Toxikologiska rådet
– expertorgan för rådgivning och samråd i toxikologiska frågor

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

REPORT 1/18

Progress report for the Toxicological Council 2017-2018

Organisation and start up

Preamble

The Toxicological Council is an expert organisation established to facilitate the rapid identification of chemical substances that can be harmful to human health or the environment. The Council includes representatives from governmental authorities and universities. The Toxicological Council identifies and evaluates signals of new, potential and emerging chemical risks and reports its findings to SamTox. SamTox is a coordination group between national authorities that ensures a structure for the rapid and systematic transfer of information and knowledge between responsible authorities and other actors, as well as cooperation in the event of a serious chemical threat.

The conclusions presented in the report represent the views of the members of the Toxicological Council and do not necessarily reflect the opinions of individual authorities and academic institutions.

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Summary

Initial organisation of an early warning system in order to identify new, potential chemical threats

In order to improve the coordination between national authorities, in 2016 the Swedish government decided to establish a coordination group to deal with new and emerging chemical threats (SamTox). SamTox comprises the Directors General of eight Swedish authorities. The purpose of this organisation is to ensure a structure for the rapid and systematic transfer of information and knowledge between responsible authorities and other actors, as well as cooperation in the event of a serious chemical threat. In 2016, the Toxicological Council was also assigned a new task in order to improve the systematic monitoring and use of scientific information and to provide updated and relevant information to SamTox. The Council shall identify and evaluate potential new or emerging chemical risks and report its findings to SamTox. The Council has also decided to include known but insufficiently managed chemical risks in its evaluations.

The Toxicological Council comprises representatives from Swedish authorities working in the field of chemical regulation and several universities that cover relevant scientific disciplines related to chemical risks. Each member of the Toxicological Council is responsible for identifying chemical risk signals within their own area of expertise. The Council jointly analyses and prioritises the signals in order to focus on areas that should be further evaluated, e.g. by gathering additional data. The Toxicological Council takes a joint decision regarding which signals should be regarded as potential new or emerging chemical risks or known but insufficiently managed risks. Such risks are reported to SamTox in an annual report. The Toxicological Council meets three times per year.

Methodological development: Case studies

In order to develop a methodology for the joint evaluation of signals, three areas in which several signals had been identified were selected for additional work from 2017–2018. Based on the adopted working procedure (see figure 1), the Toxicological Council decided to raise two areas of concern with SamTox. The first, PFAS accumulating in landfills potentially resulting in a (future) source of contamination (see case 1 below), can be regarded as a potential emerging risk chemical based on new information becoming available. The second, non-decreasing exposure levels of cadmium in the general population (see case 2 below), can be regarded as a known but insufficiently managed chemical risk.

Case 1: PFAS in landfills

The Toxicological Council has become aware of the risk that landfills and waste treatment plants may act as a source of (future) PFAS contamination.

PFAS (per- and polyfluoroalkyl substances) constitute a large group of substances with a very broad and still largely unknown use. These fluorinated substances can contaminate the environment throughout their lifecycle. Ultimately, the disposal of PFAS-containing waste can be a source of environmental contamination resulting from recycling, municipal or industrial wastewater treatment plants, or after the deposition of contaminated soil or industrial waste in landfills. Based on current knowledge, PFAS are persistent substances or can be transformed in the environment into persistent substances. Many of them are mobile

and can migrate through the soil to the groundwater. When ground-/drinking water is contaminated (such as in the Swedish regions of Ronneby and Tullinge), the societal cost of constructing new wells or remediating contaminated soil and/or water is very high.

Many regulatory activities concerning PFAS are ongoing. However, there is still uncertainty regarding the handling of PFAS-containing waste in Sweden. A recent study by the Swedish Environmental Protection Agency shows high concentrations of PFAS in Swedish landfills and in leachate from landfills.

Remediation activities could result in a need to dispose of contaminated soil. Also, some industrial waste may contain PFAS. There is a need to clarify how this can be handled safely. Currently, there is insufficient guidance regarding the criteria to use for determining which waste can be accepted at landfills or on how leachate from landfills should be handled. At present, leachate is often discharged into ground water and water recipients. In order to improve the handling of PFAS-containing waste, an investigation of what requirements that are necessary to demand from waste treatment plants accepting PFAS containing waste is needed. Also, improved guidance, as well as a focus on which PFAS-containing waste is acceptable at landfills (i.e. waste acceptance criteria) is required. Guidance is also necessary regarding how leachate should be managed, potentially requiring some kind of purification. New legislation is probably not necessary.

Case 2: Cadmium exposure in the general population

In order to reduce our exposure to cadmium from food, in 2013, in a collaboration with the Swedish Chemicals Agency, the National Food Agency, the Board of Agriculture and the Swedish EPA proposed a milestone target and 11 activities to be implemented by 2018, at the latest.

However, few of these activities have been implemented. The Toxicological Council calls for activities to reduce cadmium emissions, such as those proposed in the milestone targets in 2013, and also recommends the reassessment of food limit values with the ultimate aim of making them health-based.

Cadmium is not a new problem, but exposure to cadmium via food is not decreasing and the present level of exposure is likely to affect public health, e.g. by increasing the risk of osteoporosis or affect kidney function. Environmental emissions from fossil fuels, (mineral) fertilisers and industrial activities end up in the soil, where plant uptake of cadmium leads to contamination of our food. Thus, the Toxicological Council wants to stress the need for further measures aiming at decreasing human exposure to cadmium via food.

1 Introduction to the need of an early warning system

1.1 Emerging chemical risks are not sufficiently identified through legislative frameworks

One main objective appearing in different EU chemicals legislation is to ensure a high level of protection for human health and the environment, by identifying chemicals (including pesticides, drugs and cosmetics) that have hazardous properties and implement risk management measures that limit human and environmental risk. Despite the legislation, numerous cases of extensive harm to health and the environment caused by the production and use of chemicals have been documented. For example, 10 of the 15 late lessons from early warnings identified by the European Environment Agency[2] are directly linked to chemicals that have hazardous properties (benzene, asbestos, PCBs, halocarbons, DES, antimicrobials, MTBE, PFAS, TBT and endocrine disruptive chemicals). Half of the cases also highlighted hazards related to the persistent and bio-accumulative nature of chemicals (i.e. PCBs, halocarbons, MTBE, PFAS and TBT). The report highlighted instances in which years or decades elapsed before regulatory intervention. Although some of these lessons (i.e. cases in the report) originate from a time when REACH[3] was not in place, several of the lessons are recent enough to indicate that the current chemical regulatory framework is not efficient and fast enough to pick up signals in order to prevent and minimise damage. The early identification of chemical risks is of great importance in order to take timely measures to reduce or eliminate negative effects on human health and the environment.

1.2 Lessons learned from PFAS contamination of Swedish waters

The story of PFAS contamination of Swedish ground and surface water has similarly highlighted the need for better organisation aimed at detecting and taking action on new or emerging hazardous chemicals. A study led by Göran Enander[4] has investigated the reasons why PFAS contamination was able to continue for decades before any action was taken. Several of the conclusions are of a general nature. Enander's analysis concludes that chemical legislation is not strong enough, that groundwater issues are often disregarded, that environmental monitoring is incomplete and that coordination between and within authorities needs to be improved. The poor or absent systematic monitoring of scientific and regulatory development in the area of new or emerging contaminants was identified as an additional deficiency by the authorities. Several authorities emphasise in the report that they do not allocate time or specific resources to systematically follow and utilise scientific research findings that are relevant to the issues.

[2] Late lessons from early warnings: science, precaution, innovation. EEA report No 1/2013
[3] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)
[4] Göran Enander. Utredningen om spridning av PFAS föroreningar(M:2015 B)

2 Establishing an early warning system in order to identify new, potential chemical threats

2.1 SamTox

In order to improve the coordination between national authorities, in 2016 the Swedish government decided to establish a coordination group to deal with new and emerging chemical threats (SamTox). SamTox comprises the Directors General from eight Swedish authorities[5]. The Director General of the Swedish Chemicals Agency chairs the group. The purpose of this organisation is to ensure a structure for the rapid and systematic transfer of information and knowledge between responsible authorities and other actors, as well as cooperation in the event of the detection of a serious chemical threat. The Toxicological Council was formed in order to improve the systematic monitoring and use of scientific information and to provide updated and relevant information to SamTox. The Council was assigned the task of identifying and evaluating signals of new potential chemical risks and report its findings to SamTox.

2.2 The Toxicological Council

The Toxicological Council[6] is organised by the Swedish Chemicals Agency and comprises representatives from Swedish authorities working in the field of chemicals regulation and several universities covering relevant scientific disciplines related to chemical risks (table 1). These scientific disciplines include e.g. environmental chemistry, ecotoxicology, toxicology, human exposure, epidemiology, and work environment, as well as knowledge about substances or areas of current concern such as endocrine disruptive chemicals, inorganic substances and metals, nanoparticles and materials and micro plastics.

Table 1: Authorities and universities represented in the Toxicological Council

Umeå University	The Swedish Research Council Formas	Swedish Civil Contingencies Agency
Uppsala University	The Public Health Agency of Sweden	University of Gothenburg
Karolinska Institutet	Lund University	County Administrative Boards
Geological Survey of Sweden	Swedish National Food Agency	SweTox
Stockholm University	Swedish University of Agricultural Sciences	Swedish Geotechnical Institute
Swedish Agency for Marine and Water Management	Örebro University	The Swedish Environmental Protection Agency
Swedish Medical Products Agency	Swedish Work Environment Authority	The Swedish Chemicals Agency

[5] Geological Survey of Sweden, Swedish National Food Agency, Swedish Agency for Marine and Water Management, Swedish Medical Products Agency, Public Health Agency of Sweden, the Swedish Environmental Protection Agency, Swedish Geotechnical Institute, the Swedish Chemicals Agency.
[6] For further information and publications see https://www.kemi.se/om-kemikalieinspektionen/organisation/toxikologiska-radet

3 Work procedure for the Toxicological Council

3.1 Definition of new and emerging chemical risks

A wide variety of terms are used to define and describe emerging risk chemicals of concern (see e.g. EFSA[7], NORMAN network[8], SCENIHR[9] and RIVM[10]), such as new risk, emerging risk, emerging issue, emerging pollutant, emerging substance and contaminants of emerging concern. EFSA (2007) defines an emerging risk as: “A risk resulting from a newly identified hazard to which a significant exposure may occur, or from an unexpected new or increased significant exposure and/or susceptibility to a known hazard”.

A more elaborate definition is given by the European Agency for Safety and Health at Work (EU-OSHA) that differentiates between new and increasing (emerging) risk[11]:

New risk:

- a risk that was previously unknown and is caused by new processes, new technologies, new types of workplace, or social or organisational change; or
- a longstanding issue recently considered a risk due to a change in social or public perceptions; or
- new scientific knowledge that enables a long-standing issue to be identified as a risk.

Increasing risk:

- the number of hazards leading to the risk is growing; or
- the likelihood of exposure to the hazard leading to the risk is increasing (exposure level and/or the number of people exposed); or
- the effect of the hazard on workers’ health is getting worse (seriousness of health effects and/or the number of people affected).

The Toxicological Council finds the definition used by EU-OSHA valuable but concludes that in many cases it can be difficult to differentiate between a new and an emerging risk. It will therefore use the term “new or emerging risk chemical” (NERC) to include both increasing and new risks. This term also complies with the terminology used by the Dutch initiative RIVM-NERC[12] as well as with the recent EU Commission report *Study for the strategy for a non-toxic environment of the 7th Environment Action Programme*[13].

3.2 General approach to identification and prioritisation of new or emerging risk chemicals

The Toxicological Council has been assigned the task of identifying and evaluating potential NERCs and has also decided to include known but insufficiently managed chemical risks in its evaluations. The identification and evaluation will be based on information in e.g.

[7] https://www.efsa.europa.eu/en/topics/topic/emerging-risks
[8] http://www.norman-network.net/?q=node/19
[9] https://ec.europa.eu/health/scientific_committees/emerging_en
[10] https://www.rivm.nl/Documenten_en_publicaties/Wetenschappelijk/Wetenschappelijke_artikelen/2018/april/An_approach_to_identify_prioritize_and_provide_regulatory_follow_up_actions_for_New_or_Emerging_Risks_of_Chemicals_NERCs_for_Workers_Consumers_and_the_Environment
[11] EU-OSHA 2009
[12] Progress report on New or Emerging Risks of Chemicals (NERCs). RIVM Letter report 2014-0040 E.A. Hogendoorn et al.
[13] Study for the strategy for a non-toxic environment of the 7th Environment Action Programme, 2017. Written by Milieu Ltd, Ökopol, Risk & Policy Analysts (RPA) and RIVM (EU-KOM)

scientific literature, regulatory reports or other activities gathered by the authorities or universities, including screening and monitoring data. Each member of the Toxicological Council is responsible for identifying signals related to chemical risk within their respective area of expertise. The aim is to compile a wide variety of signals, e.g. reports of new (eco-)toxicological effects, increases in potentially chemical-related symptoms (e.g. allergies), or innovations and patents, as well as changes in use patterns, which could increase exposure to certain chemicals. The identified signals will serve as a basis for the subsequent joint prioritisation and evaluation of potential new or emerging (or not managed) chemical risks.

The compiled signals are jointly analysed by the Toxicological Council in order to identify areas that should be further evaluated, e.g. by gathering additional data and ascertaining which signals should be regarded as potential NERCs or known but insufficiently managed risks. The discussions include issues such as severity, data quality, data gaps, signals pointing in the same direction and regulatory (policy) measures already taken. The signals regarded as potential NERCs or known but insufficiently managed risks are reported to SamTox in an annual report. The Toxicological Council meets three times per year and provides one annual report to SamTox that summarises the signals and analyses. The general working procedure for the Toxicological Council and SamTox is described in figure 1.

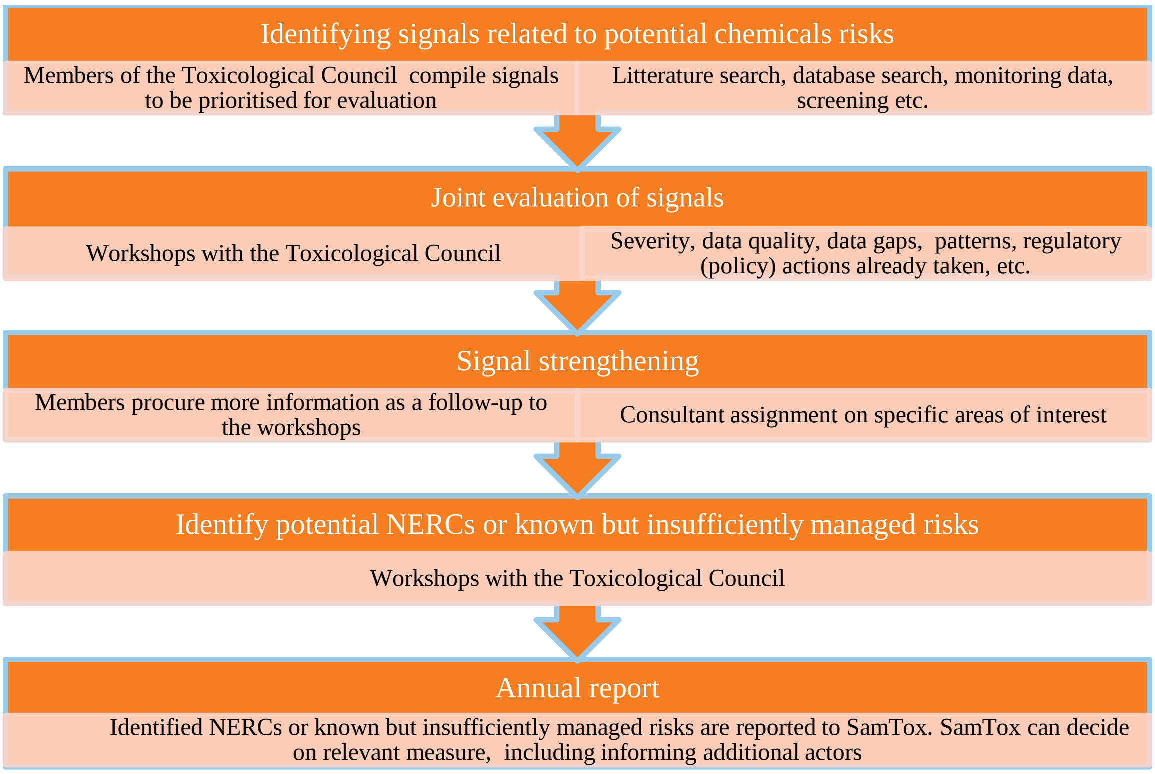

Figure 1: The general working procedure for the Toxicological Council and SamTox.

3.3 Prioritisation of potential chemical risks of concern

The Toxicological Council will compile a wide range of signals related to potential chemical risks. The aim is the systematic monitoring and utilisation of scientific information to facilitate the rapid identification of chemical substances that can harm human health or the environment. In order to determine the strength of a signal and suggest measure to be taken, a number of important aspects need to be considered. One important aspect concerns prioritisation, both in order to identify signals for further evaluation and for decisions regarding what to report to SamTox. A final prioritisation procedure has not yet been established but will be built upon the experience gained from the meetings and workshops within the Toxicological Council. Potential indicators that could be included in a prioritisation scheme have, however, been identified, e.g.:

Exposure indicators

- Production/market volume
- Uses that result in high release potential (e.g. release from industry or from articles)
- Widespread use – e.g. multiple applications or extensive use resulting in contamination of large areas or exposure of many people
- Increasing trends in usage or production
- Human exposure monitoring data
- Environmental monitoring data
- Persistence of a substance

Toxicity indicators

- Laboratory toxicity data and toxicity determined by QSARs indicating the severity of (eco-) toxicological response
- Effect on ecosystem services
- Epidemiological data

In addition, these indicators can also be considered in order to identify knowledge gaps and the need to obtain additional information.

3.4 Cooperation with other organisations

The need for early warning systems related to chemical threats to human health and the environment was also highlighted in the EU Commission report *Study for the strategy for a non-toxic environment of the 7th Environment Action Programme*[14]. In this study a general need for more cooperation and exchange of information on NERCs at an EU level, including a supra-national platform for coordination, has been emphasised. The Toxicological Council has identified a range of networks or initiatives that could be relevant for collaborations and potentially form such a platform, some of which are described shortly below. Steps to initiate collaboration have been taken and will be developed further.

The **Emerging-risk exchange network (EREN)** is organised by EFSA. Through EREN, EFSA networks with Member States, EU and international agencies on exchanging data, methodologies and lessons learnt on emerging risks. The Toxicological Council, in collaboration with the Swedish EREN representative (currently at the National Food Agency), can submit briefing notes to the EREN regarding emerging risks that have been identified. The extent to which briefing notes submitted to the EREN can be more generally shared across organisations/networks has not yet been decided.

The **NORMAN network** enhances the exchange of information on emerging environmental substances, mainly focusing on ecotoxicological effects, working in close connection with the

[14] Study for the strategy for a non-toxic environment of the 7th Environment Action Programme. 2017. Written by Milieu Ltd, Ökopol, Risk & Policy Analysts (RPA) and RIVM (EU-KOM)

Water Framework Directive. The NORMAN Suspect Database comprises an extensive list (> 40,000 compounds) of monitored compounds. One work package within the network is focused on developing a risk- based prioritisation concept to enable the selection of top candidates for different measures (e.g. monitoring or generation of ecotoxicological data). As several of the representatives in the Toxicological Council also are associated with the NORMAN network, a mutual exchange of information is foreseen.

Human Biomonitoring for EU (HBM4EU) is a new joint initiative by 28 countries, the European Environment Agency and the European Commission, co-funded under Horizon 2020. The primary aim of the initiative is to coordinate and advance human biomonitoring in Europe to provide evidence for chemical policy making. The project will produce an inventory of known chemicals to be considered as exposure markers of emerging concern and set up a globally structured approach and framework for the priority setting of unknown chemicals of emerging concern. Cooperation is anticipated through the Swedish National Hub led by the Swedish EPA in which members of the Toxicological Council participate.

RIVM-NERC is a project coordinated by RIVM Bureau REACH and financed by the Dutch ministries. It was initiated in 2012 and advocates the development of a system to identify New or Emerging Risks of Chemicals (NERCs) at an early stage. The project aims to link (new) information on chemical stressors to their effects on three protection goals – workers, consumers and the environment – with the purpose of better protecting humans and the environment. The RIVM utilises text mining, scientific literature searches and non-target screening to collect the relevant information. The Toxicological Council will initially share information with the NERC project and will aim at developing further cooperation.

4 Identified potential NERCs or known but insufficiently managed chemical risks from 2017–2018

Between September and December 2017, the Toxicological Council compiled more than 50 signals related to potential NERCs or insufficiently managed chemical risks.

In order to develop a methodology for the joint evaluation of signals aimed at identifying potential NERCS or insufficiently managed chemical risks, three areas in which multiple signals had been compiled were selected for additional work from 2017–2018. Future selections of signals will be performed according to the prioritisation procedure outlined above. The three selected areas concerned PFAS-related issues, cadmium exposure and indications of increased incidences of allergies related to certain chemical exposures. After gathering additional data, according to the adopted working procedure (figure 1), the Toxicological Council decided to raise two areas of concern with SamTox. The first, PFAS accumulating in landfills potentially resulting in a (future) source of contamination (see case 1) can be regarded as a potential NERC based on new information becoming available. The second, non-decreasing exposure levels of cadmium in the general population (see case 2) can be regarded as a known but insufficiently managed chemical risk. It is likely that current cadmium exposure, primarily through dietary sources, has resulted in adverse effects in parts of the Swedish population, and there is no indication that such exposure is decreasing.

The Toxicological Council decided not to raise the issue of increased incidences of chemically-induced allergies with SamTox. The decision was based on a recognised need for additional data and further analyses in order to identify this issue as a potential NERC or insufficiently managed chemical risk.

4.1 Case 1: PFAS in landfills

4.1.1 Use

PFAS (per- and polyfluoroalkyl substances) constitute a large group of substances with a very broad and largely unknown use. PFAS are used for their unique properties. They are both fat and water repellent and are highly persistent, which makes them useful in extreme conditions such as high temperatures and corrosive environments. Their use is widespread, for example, in various types of surface treatments of paper, plastic and metal, for impregnation of textiles, in ski waxes, cosmetic products, pharmaceuticals, biocides, hydraulic oils, as well as in fire-fighting foam. It has been estimated that three to five thousand PFAS are in use. However, for the majority of PFAS, knowledge about where and how they are used is lacking.

There is ongoing, rapid development of new PFAS, as well as new applications for known PFAS. Consequently, there is a risk of regrettable substitution of PFAS, i.e. that PFAS identified as a risk are substituted with similar PFAS that are considered to exhibit a lower risk based on insufficient knowledge of the human and environmental hazards and/or exposures.

4.1.2 Monitoring and exposure

PFAS are widely dispersed in the aquatic environment and have been found, for example, in almost all fish samples taken between 2000 and 2015[15]. Environmental monitoring data for PFAS are increasing. Today, we can identify some PFAS substances in the environment, but there seems to be a large number whose identity is unknown. Thus, information about environmental concentrations of these substances is also missing. This is evident since analyses of extractable organic fluorine in samples from, for example, sludge and water from sewage treatment plants, indicate that the amount of total fluorine is higher than what can be attributed to known forms of fluorinated substances.

PFAS can be emitted to the environment throughout their entire lifecycle, including production, incorporation in articles, usage and waste treatment. The treatment of PFAS-containing waste can be a source of environmental contamination during recycling, from municipal or industrial wastewater treatment plants, or after the deposition of contaminated soil or industrial waste at landfills. A recent study has shown that high concentrations of PFAS can be found at Swedish landfills and in leachate from landfills.[16] A similar situation has been demonstrated in other countries.[17] It is not known to what extent landfills are sources of PFAS contamination to the environment. There is however sufficient evidence of high concentrations of PFAS in leachate from a number of landfills to conclude that measures are needed in order to avoid landfills becoming long-term sources of PFAS that pose a risk to human health and the environment.

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[15] https://dvsb.ivl.se/

[16] Naturvårdsverket 2016. Rapport 6709. Högfluorerade ämnen (PFAS) och bekämpningsmedel. En sammantagen bild av förekomsten i miljön.

[17] Benskin et al. (2012) "Per- and polyfluoroalkyl substances in landfill leachate – patterns, time trends, and sources", Environ. Sci. Technol. 46, 11532–11540.

4.1.3 Risks to human health and the environment

Based on current knowledge, PFAS are persistent substances or can be transformed in the environment into persistent PFAS forms. Many of them are mobile and can migrate through the soil to the groundwater. When groundwater or drinking water is contaminated (such as in the Swedish regions of Ronneby and Tullinge), the societal cost of establishing new wells or remediating contaminated soil and/or water is very high.

The previous use of PFOS (perfluorooctane sulfonate) in fire-fighting foam has resulted in the contamination of drinking water in many places in Sweden. There is growing evidence on the toxicological effects of PFOS, such as the effects on reproduction, the thyroid hormone system, the immune system and lipid metabolism. However, for most PFAS, knowledge on use, emissions and the potential effects on human health and the environment is scarce or lacking. Aquatic and terrestrial organisms are exposed to PFAS, which are then introduced into and accumulated in the food webs, eventually resulting in the exposure to top predators and humans.

4.1.4 Regulatory activities

Many different regulatory activities have been, and are being, undertaken under the EU REACH regulation that focuses on limiting the use of PFCA (perfluoroalkyl carboxylate) with varying numbers of carbon atoms, including degradation products. However, as regulations have, thus far, often led to substitution by other PFAS (with less known or unknown properties), an overall reduction in use of all PFAS is desirable. Some PFAS, including PFOS, are recognised as POPs (Persistent Organic Pollutants) and PFOS was included in the UN Stockholm Convention in 2009. There are also many research initiatives that focus on the substitution of PFAS and the remediation of soil and water contaminated by PFAS.

The EU limit values of some PFAS in food (TDI) are currently being revised by EFSA and two new EU limit values (for individual PFAS and the sum of PFAS, respectively) for drinking water are being discussed.

Although many regulatory activities are ongoing, the Toxicological Council would like to draw attention to the very ambiguous regulatory situation for handling PFAS-containing waste in Sweden. Some waste treatment plants (landfills) accept PFAS-contaminated soil and industrial waste, whereas others refuse to do so. Currently, there is insufficient guidance on the criteria to use for determining which waste can be accepted at landfills or on how leachate from landfills should be handled. At present, leachates are often discharged into ground water and water recipients. There is also uncertainty regarding the responsibility for enforcement and supervision of landfills as several authorities are involved at different levels and to a different extent. In order to prevent continuous accumulation and emissions of PFAS from landfills into the environment, concerted regulatory action is needed, see below.

4.1.5 Further needs

Remediation activities can result in a requirement to dispose of PFAS-contaminated soil. A certain amount of industrial waste may also contain PFAS. There is a need to clarify how PFAS-containing soils or other types of waste can be handled and disposed of safely. The Toxicological Council has identified a need for improved knowledge about the presence of PFAS in waste, how these substances are transformed within landfills and to what extent they spread from landfills via leachate and gas emission. This knowledge is necessary in order to design measures that can prevent further leakage of PFAS into the environment from landfills.

There is also a need to clarify the applicable rules, limit values and responsibilities concerning the disposal of PFAS-containing waste. New legislation is probably not necessary; better guidance is preferable, to include the following identified essential points:

It should be investigated if it is feasible to determine limit values for PFAS in waste and soil (i.e. waste acceptance criteria for landfills) or if generic guideline values[18] for PFAS in waste is sufficient.

Improved guidance regarding how leachate should be managed, including the possibility of requiring purification of leachate by the waste treatment plants.

An investigation of what requirements will be necessary to demand from waste treatment plants that accept PFAS-containing waste in order to handle such waste safely. This should include management of leachate and, if feasible, generic guideline values concerning emissions of PFAS from the waste treatment plants.

Guidance on the design and implementation of monitoring programmes for waste treatment plants, taking into consideration what PFAS should and can be monitored.

4.2 Case 2: Cadmium exposure in the general population

4.2.1 Use

The largest active use of cadmium is in batteries. This use, including the waste stage, is considered to be well controlled, with limited emissions to the environment. The major source of emissions to the environment is believed to be products in which cadmium is a contaminant, such as fossil fuels and (mineral) fertilisers. Also, industrial activities such as the production of energy, biofuels, biofertilisers, combustion plants and the metal industry release cadmium to the environment.

4.2.2 Monitoring and exposure

Cadmium occur naturally in soil, with geographical variations based on type of bedrock[19]. Airborne deposition of cadmium (from fossil fuel and biofuel) and the use of fertilisers and lime are main additional contributors to cadmium concentrations in agricultural soil. Plants take up cadmium from the soil, leading to contamination of our food.

Estimates of cadmium exposure through food indicate that part of the adult population (0.1-10 percent depending on study) may exceed the tolerable weekly intake level (TWI) of 2.5 µg cadmium/kg body weight established by EFSA in 2009.[20, 21, 22] Besides food, there is also considerable exposure from smoking.

Analyses of Swedish food have shown that levels of cadmium are not decreasing. This is, for example, indicated by results from 1999, 2010 and 2015, which describe a similar (or increasing) per capita exposure to cadmium. Likewise, no decreasing trend of cadmium in

[18] Generic guideline values translates as “riktvärden”

[19] Andersson M, Carlsson M, et al. Geokemisk atlas över Sverige/Geochemical atlas of Sweden. Sveriges geologiska undersökning 2014.

[20] Sand S, and Becker W. 2012. Assessment of dietary cadmium exposure in Sweden and population health concern including scenario analysis. Food Chem. Toxicol. 50, 536-544.

[21] Sand S, Héraud F, Arcella D. 2013. The use of chemical occurrence data at European vs. national level in dietary exposure assessments: a methodological study. Food Chem. Toxicol. 62, 7-15.

[22] Livsmedelsverket. 2018. Kadmium i Livsmedel. Riskvärderingsrapport. SLV rapport, utkast.

blood has been observed over time (1994 and 2014) among never-smoking participants from the Västerbotten Intervention Programme. Nor did the time trend study of cadmium in urine in non-smoking women from 2002–2016[23] give any clear indication of decreasing exposure.

The concentration of cadmium in the aquatic environment also seems stable and data from the Swedish environmental monitoring programme show that the cadmium concentration in herring (*Clupea harengus*) remains at the levels seen in the 1980s.

4.2.3 Risks to human health

Cadmium is well known to be toxic to humans. In experimental animals, a high exposure to cadmium may more or less affect all organ systems. Cadmium also accumulates in the body over time, so even long-term, low-level human exposure can lead to osteoporosis in elderly people[24] and affect kidney function. Iron deficiency, which is rather common in Swedish women, increases the uptake of cadmium in the body. Recent studies have also shown the effects on micronutrient transfer to the foetus[25] and the effects on cognitive function in exposed children[26,27]. It has been estimated that the economic cost in Sweden of fractures caused by cadmium from food amounts to approximately SEK 4.2 billion per year[28].

The current health risk assessment of cadmium, conducted by EFSA in 2009, is based on the association between urinary cadmium and increased excretion of low-molecular weight proteins – reflecting tubular kidney damage. The urinary cadmium concentration of 1 µg/g creatinine is considered the reference dose below which the risk of tubular dysfunction is low. Epidemiological studies performed among various Swedish populations with a fairly low average exposure (<1 µg/g creatinine) show associations between various biomarkers of cadmium exposure and an increased risk of osteoporosis and fractures, as well as cardiovascular disease. International studies summarised in a meta-analysis indicate an association with mortality.[29] Annex 2 presents some recent scientific studies showing an association between current cadmium exposure and health effects. Thus, it cannot be excluded that a proportion of the Swedish population is currently adversely affected by cadmium.

4.2.4 Environmental risks

The release of cadmium is also an environmental problem and is included in the EU Directive on environmental quality standards[30] as a priority substance. The environmental quality standard for cadmium[31] is exceeded in some Swedish lakes, water courses and coastal waters. The environmental quality standard is also exceeded in offshore sediment in the Baltic

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[23] Health-related environmental monitoring programme; https://ki.se/imm/tidsserier-och-data

[24] Åkesson et al 2014, Non-renal effects and the risk assessment of environmental cadmium exposure, Environmental Health Perspectives, 112, 5, 431–8.

[25] Kippler M, Hoque AM et al. Accumulation of cadmium in human placenta interacts with the transport of micronutrients to the fetus, Toxicology Letters, 2010; 192(2):162–8.

[26] Kippler M, Tofail F, et al. Early-Life Cadmium Exposure and Child Development in 5-Year-Old Girls and Boys: a Cohort Study in Rural Bangladesh, Environ Health Perspect. 2012;120(10):1462-8.

[27] K. Gustin, F. Tofail, et al. Cadmium exposure and cognitive abilities and behavior at 10 years of age: A prospective cohort study. Environment International. 2018;113(April):259–68.

[28] KemI 2013. Report 4/13. Economic cost of fractures caused by dietary cadmium exposure.

[29] Larsson SC, Wolk A. Urinary cadmium and mortality from all causes, cancer and cardiovascular disease in the general population: systematic review and meta-analysis of cohort studies. Int J Epidemiol. 2016;45(3):782–912

[30] 2008/105/EG

[31] HVMFS 2013:19 including HVMFS 2015:4

Proper[32]. Cadmium contamination results in some surface water bodies not achieving good chemical status.

4.2.5 Regulatory activities

Most uses and emissions of cadmium have been regulated to some extent and there are EU limit values for cadmium in certain foodstuffs, as well as limit values for certain additives, flavourings and materials that come into contact with food. However, monitoring of food items shows that measures taken to reduce cadmium exposure have not been sufficient. Human exposure to cadmium via food needs to further decrease. Thus, emissions to the environment need to be reduced.

There are ongoing discussions regarding a Swedish tax on cadmium in certain products e.g. certain animal feed, mineral fertilisers, sewage sludge and lime for use in agriculture.[33] The EU fertilisers legislation[34] are being reviewed for the time being and new limits on cadmium in mineral fertilisers are tabled for discussion. Regarding activities on cadmium within CLP[35] and REACH, additional cadmium compounds have been classified according to CLP; there are currently 15 entries for cadmium and cadmium compounds with EU harmonised classification. Cadmium and eight cadmium salts have also now been included on the EU candidate list under REACH.

A minor use of cadmium that has never been regulated is in artist paint. It has been shown that artist studios discharge cadmium to the sewage system, in some cases contributing around 10% of the cadmium found in sewage water. A Swedish proposal to restrict the use of cadmium in artist paint in the EU has, however, been rejected.

In 2013 the Swedish EPA[36], in collaboration with the Swedish Chemicals Agency, National Food Agency and the Swedish Board of Agriculture, proposed a number of activities (and an Environmental Milestone target) in order to decrease exposure in Sweden to cadmium from food. This should be implemented by 2018, at the latest. An excerpt from the proposal, with the proposed activities, is shown in Annex 1 (in Swedish).

4.2.6 Uncertainty in the data

There are few other chemicals for which the evidence of adverse effects in the population at current exposure levels is so consistent. However, estimates of our current exposure to cadmium varies between studies, as do estimates of the number people at risk of cadmium-induced adverse effects. There is also uncertainty regarding how to reduce the environmental exposure most effectively.

4.2.7 Further needs

Although some measures have been taken or are being discussed, exposure through food has not decreased since the Swedish EPA proposal in 2013, and there is a need to consider additional activities. We require robust measures to reduce cadmium emissions in order to reduce the risk to human health and the environment. However, as there are many sources of

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[32] Apler A, Josefsson S. Chemical contamination in offshore sediments 2003-2014. Geological Survey of Sweden, 2016, SGU report 2016:04.
[33] SOU 2017:102
[34] Regulation (EC) No 2003/2003 of the European Parliament and of the Council of 13 October 2003 relating to fertilisers.
[35] Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures.
[36] NV-00336-13, Förslag till etappmål - Exponering för kadmium via livsmedel

cadmium, an investigation must be conducted into how to achieve the most effective and proportionate long-term reduction in emissions.

Activities proposed by the Swedish EPA in 2013 (see Annex 1) that have not yet been implemented could be first-hand choices for implementation. These activities include decreasing the concentration of cadmium in fertilisers, decreasing emissions of cadmium to the atmosphere in Sweden and elsewhere, decreasing the emissions of cadmium from artist paint, choosing crops with less uptake of cadmium, implement instruments aimed at lowering the consumption of food that has a high cadmium concentration, and implementing activities on cadmium within CLP and REACH. From a circular economy point of view, it is desirable to use digested/limed sewage sludge from sewage treatment plants as fertilisers. However, such usage also adds cadmium to the soil, unless it is removed, and this needs to be taken into account in these discussions. The possibility of further reducing industrial emissions also needs to be reassessed, e.g. from the energy production sector and from the metal industry.

Furthermore, from a scientific perspective, the EU limit values for cadmium in certain foodstuffs and additives, flavourings and materials that come into contact with food should be re-assessed with the ultimate aim of making them health-based, without considering the actual levels of cadmium in such products, which is currently the primary factor behind these limit values.

Annex 1. Excerpt from NV-00336-13

Excerpt from NV-00336-13 (Förslag till etappmål - Exponering för kadmium via livsmedel) pages 6-8.

Etappmål för exponering för kadmium via livsmedel
Senast år 2018 är styrmedel beslutade som minskar befolkningens exponering för kadmium via livsmedel

Vi föreslår 11 åtgärder vilka närmare beskrivs i kapitel 5, förslag till åtgärder och styrmedel, och i bilagan med den samhällsekonomiska analysen. De 11 åtgärderna är, utan rangordning:

1. Begränsa kadmiumanvändningen i konstnärsfärger
2. Minska tillförsel av kadmium genom att minska mängden inköpta fodermedel
3. Förhindra användningen av mineralgödsel med höga kadmiumhalter
4. Minska halten växttillgängligt kadmium i åkermarken
5. Riktad odling av salix för att bortföra kadmium från åkermark[37]
6. Minska odlingen av grödor med naturligt höga upptag av kadmium på jordar med höga kadmiumhalter
7. Minskat intag av livsmedel som innehåller mycket höga halter kadmium
8. Rätt råvara till rätt livsmedel
9. Verka för att kadmium och dess föreningar förs upp på kandidatförteckningen i Reach
10. Verka för harmoniserad klassificering av kadmiumföreningar
11. Minska luftdepositionen av kadmium från internationella källor

För att åtgärderna ska genomföras behövs styrmedel som initierar och stödjer aktörernas arbete med åtgärder. Vi föreslår följande styrmedel:

För att minska kadmium i växtnäring och åkermark

- Förbud mot kadmiumanvändning i konstnärsfärger
- Information för att minska kadmiumhalten i foder
- Skatt/avgift på kadmium i mineralgödsel och låga gränsvärden för kadmium i mineralgödsel inom EU
- Rådgivning för att minska växttillgängligt kadmium i åkermarken
- Rådgivning samt stöd till riktad odling av salix för att bortföra kadmium i åkermark

För att minska kadmium i livsmedel
Information såsom kostråd till konsumenter, information samt ev. sänkta gränsvärden till livsmedelsproducenter, samt frivilliga åtaganden av livsmedelsproducenter

Kompletterande insatser internationellt

- Verka för att kadmium och dess föreningar förs upp på kandidatförteckningen (Reach),
- verka för harmoniserad klassificering av kadmiumföreningar (CLP),
- verka för ytterligare begränsning av kadmiumanvändning (Reach),

verka för lägre gränsvärden och bättre regelefterlevnad i metallprotokollet i FN:s luftvårdskonvention

[37] Notera att förbränning av biomassa är en stor källa till kadmiumutsläpp, vilket kan behöva beaktas. http://www.naturvardsverket.se/Sa-mar-miljon/Statistik-A-O/Kadmium-utslapp-till-luft/

Annex 2. Scientific references with brief summaries

Engstrom A, Michaelsson K, Suwazono Y, Wolk A, Vahter M, Akesson A. Long-term cadmium exposure and the association with bone mineral density and fractures in a population-based study among women. J Bone Miner Res. 2011;26(3):486–95.
In linear regression, U-Cd was inversely associated with BMD at the total body ($p < .001$), femoral neck ($p = .025$), total hip ($p = .004$), lumbar spine ($p = .088$), and volumetric femoral neck ($p = .013$). In comparison with women with U-Cd < 0.50 µg/g of cr, those with U-Cd≥ 0.75 µg/g of cr had odds ratios (ORs) of 2.45 [95% confidence interval (CI) 1.51-3.97] and 1.97 (95% CI 1.24-3.14) for osteoporosis at the femoral neck and lumbar spine, respectively. Among never-smokers, the corresponding ORs were 3.47 (95% CI 1.46-8.23) and 3.26 (95% CI 1.44-7.38). For any first fracture (n = 395), the OR was 1.16 (95% CI 0.89-1.50) comparing U-Cd ≥ 0.50 µg/g of cr with lower levels. Among never-smokers, the ORs (95% CIs) were 2.03 (1.33-3.09) for any first fracture, 2.06 (1.28-3.32) for first osteoporotic fracture, 2.18 (1.20-3.94) for first distal forearm fracture and 1.89 (1.25-2.85) for multiple incident fractures. U-Cd at low environmental exposure from food in a general population of women showed a modest but significant association with both BMD and fractures, especially in never-smokers, indicating a larger concern than previously known.

Engstrom A, Michaelsson K, Vahter M, Julin B, Wolk A, Akesson A. Associations between dietary cadmium exposure and bone mineral density and risk of osteoporosis and fractures among women. Bone. 2012;50(6):1372–8.
A 32% increased risk of osteoporosis (95% CI: 2-71%) and 31% increased risk of any first incident fracture (95% CI: 2-69%) were observed comparing high dietary cadmium exposure (≥13 µg/day, median) with lower exposures (<13 µg/day). By combining high dietary with high urinary cadmium (≥0.50 µg/g creatinine), odds ratios among never-smokers were 2.65 (95% CI: 1.43-4.91) for osteoporosis and 3.05 (95% CI: 1.66-5.59) for fractures. In conclusion, even low-level cadmium exposure from food is associated with low BMD and an increased risk of osteoporosis and fractures. In separate analyses, dietary and urinary cadmium underestimated the association with bone effects.

Akesson A, Barregard L, Bergdahl IA, Nordberg GF, Nordberg M, Skerfving S. Non-renal effects and the risk assessment of environmental cadmium exposure. Environ Health Perspect. 2014;122(5):431–8.
The associations between U-Cd and urinary proteins at very low exposure may not be due to Cd toxicity, and the clinical significance of slight proteinuria may also be limited. More importantly, other effects have been reported at very low Cd exposure. There is reason to challenge the basis of the existing health risk assessment for Cd. Our review of the literature found that exposure to low concentrations of Cd is associated with effects on bone, including increased risk of osteoporosis and fractures, and that this observation has implications for the health risk assessment of Cd. Other effects associated with Cd should also be considered, in particular cancer, although the information is still too limited for appropriate use in quantitative risk assessment. CONCLUSION: Non-renal effects should be considered critical effects in the health risk assessment of Cd.

Larsson SC, Wolk A. Urinary cadmium and mortality from all causes, cancer and cardiovascular disease in the general population: systematic review and meta-analysis of cohort studies. Int J Epidemiol. 2016;45(3):782–912
A meta-analysis providing summary estimates of several cohort studies on urinary cadmium and mortality. In an analysis restricted to six cohort studies conducted in populations with a

mean urinary cadmium concentration of 1 mg/g creatinine, the hazard ratios were 1.38 (95% CI, 1.17–1.63) for all-cause mortality, 1.56 (95% CI, 0.98–2.47) for cancer mortality and 1.50 (95% CI, 1.18–1.91) for cardiovascular mortality (comparing highest vs lowest exposure category). CONCLUSIONS: Even at low-level exposure, cadmium appears to be associated with increased mortality.

Kippler M, Bottai M, Georgiou V, Koutra K, Chalkiadaki G, Kampouri M, et al. Impact of prenatal exposure to cadmium on cognitive development at pre-school age and the importance of selenium and iodine. Eur J Epidemiol. 2016.
Maternal elevated urinary cadmium concentrations (≥0.8 μg/L) were inversely associated with children's general cognitive score [mean change: -6.1 points (95% CI -12; -0.33) per doubling of urinary cadmium; corresponding to ~0.4 SD]. Stratifying by smoking status (pfor interaction 0.014), the association was restricted to smokers. In conclusion, elevated cadmium exposure in pregnancy of smoking women was inversely associated with children's cognitive function at pre-school age. The results indicate that cadmium may adversely affect neurodevelopment at doses commonly found in smokers, or that there is an interaction with other toxicants in tobacco smoke. Additionally, possible residual confounding cannot be ruled out.

Barregard L, Sallsten G, Fagerberg B, Borne Y, Persson M, Hedblad B, et al. Blood Cadmium Levels and Incident Cardiovascular Events during Follow-up in a Population-Based Cohort of Swedish Adults: The Malmo Diet and Cancer Study. Environ Health Perspect. 2016;124(5):594–600.
Hazard ratios for all cardiovascular endpoints consistently increased for participants in the 4th blood cadmium quartile (median, 0.99 μg/L). In models that also included gender, smoking, waist circumference, education, physical activity, alcohol intake, serum triglycerides, HbA1c and C-reactive protein, the hazard ratios comparing the highest and lowest quartiles of exposure were 1.8 (95% CI: 1.2, 2.7) for acute coronary events and 1.9 (1.3, 2.9) for stroke. Hazard ratios in never-smokers were consistent with these estimates. CONCLUSIONS: Blood cadmium in the highest quartile was associated with incident cardiovascular disease and mortality in our population-based samples of Swedish adults. The consistent results among never-smokers are important because smoking is a strong confounder. Our findings suggest that measures to reduce cadmium exposures are warranted, even in populations without unusual sources of exposure.

Wallin M, Barregard L, Sallsten G, Lundh T, Karlsson MK, Lorentzon M, et al. Low-Level Cadmium Exposure Is Associated With Decreased Bone Mineral Density and Increased Risk of Incident Fractures in Elderly Men: The MrOS Sweden Study. J Bone Miner Res. 2016;31(4):732–41.
We found significant negative associations between U-Cd and BMD, with lower BMD (4% to 8%) for all sites in the fourth quartile of U-Cd, using the first quartile as the reference. In addition, we found positive associations between U-Cd and incident fractures, especially nonvertebral osteoporosis fractures in the fourth quartile of U-Cd, with hazard ratios of 1.8 to 3.3 in the various models. U-Cd as a continuous variable was significantly associated with nonvertebral osteoporosis fractures (adjusted hazard ratio 1.3 to 1.4 per μg Cd/g creatinine), also in never-smokers, but not in the other fracture groups (all fractures, hip fractures, vertebral fractures and other fractures). Our results indicate that even relatively low cadmium exposure through diet and smoking increases the risk of low BMD and osteoporosis-related fractures in elderly men.