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SWEDISH ENVIRONMENTAL PROTECTION AGENCY

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Report to the Swedish EPA (the Health-Related Environmental Monitoring Program)

Jämförelser av tidstrender av miljöföroreningarna PCBer, HCB, dioxiner, bromerade flamskyddsmedel och perfluorerade alkylsyror i biota och människa – vilka faktorer bidrar till skillnader?

Anders Glynn[1], Anders Bignert[2], Elisabeth Nyberg[3], Irina Gyllenhammar[1,4], Sanna Lignell[4], Ulrika Fridén[5], Marie Aune[5]

[1]Institutionen för biomedicin och veterinär folkhälsovetenskap, Sveriges lantbruksuniversitet (SLU), Uppsala

[2] Enheten för miljögiftsforskning och –övervakning, Naturhistoriska riksmuseet, Stockholm

[3]Miljögiftsenheten, Naturvårdsverket, Stockholm

[4]Risk- och nyttovärderingsavdelningen, Livsmedelsverket, Uppsala

[5]Kemiavdelningen, Livsmedelsverket, Uppsala

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Rapportförfattare

Anders Glynn, SLU

Anders Bignert, NRM

Elisabeth Nyberg, SNV

Irina Gyllenhammar, SLU/SLV

Sanna Lignell, SLV

Ulrika Fridén, SLV

Marie Aune, SLV

Utgivare

SLU

Postadress
Box 7028, 750 07 Uppsala

Telefon
018-671000

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Sammanfattning

Naturvårdsverket har under flera decennier, inom den nationella miljöövervakningen, undersökt tidstrender av bioackumulerande/biomagnifierande organiska miljöföroreningar (persistent organic pollutants, POPs) i biota och människor, eftersom POPs kan utgöra hälsorisker för djur och människor. Ett viktigt syfte med detta monitoreringsprogram är att följa miljötillståndet i Sverige. Programmet används också för att följa upp resultat av de åtgärder som vidtagits nationellt och internationellt för att begränsa POP-förororeningen av miljön. I denna rapport undersöks tidstrender av POPs i människor från Sverige (modersmjölk och blodserum), sillgrisslor från Östersjön (ägg) och sill/strömming (muskel och lever) från svenska ost- och västkusten, och dessa trender kopplas samman med de viktigaste nationella/internationella åtgärderna (lagstiftning, råd/rekommendationer, frivilliga åtgärder, mm) som införts för att begränsa utsläppen i miljön. Syftet är att undersöka om det finns samband mellan åtgärder och förändringar av tidstrender i biota och människor. De studerade POPs omfattar industrikemikalierna polyklorerade bifenyler (PCB), de oavsiktligt bildade föroreningarna polyklorerade dibenso-*para*-dioxiner och dibensofuraner (PCDD/F), fungiciden hexaklorbensen (HCB), de bromerade flamskyddsmedlen (BFR) polybromerade difenyletrar (PBDE) och hexabromcyklododekan (HBCDD), och industrikemikalierna per- och polyfluorerade alkylsubstanser (PFAS).

Resultaten visar att nationella/internationella förbud av produktion och användning av PCB och HCB relativt snabbt resulterade i minskande halter i alla studerade matriser. Liknande effekter observerades efter mer eller mindre frivilliga utfasningar av produktion och användning av vissa BFR och PFAS. Halterna av PCDD/F, som förekom som förorening i tekniska PCB-blandningar, minskade också efter att förbud mot PCB-produktion och användning infördes. Detta visar att eliminering av primära källor för utsläpp i miljön är en mycket effektiv åtgärd, som relativt snabbt leder till sjunkande halter i biota och människor även när det gäller så pass svårnedbrytbara substanser som de studerade POPs.

När de flesta viktiga primära källorna har eliminerats finns det dock sekundära källor som kan vara mycket svårare, eller helt omöjliga, att eliminera. Detta illustreras av HCB, som för närvarande tycks öka i vissa delar av den svenska miljön. Det har föreslagits att detta fenomen till viss del beror på avdunstning av HCB från förorenad mark i områden som har haft en historiskt högre användning av fungiciden än i Sverige. När det avdunstade HCB med vindarna når Sverige sker en deposition på grund av ett kallare klimat. Diffusa primära källor för PCDD/F, som nu tycks dominera i Sverige, är också svåra att åtgärda, vilket kan förklara

varför minskningen av halterna i flera av de studerade matriserna nu verkar gå långsammare än tidigare.

Resultaten visar också att stegvis eliminering av produktion och användning av några få substanser i taget inom en grupp av POPs är ineffektivt ur miljömässig synvinkel. Detta exemplifieras av de studerade BFR och PFAS, som i motsats till PCB inte har reglerats gruppvis. Stegvisa åtgärder ger en mycket mer utdragen förbättringsprocess i miljön, där minskande halter av reglerade substanser motverkas av ökande halter av oreglerade substanser med liknande egenskaper. För att undvika denna, ur miljöns synvinkel, utdragna process bör ämnen med liknande egenskaper inom en POP-grupp regleras samtidigt.

För vissa av de undersökta POPs har olika delar av den svenska miljön ”svarat” olika snabbt på vidtagna åtgärder. För tetra-pentaBDE vändes en ökning av halter till en minskning mer än 10 år tidigare i sillgrissla och strömming/sill än i modersmjölk. Även om det inte klart går att bevisa, så kan detta bero på att det vidtogs regionala åtgärder i ett tidigt skede som hade positiv effekt på utsläpp i Östersjön utan att nämnvärt påverka den svenska befolkningens exponering. Tidstrenderna i modersmjölk följde istället i hög grad förändringarna i världsproduktion av dessa PBDE.

De retrospektiva studierna av BFR och PFAS trender visar att en oreglerad ökning av världsproduktion och -användning har resulterat i exponentiella ökningar av föroreningen av den svenska miljön. Det är därför av yttersta vikt att reglerande myndigheter/organisationer och industrin tillsammans anstränger sig att införa effektiva och snabba åtgärder på global nivå som minimerar risken för framtida miljöproblem orsakade av hittills ”okända” substansgrupper med POP-liknande egenskaper.

Temporal trends of persistent organic pollutants in Baltic Sea biota and humans from Sweden – comparisons of trends and relations to actions against pollution

Anders Glynn[1], Anders Bignert[2], Elisabeth Nyberg[3], Irina Gyllenhammar[1,4], Sanna Lignell[4], Ulrika Fridén[5], Marie Aune[5]

[1]Institutionen för biomedicin och veterinär folkhälsovetenskap, Sveriges lantbruksuniversitet (SLU), Uppsala

[2] Enheten för miljögiftsforskning och –övervakning, Naturhistoriska riksmuseet, Stockholm

[3]Miljögiftsenheten, Naturvårdsverket, Stockholm

[4]Risk- och nyttovärderingsavdelningen, Livsmedelsverket, Uppsala

[5]Kemiavdelningen, Livsmedelsverket, Uppsala

Contents

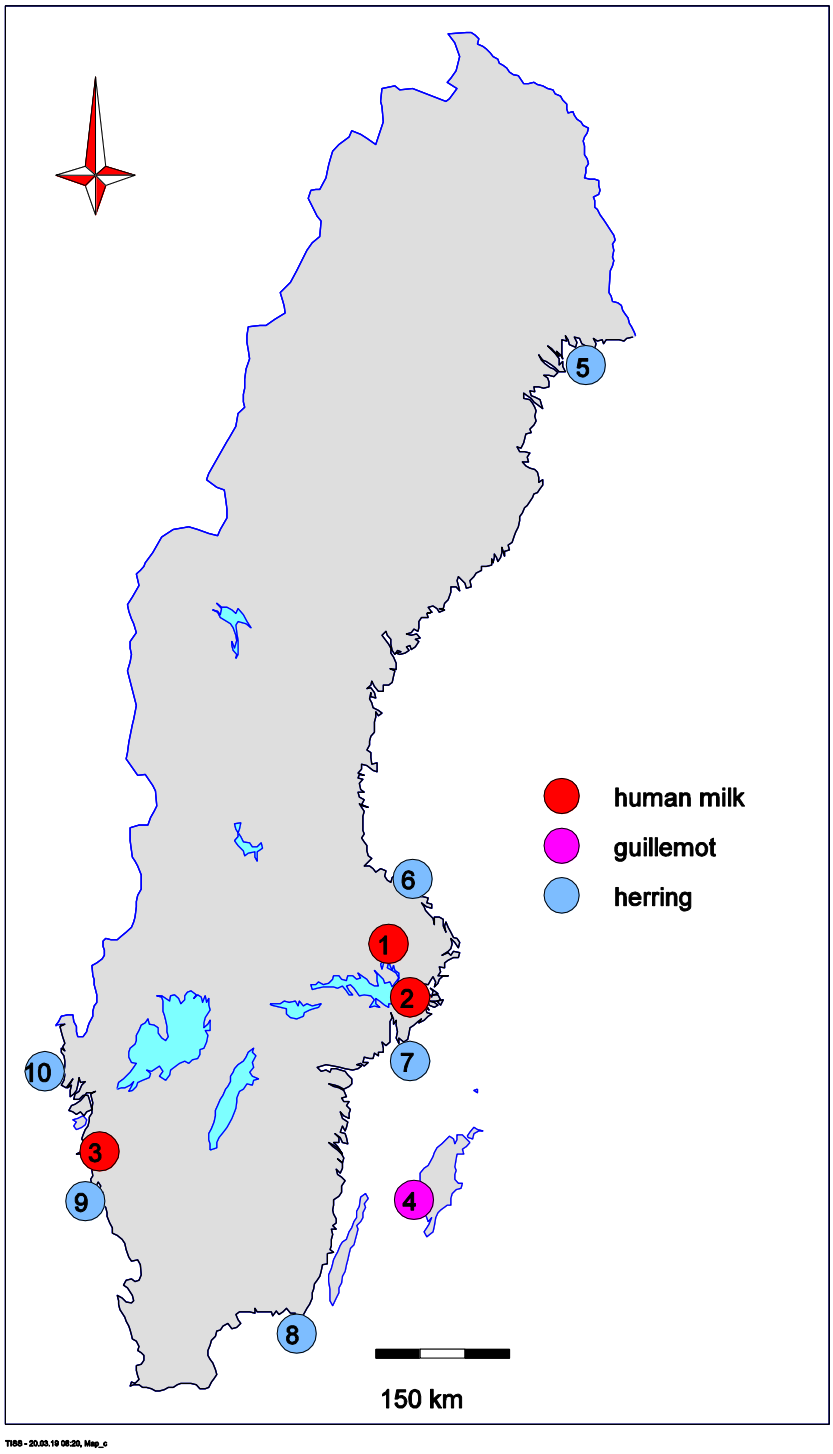
Summary

The Swedish Environmental Protection Agency (SEPA) has for decades, within the national environmental program, commissioned temporal trend studies of bioaccumulating/biomagnifying persistent organic pollutants (POPs) in wildlife and humans, due to the health threat that POPs pose to animals and humans. An important aim is to follow the general trends in the environmental conditions in Sweden. Moreover, the program is used to follow up if actions to mitigate environmental pollution of POPs results in reduced POP exposures of wildlife and humans in Sweden. The aim of the present study was to evaluate the temporal trends of POPs in humans in Sweden (human milk and blood serum), and in guillemots (eggs, Baltic Sea), and herring (muscle and liver), the latter sampled along the Swedish east and west coasts. Moreover, information about the national/international actions (regulation/advice, agreements, voluntary actions, etc.) to limit environmental pollution was collected, with the aim to study the relations between actions and changes in temporal trends.

The POPs studied were the industrial chemicals PCBs, the unintentionally formed PCDD/Fs, the agricultural chemical hexachlorobenzene (HCB), the brominated flame retardants (BFRs) PBDEs and hexabromocyclododecane (HBCDD), and the industrial chemicals PFASs. The results show that initial national and international bans of production and use of PCBs and HCB fairly rapidly resulted in decreasing temporal trends in all studied matrices. Similarly effects were observed after more or less voluntary phase-out of production and use of certain BFRs and PFASs. For PCDD/Fs, that are contaminants of technical PCB mixtures, the initial ban of PCB production and use also had positive effects on environmental pollution. Thus elimination of primary sources of pollution are effective risk managing actions against pollution, even when the substances degrades slowly and persists in the environment as in the case of POPs. However, when the majority of the primary sources of pollution have been eliminated there may be secondary sources of pollution that are much harder, or even impossible, to eliminate. This is illustrated by HCB that currently seems to increase in some parts of the Swedish environment, which at least partially may be due to evaporation from contaminated soils in southern areas with historical extensive use and subsequent deposition in more northern areas with colder climate. The diffuse primary sources of PCDD/F pollution, now dominating in Sweden, are also much more difficult to eliminate than the previous primary sources. This is may contribute to the indicated slowing down of PCDD/F rates of decline in humans and biota in Sweden.

For some of the investigated POPs the results suggest that different parts the Swedish environment have responded in different ways after actions to limit pollution have been initiated. For instance, levels of tetra-pentaPBDEs in gullemot eggs and herring muscle peaked more than a decade earlier than levels in human milk. This suggests that regional actions were initially taken that had pronounced effects on pollution of the Baltic Sea without affecting human exposure in Sweden.

Our results also show that the current approach to initially regulate only a few of the substances within a group of POPs is ineffective. As illustrated by BFRs and PFASs, this approach leads to a step-wise elimination of pollution of POPs with very similar environmental/toxicity properties, thus slowing down the improvement of the environment. Instead the whole group of POPs with similar properties should be regulated simultaneously in order to as soon as possible eliminate pollution to a minimum. The retrospective temporal trends of BFRs and PFASs clearly show that worldwide increase in production and use of substances with POP properties leads to exponential increases in environmental pollution. Thus it is of utmost importance that the regulators and industry get together and create effective measures/regulation that limits the possibility for future emergence of new POPs in the environment.



Sampling sites. 1=Uppsala, 2=Stockholm, 3=Göteborg, 4=St Karlsö, 5=Harufjärden, 6=Ängskärsklubb, 7=Landsort, 8=Utlängan, 9=Fladen, 10=Väderöarna,

Introduction

The Swedish Environmental Protection Agency (SEPA) has for decades, within the national environmental program, commissioned temporal trend studies of bioaccumulating/biomagnifying persistent organic pollutants (POPs) in wildlife and humans, due to the health threat that these types of pollutants pose to animals and humans. An important aim of this environmental monitoring is to follow the general trends in the environmental conditions in Sweden.[1] Moreover, the program is used to follow up if actions to mitigate environmental pollution of POPs have resulted in reduced POP exposures of wildlife and humans in Sweden. The samples that are collected in these long time series are banked (stored frozen) and can therefore also be used for retrospective studies of trends of emerging POPs that are suspected to become threats to the environment.[2] Furthermore, data from the trend studies can be used to estimate how long it will take to reach threshold levels that can be regarded as acceptable from a health perspective of wildlife and humans, i.e. risk assessment.[3, 4]

These cross-sectional trend studies (time series) have been designed to display and evaluate temporal trends caused by changes of emissions/pollution of anthropogenic POPs. These time series are also designed to minimize temporal changes due to long-term alterations in age, sex or other factors of sampled wildlife and humans that may influence POP levels. Time series are designed to detect changes in temporal trends that are mainly due to alterations in the level of wildlife and human POP exposure, although in certain cases trends can be affected by physiological changes in the target organisms due for instance ecosystem changes un-related to POP pollution.[5]

POPs are mainly lipid soluble industrial/agricultural chemicals that are persistent in the environment, thus remaining for decades after production and use have been banned.[6] Moreover, some lipid soluble POPs are unintentionally formed in industrial and combustion processes.[7] An exception from the lipid-soluble theme of POPs is the group of poly- and perfluorinated alkyl substances (PFASs) that are water soluble industrial chemicals, some of them being very persistent and bioaccumulating in wildlife and in humans.[8]

Food is a major source of human POP exposure, and some POPs, such as polychlorinated biphenyls (PCBs), dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs) are potential human health threats in Sweden.[9] The Swedish National Food Agency (SNFA) has for decades had food control programs with the aim to monitor the compliance of the Swedish food production with regulations to limit human exposure to POPs. Due to the

annual sampling of food products and food producing animals, and frequent measurements of POPs, these food control programs can be used to study temporal trends of POP contamination of Swedish food production, and consequently also human POP exposures.[10]

A pilot study from 2013 showed that there were differences in temporal trends of the brominated flame retardants: polybrominated diphenyl ethers (PBDEs) and the PFAS perfluorooctane sulfonate (PFOS) between the guillemot from the Baltic Sea (eggs from St Karlsö in the south Baltic Proper) and humans (young women from Uppsala; human milk, blood serum).[11] This suggested that efforts to mitigate environmental pollution of PBDEs and PFOS affected the exposure of guillemots differently than exposure of humans, which could be due to differences in response rates of the guillemot and human environment to the implemented actions. It was suggested that relations between risk reducing actions and similarities/differences in temporal changes in POPs in biota and human can give important information about which actions that are most effective in reducing pollution of nature and the human environment.[11]

The aim of the present study was to evaluate the temporal trends of POPs in guillemots and humans, and in important exposure sources such as herring (guillemots) and food of animal origin (humans). Moreover, information about the national/international actions (regulation/advice, agreements, voluntary actions, etc.) to limit environmental POP pollution and human exposure was collected, with the aim to study the relations between actions and changes in temporal trends. The POPs studied were the industrial chemicals PCBs, the unintentionally formed PCDD/Fs, the agricultural chemical hexachlorobenzene (HCB), the brominated flame retardants (BFRs) PBDEs and hexabromocyclododecane (HBCDD), and the industrial chemicals PFASs.

Materials and methods

Biological samples

Herring muscle has for decades been sampled from the Baltic Sea coast and the west coast of Sweden each year at 17 locations.[12] Herring is a suitable species for monitoring of POPs since herring muscle has a high fat content, which simplifies measurements of the fat-soluble POPs due to higher concentrations than in less fat-rich fish species. Herring is an important commercial species for animal feed production and for human consumption. Sampling is

controlled so that mainly female herring of ages 2-5 years are sampled. In the present study the focus is on temporal trends of the POPs in herring muscle sampled in autumn at a background sampling site in the southern Baltic Proper (Utlängan) with no known local pollution. Temporal trends from other herring sampling sites are used to broaden the picture of how pollution of the Swedish marine environment have responded to different actions to limit pollution. Time series of PFASs in herring were based on liver samples instead of muscle samples. This was due to the fact that levels of some PFASs in fish muscle are low and hard to detect.[13]

The sampling of guillemots also takes place in the southern Baltic Proper (Stora Karlsö).[14] The guillemot is suitable for monitoring of POPs since the birds generally do not migrate further than the southern parts of the Baltic Proper. Eggs are sampled annually, and are rich in fat thus accumulating the lipid soluble POPs at high concentrations.[14] Eggs also accumulate high concentrations of some environmentally important PFASs, adding to the usefulness of guillemot eggs for environmental monitoring of POPs.[15]

Within the SEPA POP monitoring program human milk is sampled annually in Uppsala (POPUP study),[16] Stockholm and Göteborg.[17] Due to the long half-lives of POPs in humans and the effective transfer of maternal POPs to human milk, POP levels in human milk gives a good estimate on the long-term cumulative POP exposure in pregnant and nursing women.[18] Human milk is also the most important food for exclusively breastfed newborns and infants, who are sensitive to health effects of POPs. Moreover, POP levels in human milk give good estimates of POP exposure of the sensitive fetus.[19] The milk can be sampled by the mothers themselves without invasive techniques, and the relatively high fat content simplifies POP measurements.[19] For the water soluble PFASs human milk can be used for monitoring of cumulative human exposure, but human blood serum is more suitable for monitoring due to less effective maternal transfer of PFASs to human and a strong binding to serum albumin.[20] Nevertheless, development of sensitive analytic methods for PFAS analyses in human milk has proved that this matrix also can be used for studies of temporal trends of certain PFASs in young women, as in the studies from Stockholm and Göteborg.[17] In the present study time series of PFAS in serum from the POPUP study and human milk from Stockholm and Göteborg were used.

Foods of animal origin are the most important human exposure source of many POPs. Fat-rich tissues/matrices from food producing animals, such as animal fat tissue, milk, and eggs, are suitable for monitoring of POP contamination of the food chain.[21] POPs can enter the food chain either thought environmental exposure of food-producing animals due to

general contamination of the environment, or through exposure from accidental POP contaminated animal feed components.[22] In contrast to the SEPA monitoring of POPs in herring, guillemot and humans, the SNFA control programs of food contaminants only include POPs with regulatory maximum limits in food, such as PCBs, PCDD/Fs, and chlorinated agricultural chemicals including HCB. BFRs and PFASs are not measured in the control programs. However, BFRs and PFASs are measured, together with the other POPs, in the Market Basket Study, which covers about 90% of the foods on the Swedish market.[23] Market basket data for the POPs were available from 1999, 2005, 2010 and 2015, making it possible to follow temporal trends in human POP exposure in Sweden the last decades.[23] The market basket data are in the present study used to complement the temporal trend data from matrices from food-producing animals analyzed, in order to get a better picture of trends in human POP exposure during the recent decades.

POPs

PCBs

Polychlorinated biphenyls (PCBs) are a series of 209 single substances (congeners), substituted with 1 and 10 chlorine atoms. The congeners can be divided into two groups, depending on mechanisms of toxicity, dioxin-like (dl) and non-dioxin-like (ndl) congeners. Since the late 1970s new use of PCBs has been banned in Sweden, but before that they were extensively used in for instance electrical installations and products, heat exchangers, paint and in house sealants.[7] However, PCBs may also be un-intentionally produced in combustion processes.[7] The present study focuses on the ndl-PCB congeners CB-28 and -153 and the dl-congeners CB-118 and CB-126. These congeners are generally found in higher levels than other similar congeners in environmental and human samples. The toxicity equivalent (TEF) system is used to estimate the total concentration of the 12 dl-PCBs, as toxicity equivalents (TEQs) in environmental, food and human samples.[24] In short, each dl-congener has been assigned a TEF which is related to the toxicity of the most toxic dioxin, tetrachlorodibenzo-*p*-dioxin (TCDD) (TEF=1). The concentration of each congener in a sample is multiplied with its specified TEF and the estimated TEQ concentration of each congener in the sample is then summarized to a total TEQ concentration. Among the dl-PCBs, CB-126 has the highest TEF (0.1).[24]

PCDD/Fs

Un-intentionally produced in chemical and combustion processes, polychlorinated dibenzo-*p*-dioxins (PCDD) and polychlorinated dibenzofurans (PCDFs) consists of 75 PCDD and 135 PCDF congeners.[24] Of these, 17 are regarded as toxic and therefore measured in environmental and human samples. Together with the 12 dl-PCBs, these toxic PCDD/Fs are included in the TEF system for substances with dioxin-like effects.[24] The present study includes temporal trends of PCB TEQ, PCDD/F TEQ and total TEQ levels. Moreover, specific trends for TCDD, 1,2,3,7,8-pentaCDD, and 2,3,4,7,8-pentaCDF are investigated, since these PCDD/Fs to a large degree contribute to the total TEQ levels in environmental and human samples.[24]

HCB

The chlorinated fungicidal pesticide hexachlorobenzene (HCB) is also un-intentionally produced in industrial and combustion processes. The use of HCB as a pesticide in Sweden was banned in 1980.[25]

PBDEs and HBCDD

Brominated flame retardants are added to flammable products to decrease the fire hazard. Polybrominated diphenyl ethers (PBDEs) are bromine substituted organic compounds that recently have more or less been banned in the EU.[26] Hexabromocyclododecane (HBCDD) is currently mostly used in polystyrene, after HBCDD in 2013 was listed in the Stockholm Convention for elimination.[27] In the present study, HBCDD and the PBDEs BDE-47 (tetraBDE), BDE-99 (pentaBDE), BDE-153 (hexaBDE) are specifically studied, since these are the BFRs that generally are present at the highest levels in the environment and humans.

PFASs

The stability and surface active properties of the per- and polyflouroalkyl substances (PFASs) have resulted in an extensive use in certain industrial processes and in commercial products. One well known use is as additives in textiles for water and dirt proofing.[28] Another use that has caused severe contamination of important drinking water sources in Sweden and abroad is as surfactants in fire-fighting foam.[28] This very complex group of highly fluorinated organic compounds consists of over 4000 known substances.[29] Some of the PFASs are very persistent and bioaccumulative in the environment and humans, especially the perfluoroalkyl sulfonic acids (PFSAs) and perfluoroalkyl carboxylic acids (PFCAs). Only two PFASs have recently entered into the process of regulation to limit production and use, i.e. PFOS and

PFOA.[29] The present study more specifically focus on the commonly detected homologues PFOA, PFNA, PFUnDA, PFHxS and PFOS in biota and humans.

Chemical analyses

In temporal trend studies it is important to use high-quality methods for chemical analyses of POPs. One problem can be that different analytical laboratory has used during the study period, or that the laboratory has made changes in the analytical method during the course of the study. In this case it is important to do a laboratory/method comparison in order confirm that the results from the different laboratories/methods are comparable. If the samples in the time series have been stored frozen, the old samples can be re-analyzed by the new laboratory/method.

PCBs, PCDD/Fs, HCB, PBDE and HBCDD in human milk from the POPUP, Stockholm and Göteborg time series, in samples from food-producing animals and in food samples, and in herring muscle, were analyzed by gas chromatography (GC) with different detection methods, in some cases also including mass spectroscopy.[30, 31] PFASs in human milk from Stockholm and Göteborg, in human serum from Uppsala (POPUP), in food samples, and in herring liver, were measured by ultra performance liquid chromatography (UPLC) or high performance liquid chromatography(HPLC) coupled to different types of mass spectrometers.[31, 32]

Statistical analyses

For each time point of sampling, geometric means were used. In some cases individual data were used. Temporal trends were analyzed by log-linear regression analysis, and consequently the rates of change in concentrations are expressed in units of % per year. Change-points (CPs) in temporal trends were identified by a technique similar to that reported by Sturludottir *et al*.[33] The entire time-series was repeatedly divided into two parts with at least 3 years in each part. To each part log-linear regression lines were fitted and the residual variance was recorded for each combination. An F-test was used to compare the regression line combinations that resulted in the lowest variance with the variance of the log-linear regression line for the whole time period. The less restrained situation with two regression lines compared to a single regression line was compensated for by down-adjustment of the degrees of freedoms. The following scenarios were considered in the CP analyses: (i) Only one change-point during the study period; (ii) Data from the identified

change-point year was included in both pre- and post-CP time series. This reduces the influence of abrupt changes from one year to the next (which may be an artefact). However, this approach may also reduce the chance to detect significant trends on either side of the CP; (iii) The two parts on either side of the CP may point in different directions (increasing-decreasing) and may not show significant slopes separately, but will nevertheless have a significantly lower residual variance than the mean or a regression line for the whole period; (iv) CP analysis was performed for time series with 7 or more sampling time-points.

Search for implemented actions against environmental pollution

As a first step the National Implementation Plans (NIPs) reported to the Stockholm Convention and the home-pages of the SEPA, the Swedish Chemicals Agency, and the SNFA were screened for implemented actions. Moreover, certain key experts (still active or retired) in the agencies were interviewed. Based on this screening, literature/homepage references of implemented actions against pollution was searched for and retrieved from the Internet.

Table 1 Temporal trends of the ndl-PCB congeners CB-28 and CB-153 in different matrices sampled in Sweden. Human milk trend from Uppsala adjusted for participant´s age, pre-pregnancy BMI, weight gain during pregnancy, weight loss after pregnancy and education. N=number of measured samples included. Trend=annual change in levels (mean (95% confidence interval)). Only statistically significant trends are reported (p≤0.05). CP=change point year for which a change in the slope has been detected (only given for statistically significant CPs (p≤0.05)). CP change=visually determined change in trend at CP. Slower decrease=decreasing levels before CP and slowing down after. Decrease/increase= decreasing levels before CP and thereafter increasing. Increase/decrease= increase in levels before CP and decrease after. Empty cell=change in slope not possible to determine visually.

Matrix	N	Years	Trend (% per year)	CP	p-value	CP change
ndl-PCBs						
CB-28						
Human milk, Uppsala	469	1996-2017	-4,8 (-5.5, -4.0)			
Cow´s milk	65	2003-2017				
Guillemot egg	316	1988-2016	-5.9 (-6.5, -5.3)	1998	<0.001	Slower decrease
Herring, Harufjärden	287	1987-2016	-2.6 (-3.0, -2.1)	1996	<0.001	Slower decrease
Herring, Ängskärsklubb	281	1989-2015	-4.9 (-5.5, -4.3)	1996	0.039	Slower decrease
Herring, Landsort	402	1987-2016	-5.5 (-6.0, -5.0)	1999	0.006	Slower decrease
Herring, Utlängan	345	1988-2016	-3.9 (-4.4, -3.4)	1994	<0.001	Slower decrease
Herring, Fladen	371	1988-2016	-6.0 (-6.4, -5.6)	1996	0.001	Slower decrease
Herring, Väderöarna	316	1995-2016	-2.8 (-3.4, -2.3)	2009	0.046	Decrease/increase
CB-153						
Human milk, Uppsala	502	1996-2017	-6.6 (-7.0, -6.2)			
Human milk, Stockholm	29	1972-2014	-5.6 (-6.6, -4.5)	2008	0.022	
Human milk, Göteborg	35	2008-2015				
Hen´s egg	470	1999-2017	-12 (-13, -11)			
Cow´s milk	75	2003-2017	-5.5 (-7.0, -4.0)			
Cattle fat	822	1991-2018	-6.0 (-6.6, -5.3)			
Lamb fat	108	1998-2017	-6.1 (-7.9, -4.3)			
Swine fat	198	2009-2017	-4.9 (-8.0, -1.8)			
Reindeer fat	199	2000-2017	-4.2 (-5.8, -2.7)			
Guillemot egg	306	1988-2016	-7.4 (-7.9, -6.9)	2012	0.041	Slower decrease
Herring, Harufjärden	399	1987-2016	-2.0 (-2.6, -1.3)			
Herring, Ängskärsklubb	364	1989-2015	-5.7 (-6.3, -5.0)			
Herring, Landsort	402	1987-2016	-5.4 (-6.0, -4.7)	1998	0.001	Increase/decrease
Herring, Utlängan	410	1988-2016	-2.0 (-2.6, -1.4)	1999	0.024	
Herring, Fladen	442	1988-2016	-5.2 (-5.7, -4.7)	2003	0.016	Slower decrease
Herring, Väderöarna	339	1995-2016				

Results

PCBs, PCDDFs and HCB

These groups of compounds have similar sources of contamination, i.e, from combustion sources, although PCBs and HCB contamination also have occurred by use of technical products.[34] Technical PCB mixtures were contaminated with PCDD/Fs.[34]

Table 2. Temporal trends of the dl-PCB congeners CB-118 and CB-126, and of non-ortho PCB TEQ and mono-ortho PCB TEQ, in different matrices sampled in Sweden. Human milk trend from Uppsala adjusted for participant´s age, pre-pregnancy BMI, weight gain during pregnancy, weight loss after pregnancy and education. N=number of measured samples included. Trend=annual change in levels (mean (95% confidence interval)). Only statistically significant trends are reported (p<0.05). CP=change point year for which a change in the slope has been detected (only given for statistically significant CPs (p≤0.05)). CP change=visually determined change in trend at CP. Faster decrease=decreasing levels before CP and faster decrease thereafter. Slower decrease=decreasing levels before CP and slowing down after. Empty cell=change in slope not possible to determine visually.

Matrix	N	Years	Trend (% per year)	CP	p-value	CP change
dl-PCBs						
CB-118						
Human milk, Uppsala	502	1996-2017	-7.7 (-8.2, -7.3)			
Human milk, Stockholm	35	1972-2014	-7.5 (-8.0, -7.0)	1990	0.015	Faster decrease
Human milk, Göteborg	14	2007-2015	-8.5 (-12, -5.2)			
Hen´s egg, cage	25	2003-2016	-7.3 (-10, -3.9)			
Hen´s egg, sputtering	38	2004-2016				
Hen´s egg, eco	95	2003-2017				
Cow´s milk	85	2003-2017	-6.6 (-7.7, -5.6)			
Cattle fat	53	2003-2018				
Lamb fat	34	2003-2015	-5.9 (-10, -1.3)			
Guillemot egg	319	1988-2016	-8.5 (-8.9, -8.1)			
Herring, Harufjärden	400	1987-2016	-3.8 (-4.5, -3.2)	1993	0.004	Slower decrease
Herring, Ängskärsklubb	366	1989-2015	-7.0 (-7.7, -6.3)			
Herring, Landsort	406	1987-2016	-7.0 (-7.5, -6.4)	1999	0.025	Faster decrease
Herring, Utlängan	403	1988-2016	-5.3 (-5.8, -4.7)	1999	0.031	Slower decrease
Herring, Fladen	444	1988-2016	-7.7 (-8.2, -7.3)	2010	0.001	
Herring, Väderöarna	339	1995-2016	-2.9 (-3.6, -2.1)			
CB-126						
Human milk, Uppsala	405	1996-2017	-6.2 (-6.8, -5.7)			
Human milk, Stockholm	35	1972-2014	-6.7 (-7.7, -5.9)			
Human milk, Göteborg	14	2007-2015	-8.1 (-11, -4.9)			
Hen´s egg, cage	27	2003-2016	-9.2 (-12, -6.1)			
Hen´s egg, sputtering	38	2004-2016				
Hen´s egg, eco	95	2003-2017				
Cow´s milk	85	2003-2017	-5.1 (-6.8, -3.3)			
Cattle fat	53	2003-2018				
Lamb fat	34	2003-2015				
Guillemot egg	NA					
Herring, Harufjärden	75	1995-2016				
Herring, Ängskärsklubb	42	1979-2015	-4.6 (-5.6, -3.7)			
Herring, Landsort	20	2005-2016				
Herring, Utlängan	76	1995-2016				
Herring, Fladen	83	1992-2016	-5.1 (-6.3, -3.9)	2006	0.017	Slower decrease
Herring, Väderöarna	20	2007-2016	8.7 (4.0, 14)			
Non-ortho PCB TEQ						
Human milk, Uppsala	388	1996-2017	-5.7 (-6.3, -5.1)			
Mono-ortho PCB TEQ						
Human milk, Uppsala	501	1996-2017	-6.5 (-6.9, -6.1)			

PCBs

When looking at the temporal trends of PCBs in the longest time series it is obvious that the environmental pollution of both ndl- and dl-PCBs have decreased substantially since the late 1970s-early 1970s as illustrated by the general annual decline in human milk, guillemot eggs and herring (Table 1 and 2, Appendix 1).

In human milk from Uppsala, Stockholm and Göteborg, the average decline of the ndl CB-28 and CB-153, and the dl CB-118 and CB-126, ranged from 4.8% to 8.5% per year (Table 1 and 2). The time series from Göteborg was the shortest and lacked statistical power to detect a significant trend of CB-153. Table 3 shows declining trends of almost all measured congeners in human milk from the three cities of Sweden. In the Uppsala time series the calculated PCB TEQ concentrations decreased on average about 6% per year between 1996 and 2017 (Table 2).

Table 3. Temporal trends of PCB congeners in different matrices from the Swedish environment. Green (Neg) cells are statistically significant declining trends. Red (Pos) show significant increasing trends. Empty red cells show time series with no statistically significant trend during the time period of series. NA= not analyzed. HU= human milk Uppsala, HS=human milk Stockholm, HG=human milk Göteborg, GE=guillemot eggs, C1=herring muscle Harufjärden, C2=herring muscle Ängskärsklubb, C3=herring muscle Landsort, C4=herring muscle Utlängan, C6=herring muscle Fladen, C7=herring muscle Väderöarna. Time series period given in the heading of each column.

PCB congener	HU 96-17	HS 72-14 07-14[1]	HG 07-15 08-15[1]	GE 88-16 90-16[1]	C1 87-16 95-16[1] 01-16[2]	C2 79-15 89-15[1]	C3 87-16 05-16[1]	C4 88-16 95-16[1] 01-16[2]	C6 88-16 92-16[1] 95-16[2] 01-16[3]	C7 95-16 07-16[1] 08-16[2]
CB-28	Neg	NA	NA	Neg	Neg	Neg[1]	Neg	Neg	Neg	Neg
CB-52	NA	NA	NA	Neg[1]	Neg	Neg[1]	Neg	Neg	Neg	
CB-77	NA	Neg	Neg	NA	Neg[1]	Neg	[1]	[1]	Neg[1]	[2]
CB-101	NA	NA	NA	Neg	Neg	Neg[1]	Neg	Neg[1]	Neg	Neg
CB-105	Neg	Neg	Neg	NA	[1]	Neg	[1]	Neg	Neg[1]	[1]
CB-114	NA	Neg	Neg	NA	[2]	Neg	[1]	[2]	[3]	Pos[1]
CB-118	Neg	Neg	Neg	Neg	Neg	Neg[1]	Neg	Neg	Neg	Neg
CB-123	NA	Neg	Neg	NA	[2]	Neg	[1]	[2]	Neg[3]	Pos[1]
CB-126	Neg	Neg	Neg	NA	[1]	Neg	[1]	[1]	Neg[1]	Pos[1]
CB-138	Neg	Neg[1]	Neg[1]	Neg	Neg	Neg[1]	Neg	Neg	Neg	Neg
CB-153	Neg	Neg	[1]	Neg	Neg	Neg[1]	Neg	Neg	Neg	
CB-156	Neg	Neg	Neg	NA	[1]	Neg	[1]		Neg[2]	Pos[1]
CB-157	NA	Neg	Neg	NA	[1]	Neg	[1]	[1]	Neg[2]	Pos[1]
CB-167	Neg	Neg	Neg	NA	Neg[2]	Neg	[1]	[2]	[3]	Pos[1]
CB-169	Neg	Neg	Neg	NA	Neg[1]	Neg	[1]	Neg[1]	Neg[1]	Pos[1]
CB-180	Neg	Neg[1]	Neg[1]	Neg	Neg	Neg[1]	Neg	Neg	Neg	
CB-189	NA	Neg	Neg	NA	[2]	Neg	[1]	[2]	[2]	[1]

Decreasing temporal trends of the most common PCB in different matrices from Swedish food producing animals (CB-153) were generally observed (Table 1, Fig. 1). Declining trends of CB-118 and CB-126 were also observed in some of the matrices, despite the lower statistical power in the time series for these congeners than in the series for CB-153 (Table 1 and 2). For fat from cattle there was enough statistical power to divide the time series of CB-153 depending on region of slaughter (Fig. 1). A similar temporal trend was observed in all studied regions, but there seemed to be a trend of lower concentrations towards the north of Sweden at the start of the time series.

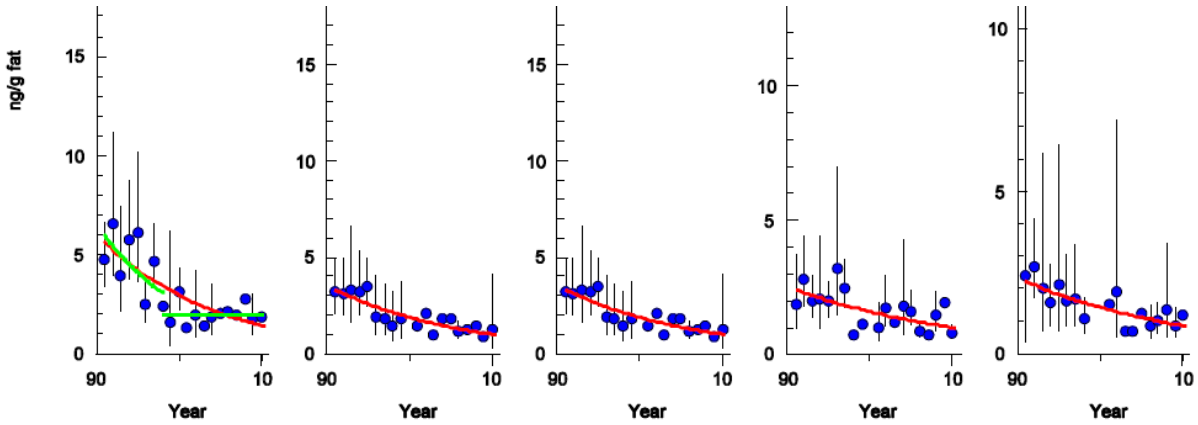


Figure 1. Temporal trends of CB-153 in cattle fat in 5 regions of Sweden from south to north. From left to right region Skåne/Blekinge, Halland/Jönköping/Kalmar/Gotland, Västra Götaland, Värmland/Örebro/Södermanland/Västmanland/Stockholm/Uppsala, and Dalarna/Gävleborg/ Jämtland/Västernorrland/Västerbotten/Norrbotten. Red line shows the log-linear regression line. Green lines show temporal trends with a statistically significant change-point.

As with human milk and Swedish food producing animals, PCB levels have decreased in guillemot eggs and herring muscle for several decades, with an annual decline of CB-28, CB-153, CB-118 and CB-126 of on average 2.0-7.7% (Table 1 and 2). No significant change in levels were observed for CB-126 in herring from several sampling locations, most likely due to a too low statistical power to detect any changes. This is also the main reason for non-significant trends of some of the other PCB congeners in herring samples (Table 3).

Although there was a general decrease in PCB levels in human milk, guillemot eggs and in herring from certain areas of the Baltic Sea, herring from the Swedish west coast (Väderöarna) showed significant increases in levels of CB-114, -123, -126, -156, -157, -167 and -169 (Table 3). Interestingly these congeners were all dl-PCBs. Of the congeners that

have been measured from 1995 at the west coast site, decreasing trends of CB-28, CB-101, CB-118, and CB-138 was observed, but the CB-153 and -180 trends were non-significant (Table 3). There was a tendency of slower declines of these congeners in the Väderöarna herring than in the Baltic Sea herring. Average annual declines in Väderöarna ranged from non-significant to less than 3% and in the Baltic Sea rates of decline were generally over 3% up to almost 8% per year (Table 1 and 2, Appendix 1).

Table 4. Statistically significant change-points (CPs) in time-series of PCB congeners in different matrices from the Swedish environment. The year in cells gives the year of the CP. Green cells show decreasing levels before CP and faster decreasing trends after the CP, as determined visually. Red cells illustrates decreasing levels before CP and slower decreasing levels after CP. Cells with a year but with no color show time series for which it was not possible to visually determine how the trend has changed after the CP. Empty cells show time series with no significant CP (p>0.05). NA= not analyzed. HU= human milk Uppsala, HS=human milk Stockholm, GE=guillemot eggs, C1=herring muscle Harufjärden, C2=herring muscle Ängskärsklubb, C3=herring muscle Landsort, C4=herring muscle Utlängan, C6=herring muscle Fladen, C7=herring muscle Väderöarna. Years in time series given in the heading of each column.

PCB congener	HU 96-17	HS 72-14	GE 88-16 90-16[1]	C1 87-16 95-16[1] 01-16[2]	C2 79-15 89-15[1]	C3 87-16 05-16[1]	C4 88-16 95-16[1] 01-16[2]	C6 88-16 92-16[1] 95-16[2] 01-16[3]	C7 95-16 07-16[1] 08-16[2]
CB-28		NA	1998	1996	1996[1]	1999	1994	1996	2009
CB-52	NA	NA	2010[1]	1993	[1]	1999	2002	2008	
CB-77	NA		NA	2010[1]		[1]	[1]	[1]	[2]
CB-101	NA	NA	2006	1993	[1]	1996	2000	2010	
CB-105				[1]		[1]	2005	2010	[1]
CB-114	NA	1995	NA	[2]		[1]	[2]	[3]	[1]
CB-118		1990		1993	[1]	1999	1999	2010	
CB-123	NA		NA	[2]		[1]	[2]	2010[3]	[1]
CB-126				[1]		[1]	[1]	2006[1]	[1]
CB-138		NA	2011	2009	[1]	1996	1999		
CB-153		2008	2012		[1]	1998	1999	2003	
CB-156		1997	NA	[1]		[1]	[1]	[2]	[1]
CB-157	NA	1995	NA	[1]		[1]	[1]	[2]	[1]
CB-167		1995	NA	[2]	1997	[1]	[2]	[3]	[1]
CB-169	1999	2000	NA	[1]		[1]	2005[1]	2005[1]	[1]
CB-180	2009	NA			[1]	1996	1999	2010	
CB-189	NA	1999	NA	[2]		2006[1]	[2]	[2]	

Although several time series showed significant CPs (Table 4), it was sometimes difficult to visually assess with certainty how the rate of decline changed after the CPs. Moreover, comparisons between time-series is complicated by varying starting points of different time-series. For instance, the time series for human milk from Uppsala (1996-2017) started almost three decades after the Stockholm series (1968-2016). Although efforts have been made to design each time series with the aim to have consistent sampling within the series, there may be differences in sampling strategy between series. As an example, the Uppsala series was based on individual samples from women giving birth to their first child (primipara), whereas the Stockholm series were mainly based on pooled samples, with some years including both primipara and multipara mothers. Milk from multipara women generally have lower PCB levels than milk from primipara women.[35]

For human milk from Stockholm significant CPs were observed for several PCB congeners, in most cases before year 2000 and with a tendency of a faster decline after the CP (Table 4). Similar patterns of CPs were not observed in Uppsala, which could be due to the time series in Uppsala starting only 4 years before year 2000. No significant CP was observed for PCB TEQ concentrations in human milk from Uppsala (Table 2). In guillemot eggs a slower decline after observed CPs were indicated for several congeners, mostly after year 2000 (Table 4). A comparison between CPs for guillemot eggs and herring muscle from the sampling site closest to the guillemot egg sampling area (C4, Utlängan) show some similarities in CPs, i.e. slower declines of CB-28, -52, and -101 after the 1990s-2000s (Table 4). There was a tendency of CPs before year 2000 in herring muscle sampled in Baltic Sea areas north of Gotland, but no consistent patterns in changes of trends after the CPs were obvious (Table 4). At sampling sites at the Swedish west coast (Fladen and Väderöarna) slower declines were indicated after observed CP at Fladen, which in contrast to Väderöarna, mostly showed declining levels during the study periods. (Table 3 and 4)

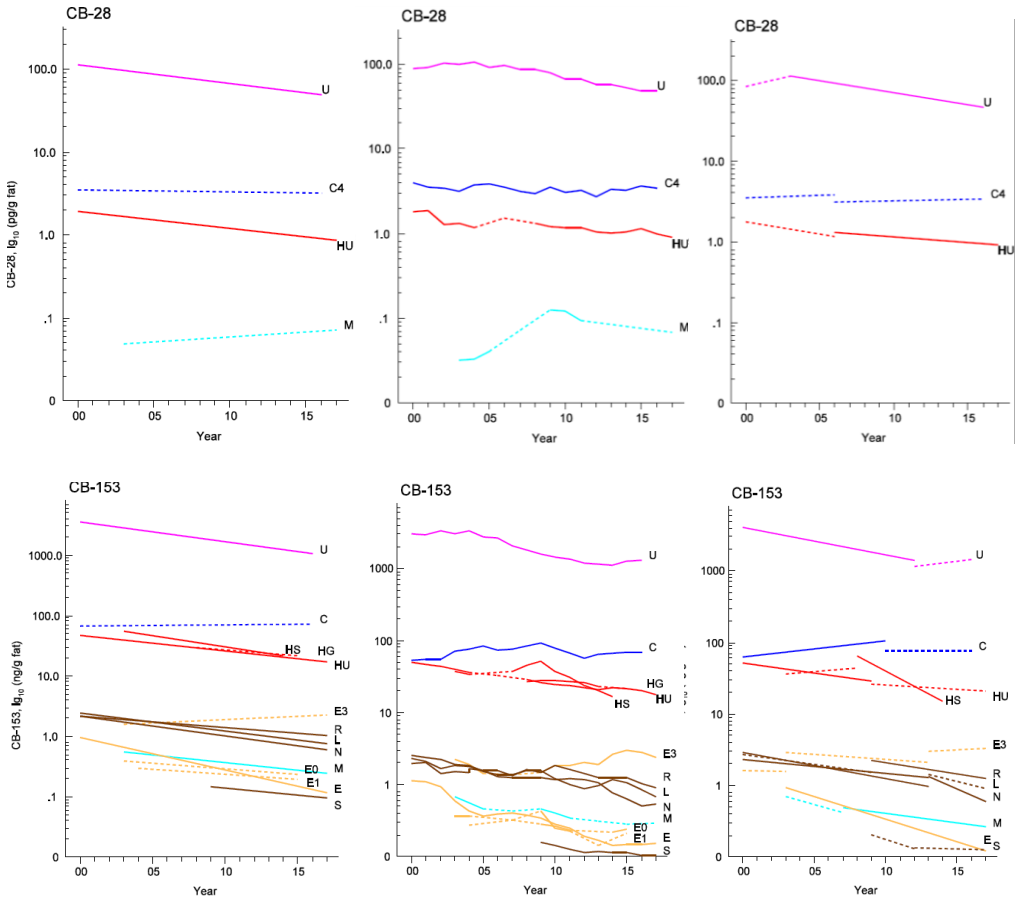


Figure 2. Left figures: log-linear regression lines for temporal trends of the ndl CB-28 and CB-153 in different matrices sampled in Sweden from year 2000 and later. Middle figures: smoothed lines. Right figures: log-linear regression lines with change point (CP). Dashed lines have non-significant slopes. U= guillemont eggs from Stora Karlsö (south Baltic Sea Proper), C/C4=herring muscle Utlängan (south Baltic Sea Proper, autumn), HU=human milk Uppsala, HS=human milk Stockholm, HG=human milk Göteborg, E0=hen´s eggs (caged), E1=hen´s eggs (sputtering), E3=hen´s eggs (eco), E=hen´s eggs (mixed), R=reindeer fat, L=lamb fat, N=cattle fat, M=cow´s milk, S=swine

A closer look at the trends for CB-28, -153, -118 and -126 since 2000 (Fig. 2 and 3) show fairly consistent declining trends for many of the analyzed matrices, and no consistent pattern in changes in trends during the study period. For human milk from the three sampling areas the trends were very similar, although the pattern of CPs differed somewhat between Uppsala and Stockholm. In the Uppsala series there is a tendency of a slower decline in CB-28, -126 and -153 concentrations in later years, but the short study period makes the results uncertain. When comparing trends in guillemot eggs and herring muscle close to Gotland (Stora Karlsö and Utlängan) there was a diverging pattern with a tendency of faster decline in

the eggs than in the herring (Fig. 2 and 3). For food-producing animals CPs with both slower and faster decline afterwards were observed.

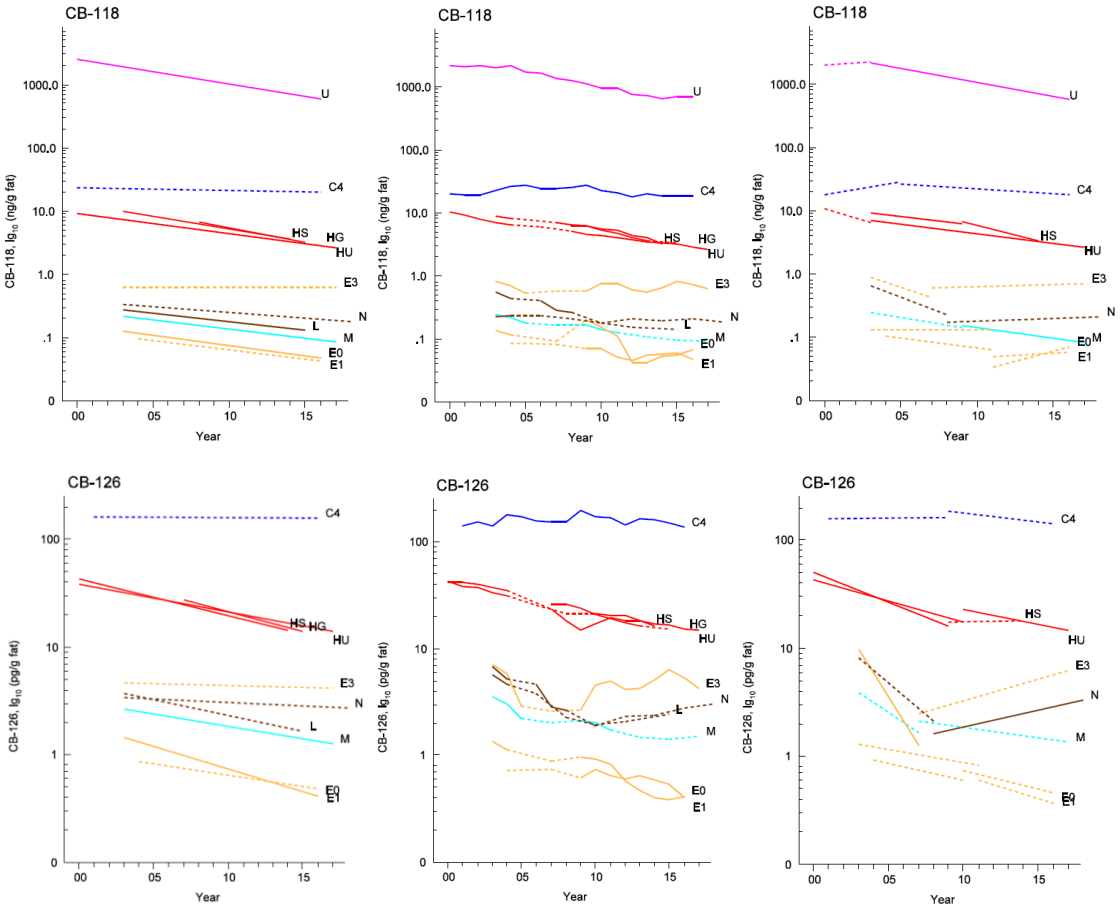


Figure 3. Left figures: log-linear regression lines for temporal trends of the dl CB-118 and CB-126 in different matrices sampled in Sweden from year 2000 and later. Middle figures: smoothed lines. Right figures: log-linear regression lines with change point (CP). Dashed lines have non-significant slopes. U= guillemont eggs from Stora Karlsö (south Baltic Sea Proper), C/C4=herring muscle Utlängan (south Baltic Sea Proper, autumn), HU=human milk Uppsala, HS=human milk Stockholm, HG=human milk Göteborg, E0=hen´s eggs (caged), E1=hen´s eggs (sputtering), E3=hen´s eggs (eco), E=hen´s eggs (mixed), R=reindeer fat, L=lamb fat, N=cattle fat, M=cow´s milk, S=swine

Actions against PCB pollution nationally and internationally

In 1966 the Swedish chemist Sören Jensen discovered that PCBs were ubiquitously present in the Swedish environment.[36] PCBs had been produced by the industry for decades before the discovery. Within a few years after the discovery national legislation restricting the use of PCBs in Sweden enforced (Table 5). During the period 1971-1980, international agreements were initiated leading to restrictions of production and use in many countries. Further

international agreements on elimination of dumping of PCB waste and long-range atmospheric transport put further pressure on the countries signing the conventions/treaties to handle the PCB problem. During this period also the first legislation dealing with PCB polluted food was enforced in Sweden (Table 5).

The period 1981-1990 saw further international agreements with the aim to put pressure on national PCB elimination. Maximum limits of PCBs in food were issued in Sweden, and the public was given consumption advice of restricted consumption of certain types of PCB-polluted fish. Further bans were enforced within the EU. In Sweden, national legislation had now dealt with most of the applications of PCBs, and now focus was set on dealing with the unintentional formation on PCBs during waste incineration. During 1991-2000, further pressure was put internationally to eliminate PCB use, and legislation about handling of PCB waste was initiated, as well as international agreements on elimination of PCB emissions. In Sweden, legislation about elimination of the remaining use in certain electrical equipment was initiated, and also work on handling the PCB problem in sealants in for instance buildings. The Swedish consumption advisories about PCB-contaminated food became more restrictive, focusing more on fatty fish from the Baltic Sea, Vänern and Vättern (Table 5).

From 2001, more focus was set on PCB waste management and handling both nationally and internationally. In Sweden, legislation about burnable waste handling most probably reduced unintentional formation during landfill fires. In 2002, legislation about maximum limits for PCDD/Fs in animal feed and food was set in force within the EU. The inclusion of animal feed in the legislation was important since animal feed is the major source of contamination of food-producing animals within the agricultural sector. Although PCBs were not included, the strong correlations between PCDD/F and PCB concentrations in feed and food indirectly also included PCBs in the legislation. In 2004, the Stockholm Convention was adopted by the international community and entered into force. By 2012 there were 176 parties to the convention, which prohibits new production and use of PCBs. The parties are required to eliminate the use of PCBs in existing equipment by 2025 and to ensure environmental sound PCB waste management by 2028. Moreover, unintentional formation of PCBs should be decreased to acceptable levels. In 2006, dl-PCBs were also included in the EU maximum limits in animal feed and in food. In Sweden the consumption advice about PCB-contaminated foods became even more restrictive. In 2012, ndl-PCBs were included in the EU legislation setting maximum limits in animal feed and in food.

Table 5. Actions against PCB pollution in Sweden and internationally.

Year	CB 153 CP (trend after CP)		National International	Comment	Reference
1966		Detection of PCB in the environment		Sören Jensen discovers PCB in a white-tailed eagle	[36]
1971-75		Sweden	National	Restriction of use	[37]
		Oslo Convention (OSPAR)	International	Restriction of PCB dumping in North-East Atlantic	[38]
		Sweden	National	Restrictions of manufacturing, import, sales of PCB products	[39]
		OECD	International	Member states agree on restrictions of production and use	[40]
		Paris Convention (OSPAR)	International	Restrictions against land-based dumping	[41]
		Sweden	National	Banning of open use (plastic, paint, paper, sealants,….	[42]
		Sweden	National	Ban of fishing in waters with PCB-contaminated seafood	[43]
1976-1980		EU	International	Banning open use in printing ink and glue	[44]
		Sweden	National	Phase-out of new use in closed systems	[45]
1981-1990		OSPAR	International	Recommendation of phase-out of production and use by member states	[46]
		Sweden	National	Maximum limits in food and food consumption advice	Not found
		EU	International	Ban of PCB as raw material/intermediate	[47]
		Sweden	National	Actions against waste incineration	[7]
		Sweden	National	More restrictive food consumption advisories	Not found
1991-2000		OSPAR	International	Elimination of all PCB use (1998)	[46]
		HELCOM	International	Ban of use in the Baltic Sea area	[48]
		Sweden	National	All use in transformers/capacitors eliminated	[45]
		Sweden	National	More restrictive food consumption advisories	Not found
		EU	International	Legislation about handling, removal and elimination of PCB waste	[49]
		UNECE	International	Aarhus protocol. Elimination of PCB emissions	[50]
		Sweden	National	Removal/elimination of PCB-sealants in buildings is initiated	[51]
		Sweden	National	Ban on “backyard burning”	[52]
2001-2010		EU	International	WEE and RoHS Directives. Electronic/electrical waste management. Restrictions of toxic substances,	[47]
		EU	International	Maximum limits of dioxins in feed and food	[53]
		Sweden	National	Ban of burnable waste in landfills	[54]
		Stockholm Convention	International	Elimination of PCB production and use	[55]
		Sweden	National	Treatment of waste (electric) (NFS 2005:10)	[56]
		EU	International	Maximum limits in feed and food, dioxinlike PCBs	[57]
		Sweden	National	Further restrictions to completely eliminate PCB in sealants	[58]
		Sweden	National	More restrictive food consumption advisories	[59]
2011-2012		EU	International	Maximum limits in feed and food, non-dioxinlike PCBs	[57]

Table 6. Temporal trends of TCDD, 1,2,3,7,8-PeCDD, 2,3,4,7,8-PeCDF, PCDD TEQ and PCDF TEQ in different matrices sampled in Sweden. Human milk trend from Uppsala adjusted for participant´s age, pre-pregnancy BMI, weight gain during pregnancy, weight loss after pregnancy and education. N=number of measured samples included. Trend=annual change in levels (mean (95% confidence interval)). Only statistically significant trends are reported (p≤0.05). CP=change point year for which a change in the slope has been detected (only given for statistically significant CPs (p≤0.05)). CP change=visually determined change in trend at CP. Faster decrease=decreasing levels before CP and faster decrease after. Slower decrease=decreasing levels before CP and slowing down after. Empty cell=not possible to determine visually.

Matrix	N	Years	Trend (% per year)	CP	P-value	CP change
PCDD/F						
TCDD						
Human milk, Uppsala	366	1996-2017	-6.8 (-7.3, -6.3)			
Human milk, Stockholm	35	1972-2014	-6.5 (-7.5, -5.5)	1992	<0.001	Faster decrease
Human milk, Göteborg	14	2007-2015	-5.8 (-8.4, -3.3)			
Guillemot egg	128	1968-2016	-4.5 (-4.9, -4.1)	1995	<0.001	
Herring, Harufjärden	75	1995-2016	-4.4 (-6.3-2.5)			
Herring, Ängskärsklubb	42	1979-2015	-9.2 (-10, -7.9)	1989		Slower decrease
Herring, Landsort	20	2005-2016				
Herring, Utlängan	76	1995-2016	-3.9 (-5.5, -2.3)			
Herring, Fladen	74	1995-2016	-5.2 (-7.0, -3.5)	2005	0.037	
Herring, Väderöarna	20	2007-2016	11 (5.0, 18)			
1,2,3,7,8-PeCDD						
Human milk, Uppsala	354	1996-2017	-6.0 (-6.4, -5.6)			
Human milk, Stockholm	35	1972-2014	-5.7 (-6.2, -5.2)	2007	0.0014	Slower decrease
Human milk, Göteborg	14	2007-2015	-7.6 (-10, -4.8)			
Hen´s egg, cage	27	2003-2016	-9.9 (-15, -5.0)			
Hen´s egg, sputtering	38	2004-2016				
Hen´s egg, eco	95	2003-2017	-6.3 (-8.8, -3.7)	2007	0.012	Slower decrease
Guillemot egg	128	1968-2016	-2.8 (-3.2, -2.4)	2002	<0.001	
Herring, Harufjärden	75	1995-2016	-4.2 (-6.4, -2.1)			
Herring, Ängskärsklubb	42	1979-2015	-6.0 (-7.3, -4.6)			
Herring, Landsort	20	2005-2016				
Herring, Utlängan	76	1995-2016	-3.6 (-5.1, -2.0)			
Herring, Fladen	75	1995-2016	-4.1 (-6.2, -2.0)			
Herring, Väderöarna	20	2007-2016				
2,3,4,7,8-PeCDF						
Human milk, Uppsala	354	1996-2017	-4.2 (-4.7, -3.7)	2008	0.019	Slower decrease
Human milk, Stockholm	35	1972-2014	-5.7 (-6.2, -5.2)	2007	0.015	Slower decrease
Human milk, Göteborg	14	2007-2015	-6.3 (-9.8, -2.6)			
Hen´s egg, cage	27	2003-2016				
Hen´s egg, sputtering	38	2004-2016				
Hen´s egg, eco	95	2003-2017		2007	0.001	Slower decrease
Lamb fat	34	2003-2015				
Guillemot egg	171	1968-2016	-1.8 (-2.4, -1.2)	1993	<0.001	Slower decrease
Herring, Harufjärden	75	1995-2016				
Herring, Ängskärsklubb	42	1979-2015	-4.7 (-6.2, -3.2)			
Herring, Landsort	20	2005-2016				
Herring, Utlängan	76	1995-2016	-2.4 (-4.0, -0.86)			
Herring, Fladen	75	1995-2016	-2.4 (-3.9, -0.85)			
Herring, Väderöarna	20	2007-2016				
PCDD TEQ$_{2005}$						
Human milk, Uppsala	360	1996-2016	-6.8 (-7.2; -6.4)			
PCDF TEQ$_{2005}$						
Human milk, Uppsala	360	1996-2016	-3.8 (-4.3; -3.3)			

PCDD/Fs

As with PCBs, the environmental pollution of both PCDDs and PCDFs has decreased substantially since the early 1970s, as illustrated by the general annual decline of on average 4.7-9.2% for TCDD, 1,2,3,7,8-PeCDD and 2,3,4,7,8-PeCDF in human milk from Stockholm, guillemot eggs and herring muscle (Table 6). Also in some of the shorter more recent time series of these matrices a decline was observed. When looking at the trend pattern for all detected PCDD/F congeners, decreasing trends dominated for human milk and guillemot eggs, and for herring muscle from Ängskärsklubb (Table 7). For other sampling areas of herring muscle, the time series were more than 10 years shorter than that from Ängskärsklubb (1979-2015) (Table 7), making it more difficult to detect significant trends. Nevertheless, for PCDDs declining levels were evident for several congeners in herring muscle from Baltic Sea sites and one of the west coast sites (Fladen) sampled between 1995 and 2016 (Table 7). Contrary to this, increasing trends were observed for some PCDD congeners in herring muscle from Väderöarna on the Swedish west coast (Table 7).

Table 7. Temporal trends of PCDD/Fs congeners in different matrices from the Swedish environment. Green (Neg) cells are statistically significant declining trends. Red (Pos) show significant increasing trends. Empty red cells show time series with no statistically significant trend during the time period of series. NA= not analyzed. HU= human milk Uppsala, HS=human milk Stockholm, HG=human milk Göteborg, GE=guillemot eggs, C1=herring muscle Harufjärden, C2=herring muscle Ängskärsklubb, C3=herring muscle Landsort, C4=herring muscle Utlängan, C6=herring muscle Fladen, C7=herring muscle Väderöarna. Years in time series given in the heading of each column.

PCDD/F congener	HU 96-17	HS 72-14	HG 07-15	GE 68-16	C1 95-16	C2 79-15	C3 05-16	C4 95-16	C6 95-16	C7 07-16
TCDD	Neg	Neg	Neg	Neg	Neg	Neg		Neg	Neg	Pos
1,2,3,7,8-PeCDD	Neg	Neg	Neg	Neg	Neg	Neg		Neg	Neg	
1,2,3,4,7,8-HxCDD	Neg	Neg	Neg	Neg	Neg	Neg		Neg	Neg	Pos
1,2,3,6,7,8-HxCDD	Neg	Neg	Neg	Neg		Neg		Neg		Pos
1,2,3,7,8,9-HxCDD	Neg	Neg	Neg	Neg	Neg	Neg			Neg	
1,2,3,4,6,7,8-HpCDD	Neg	Neg	Neg	Neg	Neg	Neg			Neg	
OCDD	Neg	Neg	Neg	Neg	Neg	Neg			Neg	
TCDF	Neg	Neg	Neg			Neg			Neg	
1,2,3,7,8-PeCDF		Neg		Neg		Neg		Neg	Neg	
2,3,4,7,8-PeCDF	Neg	Neg	Neg	Neg		Neg		Neg	Neg	
1,2,3,4,7,8-HxCDF	Neg	Neg		Neg		Neg		Neg	Neg	
1,2,3,6,7,8-HxCDF	NA	Neg		Neg		Neg		Neg		Pos
1,2,3,7,8,9-HxCDF		NA	NA	Neg		Neg		Neg		
2,3,4,6,7,8-HxCDF		Neg			Neg	Neg			Neg	
1,2,3,4,6,7,8-HpCDF	Neg	Neg	Neg	Neg						
1,2,3,4,7,8,9-HpCDF	NA	NA	NA	Neg		Neg				
OCDF	NA	Neg	Neg	Neg						

When looking at the PCDFs, fewer congeners showed declining trends in comparison with the PCDD congeners, especially in the shorter time series (Table 7). Between 1996 and 2016 an average decline of PCDD TEQs of 6.8% per year was observed in human milk from Uppsala but for PCDF TEQs the decline was slower, 3.8% per year on average (Table 6). Similar results, with a slower decrease of PCDFs than of PCDDs were indicated for guillemot eggs when comparing TCDD (-4.5/year) and 1,2,3,7,8-PeCDD (-2.8%/year) with 2,3,4,7,8-PeCDF (-1.8%/year) (Table 6). This tendency was also suggested for herring samples (Table 6).

Many matrices from food-producing animals in Sweden had levels below the limit of detection (LOD), so no trend analyses could be performed. For those few matrices with enough samples with levels above LOD (eggs and lamb fat), only organic eggs showed a decreasing trend of 1,2,3,7,8-PeCDD between 2003 and 2016 (Table 6). These time series were relatively short, and consisted of a relatively low number of samples.

Statistically significant CPs were observed mainly in human milk, guillemot egg and the longest herring muscle (Ängskärsklubb) time series (Table 8). The human milk series from Stockholm showed CPs for several PCDD congeners during the period 1980-1997, with a tendency of a more rapid decline after the CP (Table 8, Appendix 2). Among the PCDFs later CPs were observed with a tendency of a slower decline afterwards. In the Uppsala time series, CPs of PCDDs and PCDFs with indicated slower declines around 2010 were also observed (Table 8).

For guillemot eggs significant CPs, with indicated slower declines afterwards, were observed for some PCDD/F congeners, occurring earlier than in human milk (Table 8, Appendix 2). In herring muscle CPs were mainly observed in the longest time-series from Ängskärsklubb. In this case it was in most cases difficult to visually determine if the decline became slower or not after the CPs (Appendix 2).

Table 8. Statistically significant change-points (CPs) in time-series of PCDD/F congeners in different matrices from the Swedish environment. The year in cells gives the year of the CP. Green cells show suggested faster decreasing trends after the CP, as determined visually. Red cells suggest slower decreasing trends after CP. Cells with a year but with no color show time series for which it was not possible to visually determine how the trend have changed after the CP. Empty cells show time series with no significant CPs (p>0.05). NA= not analyzed. HU= human milk Uppsala, HS=human milk Stockholm, GE=guillemot eggs, C1=herring muscle Harufjärden, C2=herring muscle Ängskärsklubb, C3=herring muscle Landsort, C4=herring muscle Utlängan, C6=herring muscle Fladen, C7=herring muscle Väderöarna. Years in time series given in the heading of each column.

PCDD/F congener	HU 96-17	HS 72-14	GE 68-16	C1 95-16	C2 79-15	C3 05-16	C4 95-16	C6 95-16	C7 07-16
TCDD		1992	1995		1989			2005	
1,2,3,7,8-PeCDD		2007	2002						
1,2,3,4,7,8-HxCDD	2006	1980	2002						
1,2,3,6,7,8-HxCDD	2006	1990	2002					2006	
1,2,3,7,8,9-HxCDD	2008	1997	1991						
1,2,3,4,6,7,8-HpCDD		1990	2002		1997				
OCDD		1991	2004	2009					
TCDF		2009	1990						
1,2,3,7,8-PeCDF		2004	2001						
2,3,4,7,8-PeCDF	2008	2007	1993						
1,2,3,4,7,8-HxCDF	2011	2009	1993						
1,2,3,6,7,8-HxCDF	NA	2009	1995						
1,2,3,7,8,9-HxCDF	2011	NA	NA		1982				
2,3,4,6,7,8-HxCDF		2010	2004		1997				
1,2,3,4,6,7,8-HpCDF		1995	1991		2007		2003		
1,2,3,4,7,8,9-HpCDF	NA	NA	1993		2003				
OCDF	NA	2011							

When trends were analyzed during the time period 2000-2016, significant declines in TCDD and 1,2,3,7,8-PeCDD concentrations were observed in human milk, guillemot eggs and herring, and for 2,3,4,7,8-PeCDFin human milk (Fig. 4). In guillemot eggs and herring no significant trends was observed for the latter congener. In human milk, CPs with a slower decline afterwards were indicated for TCDD, 1,2,3,7,8-PeCDD, and 2,3,4,7,8-PeCDF (Fig. 4). CPs with slower declines of TCDD were also suggested both for guillemot eggs and herring muscle from Landsort (Fig. 4). For the two other congeners 1,2,3,7,8-PeCDD and 2,3,4,7,8-PeCDF the picture was not as clear. The only food-producing animal with enough samples with PCDD/F concentrations above LOD, hen´s eggs, showed a tendency of CPs with an increase in levels afterwards in the middle of the study period 2000-2016/17 (Fig. 4).

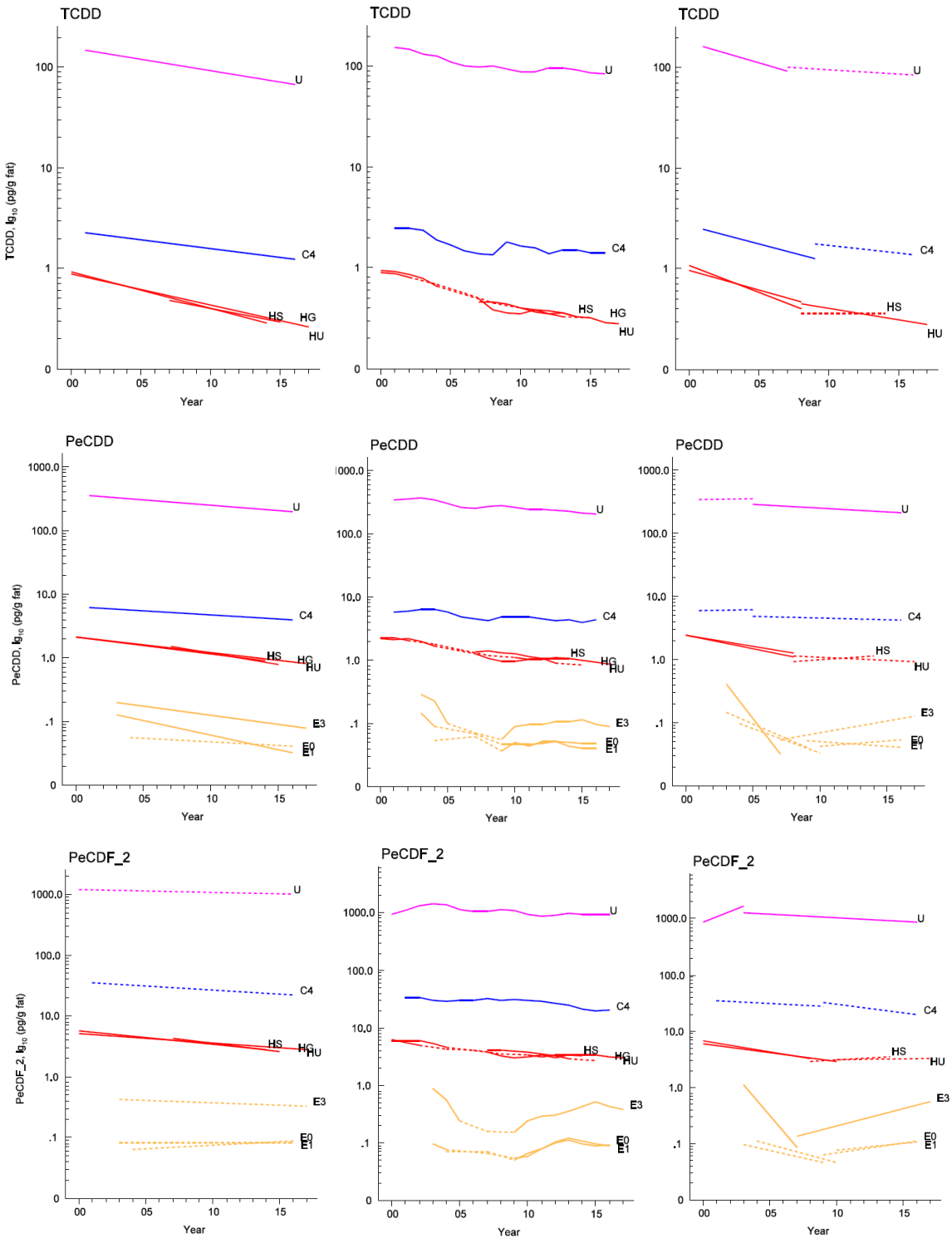


Figure 4. Left figures: log-linear regression lines for temporal trends of TCDD, 1,2,3,7,8-PeCDD and 2,3,4,7,8-PeCDF in different matrices sampled in Sweden from year 2000 and later. Middle figures: smoothed lines. Right figures: log-linear regression lines with change point (CP). Dashed lines have non-significant slopes (P>0.05). U= guillemot eggs from Stora Karlsö (south Baltic Sea Proper), C4=herring muscle Utlängan (south Baltic Sea Proper, autumn), HU=human milk Uppsala, HS=human milk Stockholm, HG=human milk Göteborg, E0=hen´s eggs (caged), E1=hen´s eggs (sputtering), and E3=hen´s eggs (eco).

Table 9. Actions against PCDD/F pollution in Sweden and internationally. For actions against PCB (PCDD/F contamination of commercial PCB mixtures, and co-formation of PCBs and PCDFs during combustion) see Table 5.

Year		National International	Comment	Reference
1957	Discovery of 2.3.7.8-TCDD causing chloracne in 2,4,5-T production		Dermatologist Sorge together with Kimmig and Schulz	[60]
1971-1980	Sweden	National	Ban of 2,4,5-T	[61]
	Sweden	National	Ban of pentachlorophenol and other chlorophenols	[62]
1981-1990	Sweden	National	Chorine industry restrictions (PVC, chlor alkali/chlorate production)t	[63]
1991-2000	Sweden	National	Chlorine gas bleaching phased out	[7]
	Sweden	National	Phase-out of lead in gasoline	[7]
	UNECE	International	Limiting emissions of PCDD/F to air	[64]
2001-2010	Stockholm Convention	International	Elimination/decrease of unintentional formation	[55]
2011-2015	Stockholm Convention	International	Elimination of pentachlorophenol with exemptions	[55]

Actions against PCDD/F pollution nationally and internationally

Chloracne was a well-known occupational disease first described in 1887 in chloro alkali workers.[65] In 1957 German dermatologists/chemists identified 2,3,7,8-TCDD as cause of chloracne (Table 9).[60] Not until 1977, PCDD/Fs were discovered in municipal waste incineration emissions.[65] Most of the actions against PCB pollution nationally and internationally (Table 5) also affected PCDD/F pollution, since PCDD/Fs were contaminants of technical PCB mixtures,[66] and PCDD/Fs are formed in the same combustion processes where PCBs are formed.[7] However, there have been some actions against pollution of other commercial chlorinated compounds that have affected PCDD/F pollution. The ban of use of pentachlorophenol (PCP) and other chlorophenols during the 1970s in Sweden affected PCDD/F pollution, since PCDD/Fs are unintentionally present as impurities in the technical mixtures.[7] The same is evident for the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T),[67] which similarly as chlorophenols was banned during the 1970s in Sweden.[61] An important source of pollution along the Baltic Sea coast, chlorine gas bleaching of pulp and paper, was eliminated during the early 1990s.[7] The phase-out of lead in gasoline during the 1990s may have contributed to decreased PCDD/F emissions.[7] In 2004 PCDD/Fs were regulated in the Stockholm Convention and in 2015 pentachlorophenol (PCP) was included.[68]

Table 10. Temporal trends of HCB in different matrices sampled in Sweden. Human milk trend from Uppsala adjusted for participant´s age, pre-pregnancy BMI, weight gain during pregnancy, weight loss after pregnancy and education. N=number of measured samples included. Trend=annual change in levels (mean (95% confidence interval)). Only statistically significant trends are reported (p≤0.05). CP=change point year for which a change in the slope has been detected (only given for statistically significant CPs (p≤0.05)). CP change=visually determined change in trend at CP. Slower decrease=decreasing levels before CP and slowing down after. Decrease/increase=decreasing levels before CP and thereafter determined to increase. Empty cell=not possible to determine visually.

Matrix	N	Years	Trend (% per year)	CP	P-value	CP change
HCB						
Human milk, Uppsala	406	1996-2016	-5.0 (-5.4, -4.6)	2006	0.012	Slower decrease
Human milk, Stockholm	25	1972-2014	-6.8 (-8.2, -5.4)	2004	0.002	Slower decrease
Human milk, Göteborg	35	2007-2015				
Hen´s egg	521	1999-2017	-7.3 (-8.4, -6.2)	2008	<0.001	Slower decrease
Cow´s milk	267	1999-2017	-3.3 (-4.2, -2.5)	2006	<0.001	Decrease/increase
Cattle fat	828	1991-2017	-2.2 (-2.6, -1.7)	1998	<0.001	Decrease/increase
Lamb fat	108	1998-2017				
Swine fat	201	2009-2017				
Reindeer fat	199	2000-2017	5.3 (3.7, 6.9)			
Guillemot egg	336	1979-2016	-5.8 (-6.1, -5.4)	1997	<0.001	Slower decrease
Herring, Harufjärden	401	1987-2016	-2.1 (-2.5, -1.7)	1993	0.008	Slower decrease
Herring, Ängskärsklubb	355	1989-2015	-4.9 (-5.6, -4.2)	2004	0.005	Decrease/increase
Herring, Landsort	401	1987-2016	-3.4 (-4.1, -2.8)	1996	<0.001	Slower decrease
Herring, Utlängan	411	1988-2016	-4.1 (-4.7, -3.6)	1995	0.0019	Slower decrease
Herring, Fladen	447	1988-2016	-4.4 (-4.8, -4.0)	2003	<0.001	Decrease/increase
Herring, Väderöarna	319	1995-2016		2010	0.013	Decrease/increase

HCB

The environmental pollution of HCB has decreased substantially since the 1980s as illustrated by the general annual decline in human milk, in some food producing animals, guillemot eggs and herring muscle (Table 10). In human milk from Uppsala (1996-2016) and Stockholm (1972-2014) the average annual decline ranged from 5.0% to 6.8% per year, with the slower annual decline in the shorter time series from Uppsala (Table 10). The time series from Göteborg is the shortest (2007-2015) and lacked statistical power to detect a significant trend of HCB.

In the food control program of contaminants performed by the SNFA, decreased levels of HCB was observed in matrices from food-producing animals in Sweden (-2.2% to-7.3% per year) (Table 10). There were, however, three exceptions to this. In the case of lamb and swine fat no significant trends were observed and for reindeer fat the concentrations increased with on average 5.3% per year between 2000 and 2017 (Table 10).

As with human milk and Swedish food producing animals, HCB levels have decreased in guillemot eggs and herring muscle for several decades, with an annual decline of on

average 2.1-5.8% (Table 10). However, no significant change in levels was observed for west coast herring at Väderöarna between 1995 and 2016.

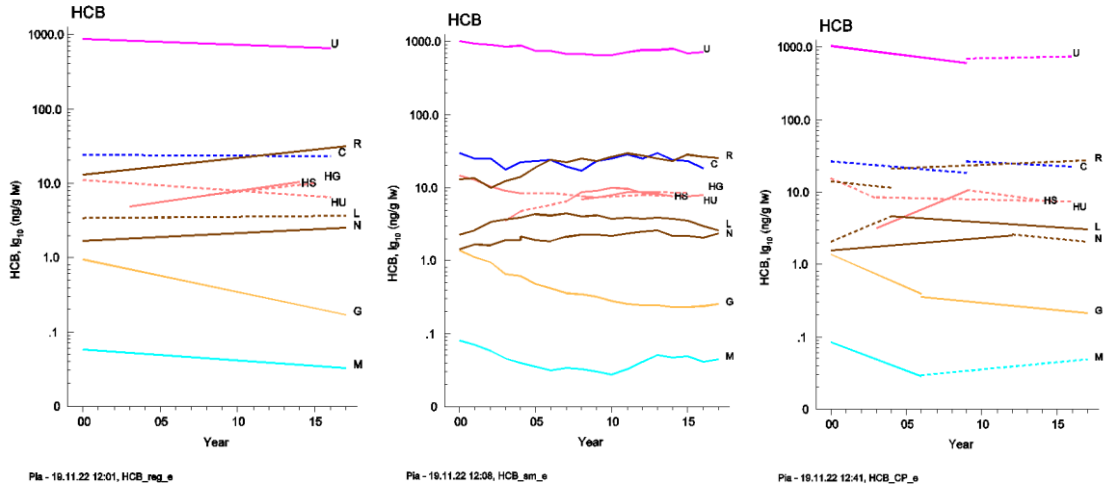


Figure 5. Left figure: log-linear regression lines for temporal trends of HCB in different matrices sampled in Sweden from year 2000 and later. Middle figure: smoothed lines. Right figure: log-linear regression lines with change point (CP). Dashed lines have non-significant slopes. U= guillemont eggs from Stora Karlsö (south Baltic Sea Proper), C=herring muscle Utlängan (south Baltic Sea Proper, autumn), HU=human milk Uppsala, HS=human milk Stockholm, HG=human milk Göteborg, R=reindeer fat, L=lamb fat, N=cattle fat, G=chicken eggs, M=cow´s milk.

For HCB, CPs were detected in human milk (2002-2004), guillemot eggs (1997) and herring muscle (1997-2010), with a general slower decline after the CP, in some cases even increasing trends were observed (Table 10, Appendix 3). A closer look at the HCB trends since 2000 (Fig. 5) shows varying trends. Some matrices showing decreasing levels (guillemot eggs, chicken eggs, cow´s milk), some showing non-significant trends (herring muscle (Utlängan), human milk Uppsala/Göteborg, lamb fat) and some matrices showing increasing trends (human milk Stockholm, cattle fat, reindeer fat. CPs were detected for all matrices, usually with a non-significant trend after CP (Fig. 4).

Actions against HCB pollution nationally and internationally

HCB was mainly used as a fungicide for decades up to 1980 when the use was banned in Sweden (Table 11). HCB may be present as a contaminant of chlorinated solvents, such as tri- and tetrachloroethylene and carbon tetrachloride,[7] and this source of pollution was banned in Sweden in 1996-1998 (Table 11). In 2001 HCB was included in the Stockholm Convention, thus eliminating the primary source of HCB pollution worldwide (Table 11).

The measures to diminish formation and emissions of PCDD/Fs from combustion processes have also, as in the case of PCBs, had positive effects on HCB pollution (Table 5).[7] However, it has been estimated that unintentional formation of HCB is larger than that of PCBs.[7] Actions against PCDD/F formation/emissions from PVC and chlor alkali production (Table 9) have also been positive for HCB emissions.[7]

Table 11. Actions against HCB pollution in Sweden and internationally. For actions against unintentionally formed HCB during combustion see Table 5.

Year		National International	Comment	Reference
1980	Sweden	National	Ban as a pesticide in Sweden	[25]
1981-1990	Sweden	National	Chorine industry restrictions (PVC, chlor alkali/chlorate production)t	[63]
1996- 1998	Sweden	National	Ban of production and use of certain chlorinated solvents	[69, 70]
	UNECE	International	Reduction of air emissions of HCB	[64]
2001	Stockholm Convention	International	Elimination of production and use	[55]
2009	UNECE	International	Further obligations to reduce air emissions of HCB	[64]

Table 12. Temporal trends of PBDEs and HBCDD in different matrices sampled in Sweden. Human milk trend from Uppsala adjusted for participant´s age, pre-pregnancy BMI, weight gain during pregnancy, weight loss after pregnancy, and education. N=number of measured samples included. Trend=annual change in levels (mean (95% confidence interval)). Only statistically significant trends are reported (p≤0.05). CP=change point year for which a change in the slope has been detected (only given for statistically significant CPs (p≤0.05)). CP change=visually determined change in trend at CP. Faster decrease=decreasing levels before CP and faster decrease thereafter. Slower decrease=decreasing levels before CP and slowing down after. Decrease/increase= decreasing levels before CP and thereafter determined to increase. Increase/decrease=increase in levels before CP and decrease after. Empty cell=not possible to determine visually.

Matrix	N	Years	Trend (% per year)	CP	P-value	CP change
BDE-47						
Human milk, Uppsala	427	1996-2016	-9.2 (-10, -8.2)	2006	0.014	Faster decrease
Human milk, Stockholm	29	1984-2016		1994	0.002	Increase/decrease
Human milk, Göteborg	38	2007-2015				
Guillemot egg	227	1969-2016	-9.4 (-10, -8.5)	1983	<0.001	Increase/decrease
Herring, Harufjärden	215	1999-2016	-3.7 (-5.0, -2.4)			
Herring, Ängskärsklubb	193	1980-2015	-7.6 (-8.7, -6.5)	1989	0.0021	Increase/decrease
Herring, Landsort	203	1999-2016	-6.5 (-7.6, -5.3)			
Herring, Utlängan	215	1999-2016	-5.6 (-6.7, -4.4)			
Herring, Fladen	212	1999-2016	-8.5 (-9.4, -7.7)	2007	0.0016	Slower decrease
Herring, Väderöarna	260	1999-2016	-9.4 (-10, -8.6)	2003	0.0042	Slower decrease
BDE-99						
Human milk, Uppsala	394	1996-2016	-14 (-15, -12)			
Human milk, Stockholm	26	1984-2014		1994	<0.001	Increase/decrease
Human milk, Göteborg	38	2007-2015				
Guillemot egg	277	1969-2016	-7.8 (-8.6, -7.0)	1982	<0.001	Increase/decrease
Herring, Harufjärden	215	1999-2016	-5.0 (-6.1, -3.9)			
Herring, Ängskärsklubb	193	1980-2015	-7.0 (-8.1, -5.8)	1990	0.0024	Increase/decrease
Herring, Landsort	202	1999-2016	-7.2 (-8.5, -5.9)			
Herring, Utlängan	215	1999-2016	-9.0 (-11, -7.3)			
Herring, Fladen	212	1999-2016	-8.6 (-9.7, -7.6)	2007	<0.001	Slower decrease
Herring, Väderöarna	260	1999-2016	-9.8 (-11, 8.9)	2007	<0.001	Slower decrease
BDE-153						
Human milk, Uppsala	428	1996-2016		2004	<0.001	Increase/decrease
Human milk, Stockholm	13	2007-2014				
Human milk, Göteborg	38	2007-2015				
Guillemot egg	170	2000-2016	-4.0 (-6.1, -1.9)	2003	0.048	Increase/decrease
Herring, Harufjärden	177	1999-2016				
Herring, Ängskärsklubb	191	1980-2015		2003	0.0085	Decrease/increase
Herring, Landsort	179	1999-2016				
Herring, Utlängan	202	1999-2016				
Herring, Fladen	198	1999-2016	-5.2 (-6.7, -3.7)	2004	0.014	Decrease/increase
Herring, Väderöarna	236	1999-2016	-5.5 (-6.6, -4.3)	2004	0.036	Decrease/increase
HBCDD						
Human milk, Uppsala	204	2002-2016	-5.9 (-7.7, -4.0)			
Human milk, Stockholm	23	1984-2014	-4.8 (-9.5, 0.021)	2002	<0.001	Increase/decrease
Human milk, Göteborg	7	2011-2015				
Guillemot egg	287	1969-2016		1985	<0.001	
Herring, Harufjärden	215	1999-2016				
Herring, Ängskärsklubb	193	1980-2016		1999	0.007	Increase/decrease
Herring, Landsort	203	1999-2016				
Herring, Utlängan	216	1999-2016	-5.4 (-7.2, -3.6)			
Herring, Fladen	211	1999-2016	-8.3 (-9.5, -7.1)			
Herring, Väderöarna	259	1999-2016	-7.5 (-8.5, -6.5)			

PBDEs and HBCDD

In the temporal trend analyses of PBDEs over the whole time series, declining levels were observed of the tetra-brominated BDE-47 and the penta-brominated BDE-99 in human milk from Uppsala (BDE-47: -9.2% per year; BDE-99: -14% per year), guillemot eggs (BDE-47: -9.4%; BDE-99: -7.8%) and herring muscle (-3.7% to -9.8%) (Table 12). No significant trends were observed for human milk from Stockholm and Göteborg. Mostly due to a short study period, the tri-brominated BDE-28 showed no significant temporal trends except in the case of decreasing levels in human milk from Göteborg and herring muscle from Harufjärden in the northern part of the Baltic Sea (Table 13). The temporal trend patterns for the penta-brominated BDE-100 was similar as for BDE-47 and -99 (Table 13).

Table 13. Temporal trends of PBDE congeners in different matrices from the Swedish environment. Green (Neg) cells are statistically significant declining trends. Red (Pos) show significant increasing trends. Empty red cells show time series with no statistically significant trend during the time period of series. NA= not analyzed. HU= human milk Uppsala, HS=human milk Stockholm, HG=human milk Göteborg, GE=guillemot eggs, C1=herring muscle Harufjärden, C2=herring muscle Ängskärsklubb, C3=herring muscle Landsort, C4=herring muscle Utlängan, C6=herring muscle Fladen, C7=herring muscle Väderöarna. Years in time series given in the heading of each column.

Substance	HU 96-16 02-16[1] 04-16[2] 09-16[3]	HS 84-14 07-14[1] 10-14[2]	HG 07-15 11-15[1]	GE 69-16 00-16[1] 11-16[2]	C1 99-16 11-16[1]	C2 80-15 11-15[1]	C3 99-16 11-16[1]	C4 99-16 11-16[1]	C6 99-16 11-16[1]	C7 99-16 11-16[1]
BDE-28	[2]	[1]	Neg	[2]	Neg[1]	[1]	[1]	[1]	[1]	[1]
BDE-47	Neg			Neg	Neg	Neg	Neg	Neg	Neg	Neg
BDE-99	Neg			Neg	Neg	Neg	Neg	Neg	Neg	Neg
BDE-100	Neg			Neg		Neg	Neg	Neg	Neg	Neg
BDE-153		[1]		Neg[1]					Neg	Neg
BDE-154	NA		NA	NA					Neg	
BDE-209	[3]	Neg[2]	[1]	NA	NA	NA	NA	NA	NA	NA
HBCDD	Neg[1]	Neg	[1]					Neg	Neg	Neg

For the hexa-brominated BDE-153 no significant trends were observed for human milk, and in herring muscle from several of the sampling sites (Table 12). However, for guillemot eggs (-4.0%) and herring muscle from the Swedish west coast (Fladen and Väderöarna) declining trends have been observed since the late 1990s (-5.2% to -5.5%) (Table 12). The other hexa-brominated congener BDE-154 showed a similar pattern. Temporal trends of the fully-brominated BDE-209 were only investigated in human milk, and a negative trend was

observed in Stockholm (2010-2014), but not in Uppsala (2009-2016) and Göteborg (2011-2015). The short study periods makes the results uncertain (Table 13).

For HBCDD declining trends were observed for human milk from Uppsala and Stockholm (-4.8% to -5.9%), and for herring muscle from Utlängan, south of Gotland, and on the Swedish west coast (-5.4% to -8.3%) (Table 12).

Table 14. Statistically significant change-points (CPs) in time-series of PBDE congeners and HBCDD in different matrices from the Swedish environment. The year in cells gives the year of the CP. Green cells show decreasing trends before the CP and suggested faster decreasing trend after the CP, as determined visually. Orange cells show increasing trends before CP and decreasing trends afterwards. Red cells show decreasing trends before CP and thereafter suggested slower decreasing trends. Cells with a year but with no color show time series for which it was not possible to visually determine how the trend have changed after the CP. Empty cells show time series with no significant CPs (p>0.05). NA= not analyzed. HU= human milk Uppsala, HS=human milk Stockholm, GE=guillemot eggs, C1=herring muscle Harufjärden, C2=herring muscle Ängskärsklubb, C3=herring muscle Landsort, C4=herring muscle Utlängan, C6=herring muscle Fladen, C7=herring muscle Väderöarna. Year in time series given in the heading of each column.

Substance	HU 96-16 02-16[1]	HS 84-14 07-14[1]	GE 69-16 00-16[1]	C1 99-16	C2 80-15	C3 99-16	C4 99-16	C6 99-16	C7 99-16
BDE-47	2006	1994	1983		1989			2007	2003
BDE-99		1994	1982		1990			2007	2007
BDE-100	2003	1992	1985		1989	2002		2007	2010
BDE-153	2003	NA	2003[1]		2003			2004	2004
BDE-154	NA	2004	NA		1989			2004	2008
HBCDD	[1]	2002	1985		1999				

When looking at the CP analyses it is obvious that the temporal trends for some BDEs have changed dramatically during the study period (Table 12 and 14). For BDE-28 the study period was too short for CP analyses, but for the tetra-hexa-brominated congeners BDE-47, -99 and -100 in the longest human milk series from Stockholm (1984-2014) CPs were observed 1992-94 with increasing levels before the CPs and declining levels thereafter (Table 14). For human milk from Uppsala, with a time series starting a few years after the CPs in the Stockholm series, BDE-47, -99 and -100 declined during the whole study period (Table 13). CPs for BDE-47 and -100 were observed 2003-2006, with a tendency of a faster decline after the CP (Table 12 and 14, Appendix 4).

In guillemot eggs the CPs for BDE-47, -99 and -100 occurred about 10 years earlier (1983-1985) than in human milk from Stockholm, going from increasing levels to decreasing levels (Table 14). The only herring time-series that covers the same period as the Stockholm human milk and guillemot eggs series was the Ängskärsklubb series. The CPs for BDE-47, -99 and -100 in herring muscle occurred somewhat later (end of 1980s) than in the guillemot eggs, but earlier than in the human milk series (Table 14). For the other sampling sites of herring muscle a CP for BDE-100 was observed 2002 at Landsort with a slower decrease after the CP (Table 14, Appendix 4). CPs 2003-2010, with slower or no declines thereafter, were also observed for BDE-47, -99 and -100 in herring muscle from Fladen and Väderöarna on the Swedish west coast (Table 14, Appendix 4).

For BDE-153, the only series long enough to cover the 1980s was the herring muscle series from Ängskärsklubb, and a significant CP was observed 2003 (Table 14). When looking closer at the changes in concentrations between 1980 and 2015 (Appendix 4), BDE-153 concentrations appeared to, similarly as for BDE-47, -99 and -100, increase to a maximum around 1990 and thereafter decline rapidly Table 14). However, in contrast to BDE-47-, -99 and -99, the levels of BDE-153 seemed to increase again in the beginning of the 2000s (Appendix 4). Similarly, significant CPs were observed 2004 with a decrease changing into an increase on the Swedish west coast (Table 12 and 14, Appendix 4). In human milk from Uppsala (1996-2017) and in guillemot eggs (2000-2016), an increasing trend was evident until 2003-2004 when the levels started decreasing (Table 12 and 14).

The other hexabrominated congener, BDE-154, in herring muscle from Ängskärsklubb (1980-2015) showed a CP in 1989 (Table 14). When looking closer at the changes in concentrations, a peak in concentrations occurred around 1990, with a decrease thereafter that leveled off around year 2000 (Appendix 4). This pattern is similar as for BDE-153 at the same sampling site. As with BDE-153, at Fladen and Väderöarna CPs were observed 2004-2008 going from decreasing to increasing levels (Table 14, Appendix 4). The series for BDE-154 in human milk from Stockholm covered the 1980s, and a CP was detected 2004 with an increasing trend before and a decreasing trend after the CP (Table 14, Appendix 4). No time series was available for BDE-154 in human milk from Uppsala and in guillemot eggs.

When looking at HBCDD, in human milk from Stockholm (1984-2014), guillemot eggs (1969-2016) and herring muscle from Ängskärsklubb (1980-2015), CPs were observed 2002, 1985 and 1999, respectively (Table 14). An increase was changed to a decrease in human milk and herring muscle, whereas the change pattern was difficult to visually interpret in guillemot eggs (Appendix 4).

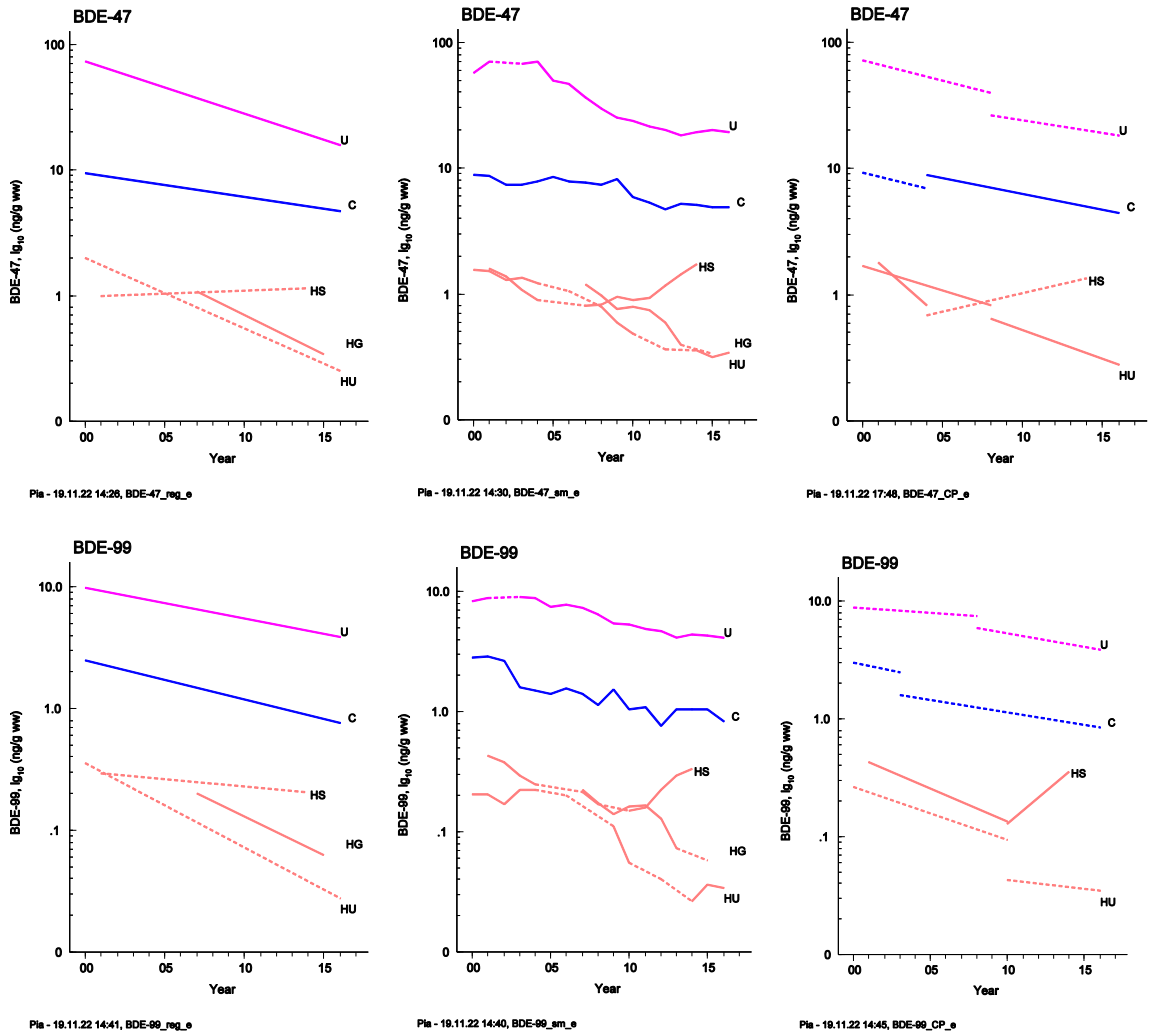


Figure 6. Left figures: log-linear regression lines for temporal trends of BDE-47 and BDE-99 in different matrices sampled in Sweden from year 2000 and later. Middle figures: smoothed lines. Right figures: log-linear regression lines with change point (CP). Dashed lines have non-significant slopes. U= guillemont eggs from Stora Karlsö (south Baltic Sea Proper), C=herring muscle Utlängan (south Baltic Sea Proper, autumn), HU=human milk Uppsala, HS=human milk Stockholm, HG=human milk Göteborg,

In the analyses of temporal trends from year 2000 and onwards, patterns for BDE-47 and BDE-99 were similar (Fig. 6). Declining trends were suggested for human milk from Uppsala and Göteborg, guillemot eggs from Stora Karlsö and herring from Utlängan, although not statistically significant in some cases. In human milk from Stockholm a CP was indicated in 2004-2010 going from declining levels to increasing levels (Fig. 6).

Similarly as for BDE-47 and BDE-99, declining trends of BDE-153 were suggested for human milk from Uppsala and Stockholm, guillemot eggs and herring muscle from year 2000 and onwards (Fig. 7), although only significant for guillemot eggs. CPs were suggested for guillemot eggs and herring muscle in the beginning of the study period, with opposite

directions in trends before and after CP. A CP was also observed for human milk from Uppsala in 2006 with a similar trend pattern as guillemot eggs (increase/decrease) (Fig. 7).

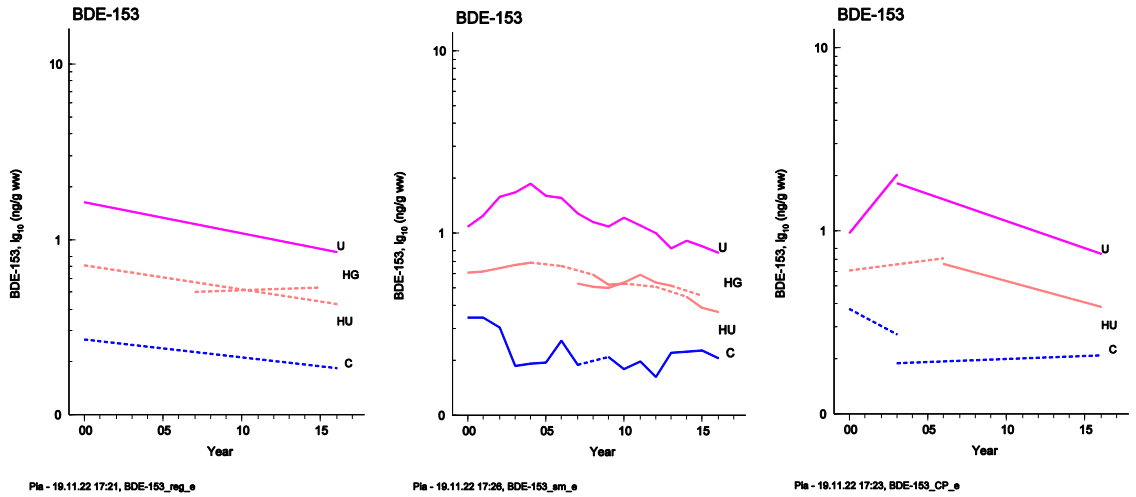


Figure 7. Left figures: log-linear regression lines for temporal trends of BDE-153 in different matrices sampled in Sweden from year 2000 and later. Middle figures: smoothed lines. Right figures: log-linear regression lines with change point. Dashed lines have non-significant slopes. U= guillemont eggs from Stora Karlsö (south Baltic Sea Proper), C=herring muscle Utlängan (south Baltic Sea Proper, autumn), HU=human milk Uppsala, HG=human milk Göteborg,

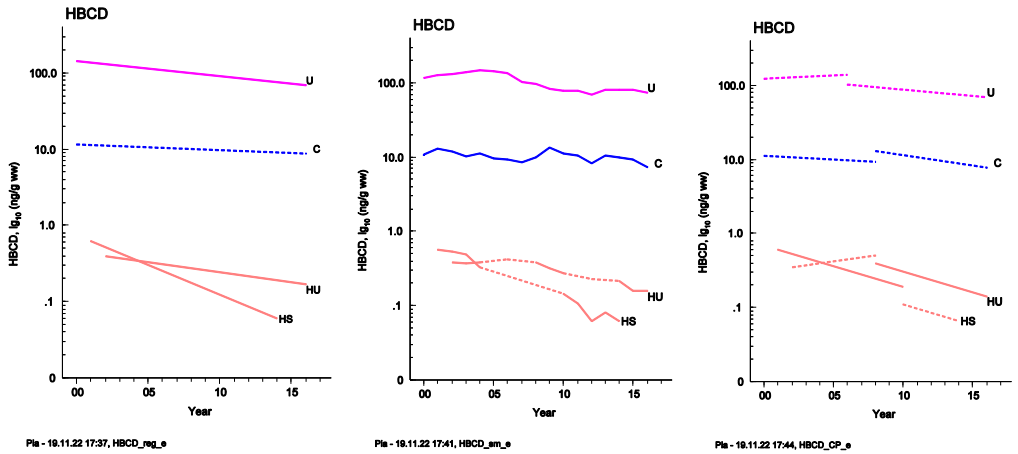


Figure 8. Left figures: log-linear regression lines for temporal trends of HBCDD in different matrices sampled in Sweden from year 2000 and later. Middle figures: smoothed lines. Right figures: log-linear regression lines with change point (CP). Dashed lines have non-significant slopes. U= guillemont eggs from Stora Karlsö (south Baltic Sea Proper), C=herring muscle Utlängan south (Baltic Sea Proper, autumn), HU=human milk Uppsala, HS=human milk Stockholm.

Declining trends of HBCDD were observed from year 2000 and onwards in guillemot eggs, and human milk from Uppsala and Stockholm (Fig. 7). No significant trend was obvious for herring muscle from Utlängan. CPs were suggested for all matrices 2006-2010, with a similar pattern of a somewhat faster decline indicated after the CPs (Fig. 7)

Table 15. Actions against PBDE and HBCDD pollution in Sweden and internationally.

Year		National/ International	Comment	Reference
1981	Sweden		First discovery of PDEs in fish	[71]
1989-1990	Germany	National	Voluntary phase-out of PBDE production and use of the plastics industry	[72]
	Sweden	National	The Government states that the most toxic BFRs should be phased out	[73]
1991-1995	TCO certification	National/International	Environmental certification of plastics in computer monitors. No BFRs	[74]
	Esbjerg Declaration	International	Decision on actions to replace BFR with less toxic flame retardants	[75]
	OECD	International	Voluntary actions of the bromine industry to limit production of BFRs	[75]
1996- 2000	Sweden	National	National organization for IT companies develops environmental certification including BFRs	[75]
	Sweden	National	Government states: important for the governmental agencies to inform companies on the Swedish market about the need to reduce BFR use.	[76]
	OSPAR	International	Strategy on toxic substances. BFR on OSPAR List of Chemicals of Chemicals for Priority Action	[75]
	Sweden		Report by Norén et al.showing exponential increases in PBDE levels in human milk from Stockholm.	[77]
	Sweden	National	The Chemicals Agency proposes ban of PBDE in certain products	[78]
2001-2005	EU	International	PentaPBDE classified as priority toxic substances in the Water Directive	[79]
	EU	International	WEEE-directive. Plastic containing BFR separated from the plastic fraction before recycling	[75]
	USA	International	Closure of the only penta-octaBDE production plant	[80]
	Great Britain	International	Closure of HBCDD production plant	[81]
	EU	International	Ban of use of penta- and octaPBDE	[75]
2006-2010	EU	International	RoHS Directive. Ban of PBDE in new electric/electronic equipment	[75]
	EU	International	Environmental quality standard - PBDE	[82]
	EU	International	HBCDD on the candidate list of toxic substances	[83]
	EU	International	HBCDD on the authorization list	[84]
	Stockholm Convention	International	Tetra-, penta-, hexa- and heptaBDE elimination of production and use	
	UNECE	International	Limiting emissions of penta- and octaBDE to air	[64]
2011-2017	Stockholm Convention	International	Elimination of production and use of HBCDD	[85]
	EU	International	HBCDD in POPs regulation	[86]
	Stockholm Convention	International	DecaBDE elimination of production and use	[27]

Actions against PBDE and HBCDD pollution nationally and internationally

In 1981, Östen Andersson and Gun Blomkvist identified PBDEs in fish samples from Viskan/Klosterfjorden on the Swedish west coast.[71] In 1998, Koidu Norén et al. presented exponential increases in levels of tri-hexa-brominated BDEs between 1972 and 1997 in human milk from Stockholm.[77] During this period no legislation to mitigate PBDE pollution had been passed in Sweden or within the EU, but voluntary measures to initiate phase-out of production and use of the most toxic PBDEs had started already in the late 1980s/early 1990s (Table 15). Not until the beginning of the 2000s, EU regulation was in place banning certain uses of penta- and octaPBDE technical mixtures. During this time period BFR-producing facilities were closed in both EU and USA. Later, more uses of these BFRs was banned within EU, and regulation about PBDE-containing waste was introduced (Table 15). HBCDD was introduced on the EU candidate and authorization lists in the late 2000s. In 2009 tetra-heptaPBDEs were included in the Stockholm Convention, and in 2017 decaBDE (Table 15). HBCDD was included in 2013.

Table 16. Temporal trends of PFCAs in different matrices sampled in Sweden. Human serum trend from Uppsala adjusted for participant´s age, pre-pregnancy BMI, weight gain during pregnancy, weight loss after pregnancy and education. PFASs were measured in herring liver. N=number of measured samples included. Trend=annual change in levels (mean (95% confidence interval)). Only statistically significant trends are reported (p≤0.05). CP=change point year for which a change in the slope has been detected (only given for statistically significant CPs (p≤0.05)). CP change=visually determined change in trend after CP. Increase/decrease= increase in levels before CP and decrease after. Increase/plateau=increase in levels before CP and no visible decreasing or increasing trend thereafter. Slower increase=increase before CP slowing down after CP. Empty cell=not possible to determine visually.

Matrix	N	Years	Trend (% per year)	CP	P-value	CP change
PFOA						
Serum, Uppsala	619	1996-2016	-4.1 (-4.6, -3.6)	2004	0.036	Increase/decrease
Serum (pooled), Uppsala	48	1996-2016	-3.3 (-4.0, -2.6)	2002	0.0077	Increase/decrease
Human milk, Stockholm	50	1972-2016		2000	<0.001	Increase/decrease
Human milk, Göteborg	27	2007-2015				
Guillemot egg	14	2003-2016	-7.6 (-13, -2.2)			
Herring, Harufjärden	19	2006-2016	-11 (-16, -5.7)			
Herring, Ängskärsklubb	32	1980-2015	2.9 (0.56, 4.2)			
Herring, Landsort	33	1980-2016	5.9 (3.6, 8.1)			
Herring, Utlängan	35	1980-2016	8.6 (6.8, 11)			
Herring, Fladen	22	2005-2016				
Herring, Väderöarna	22	2004-2016	-9.8 (-15, -3.8)			
PFNA						
Serum, Uppsala	616	1996-2016	2.1 (1.5, 2.7)			
Serum (pooled), Uppsala	48	1996-2016	2.7 (1.8, 3.6)	2007	<0.001	Increase/decrease
Human milk, Stockholm	50	1972-2016	3.1 (1.6, 4.6)	2010	0.0065	Increase/decrease
Human milk, Göteborg	27	2007-2016				
Guillemot egg	22	1973-2016	8.4 (7.2, 9.7)			
Herring, Harufjärden	22	2005-2016				
Herring, Ängskärsklubb	33	1980-2015	7.6 (5.3, 10)			
Herring, Landsort	33	1980-2016	6.8 (4.9, 8.7)	1998	<0.001	Increase/plateau
Herring, Utlängan	35	1980-2016	8.6 (6.8, 11)			
Herring, Fladen	22	2005-2016				
Herring, Väderöarna	22	2004-2016				
PFUnNA						
Serum, Uppsala	620	1996-2016	3.7 (2.8, 4.7)	2001	<0.001	Increase/plateau
Serum (pooled), Uppsala	48	1996-2016	3.4 (2.5, 4.4)	2004	0.038	Slower increase
Human milk, Stockholm	50	1972-2016	3.1 (1.6, 4.6)	1984	<0.001	Increase/plateau
Human milk, Göteborg	27	2007-2016				
Guillemot egg	22	1973-2016	11 (8.1, 13)	2007	>0.001	Increase/decrease
Herring, Harufjärden	22	2005-2016	-5.6 (-9.4, -1.7)			
Herring, Ängskärsklubb	33	1980-2015	7.8 (5.9, 9.7)	2005	0.017	Increase/decrease
Herring, Landsort	33	1980-2016	7.5 (5.9, 9.1)	2006	0.001	Increase/decrease
Herring, Utlängan	35	1980-2016	6.1 (4.7, 7.8)	2006	<0.001	Increase/decrease
Herring, Fladen	22	2005-2016				
Herring, Väderöarna	22	2004-2016	-7.7 (-12, -2.7)			

PFASs

Declining log-linear trends of PFOA were observed for blood serum from Uppsala (1996-2016) (Table 16). No significant trend was observed for the longest series using human milk from Stockholm (1972-2016) and the shortest series of human milk from Göteborg (2007-2015). Two time series of human serum from Uppsala were available, based on the same samples, one with measurements of individual samples and one using pooled samples (Table 16). In this case, PFOA decreased with 3.3-4.1% per year. Similarly as in the human time series from Uppsala, a decreasing PFOA trend was observed for guillemot eggs in the relatively short time series between 2003 and 2016 (-7.6% per year), and in herring liver from Harufjärden (-11% per year) in 2006-2016 and Väderöarna (-9.8% per year) in 2004-2016 (Table 16). For the longer series of herring liver, starting 1980, increasing log-linear trends were seen with annual increases ranging from 2.9% to 8.6% (Table 16).

In serum from Uppsala and human milk from Stockholm similar increasing log-linear trends (2.1-3.1% per year) of PFNA were observed, although the time series from Stockholm was more than 20 years longer (Table 16). No significant trend was observed in the shortest time series of human milk from Göteborg. In guillemot eggs PFNA levels increased with 8.4% per year during the period 2003-16 (Table 16). The short time series of herring liver did not show any significant log-linear trends, whereas the longer time series showed increasing trends with average annual changes of 6.8% to 8.6% (Table 16).

PFUnDA increased in human serum from Uppsala, 1996-2016, (3.4% and 3.7% per year) and in human milk from Stockholm, 1972-2016, (3.1% per year). No significant trend was observed in the shortest time series from Göteborg (Table 16). Guillemot eggs showed an average 11% per year increase between 1973 and 2016, and herring liver an increase of 6.1%-7.8% between 1980 and 2016. In the shorter herring time series decreasing levels were observed at Harufjärden (-5.6% per year) and Väderöarna (-7.7% per year) (Table 16).

Table 17. Temporal trends of PFASs in different matrices from the Swedish environment. Human serum trend from Uppsala (SU) adjusted for participant´s age, pre-pregnancy BMI, weight gain during pregnancy, weight loss after pregnancy and education. Green (Neg) cells are statistically significant declining trends. Red (Pos) show significant increasing trends. Empty red cells show time series with no statistically significant trend. NA= not analyzed. SU= human serum individual samples Uppsala, SUP=human serum Uppsala, pooled samples, HS=human milk Stockholm, HG=human milk Göteborg, GE=guillemot eggs, C1=herring liver Harufjärden, C2=herring liver Ängskärsklubb, C3=herring liver Landsort, C4=herring liver Utlängan, C6=herring liver Fladen, C7=herring liver Väderöarna. Year in time series given in the heading of each column.

PFAS homologue	SU 96-16	SUP 97-16	HS 72-16	HG 07-15	GE 73-16 08-16[1] 03-14[2]	C1 05/06-16	C2 80-14/15	C3 80-16	C4 80-16	C6 05-16	C7 04-16
PFHxS	Pos	Pos		Neg	Pos			Pos	Pos		
PFOS	Neg	Neg			Pos		Pos	Pos	Pos	Neg	
PFHpA	NA	NA	NA	NA	Neg[1]	Neg	Neg	Pos	Pos	Neg	Neg
PFOA	Neg	Neg		Neg	Neg[2]	Neg	Pos	Pos	Pos		Neg
PFNA	Pos	Pos			Pos		Pos	Pos	Pos		
PFDA	Pos	Pos	Pos		Pos		Pos	Pos	Pos	Neg	
PFUnDA	Pos	Pos	Pos		Pos	Neg	Pos	Pos	Pos		Neg
PFDoDA	NA	Pos		Neg	Pos	Neg	Pos	Pos	Pos		
PFTrDA	NA		Pos		Pos		Pos	Pos	Pos		

For the other PFCAs, PFDA showed increasing log-linear trends in several of the matrices with time series of spanning over 2 decades or more (Table 17). For shorter time series no significant trends were observed except for a decreasing trend in herring liver from Landsort. Similarly, increasing log-linear trends of PFDoDA and PFTrDA were observed in Uppsala pooled serum (PFDoDA), Stockholm human milk (PFTrDA), guillemot eggs and herring liver (in the long series) (Table 17). Negative trends of PFDoDA were observed in human milk from Göteborg 2007-2015, and in herring liver from Harufjärden 2005-2016.

Among the PFSAs, PFHxS showed increasing log-linear trends in human serum from Uppsala 1996-2016 (3.6-5.3% per year) and in human milk from Stockholm 1972-2016 (3.1% per year) (Table 18). No trend was observed for human milk from Göteborg 2007-2016. Also in guillemot eggs PFHxS concentrations increased on average 4% per year between 1973 and 2016 (Table 18), and in herring liver from Landsort and Utlängan (1980-2016) the increase was 1.8-1.9% per year (Table 18). No significant trend was obvious in the other four herring time series.

Table 18. Temporal trends of PFSAs in different matrices sampled in Sweden. Human serum trend from Uppsala adjusted for participant´s age, pre-pregnancy BMI, weight gain during pregnancy, weight loss after pregnancy and education. N=number of measured samples included. Trend=annual change in levels (mean (95% confidence interval)). Only statistically significant trends are reported (p≤0.05). CP=change point year for which a change in the slope has been detected (only given for statistically significant CPs (p≤0.05)). CP change=visually determined change in trend after CP. Increase/decrease= increase in levels before CP and decrease after. Plateau/decrease=no visible trend before CP and decreasing levels thereafter. Faster decrease=decreasing levels before CP becoming faster after. Slower decrease=decreasing levels before CP slowing down after. Increase/plateau=increasing levels before CP with increase plateauing after. Empty cell=not possible to determine visually.

Matrix	N	Years	Trend (% per year)	CP	P-value	CP change
PFHxS						
Serum, Uppsala	615	1996-2016	3.6 (2.6, 4.6)	2008	0.025	Increase/decrease
Serum (pooled), Uppsala	48	1996-2016	5.3 (3.6, 6.9)	2009	0.004	Increase/decrease
Human milk, Stockholm	50	1972-2016	3.1 (1.6, 4.6)	2004	<0.001	Increase/decrease
Human milk, Göteborg	27	2007-2016				
Guillemot egg	22	1973-2016	4.0 (1.5, 6.5)	2006	>0.001	Increase/decrease
Herring, Harufjärden	22	2005-2016				
Herring, Ängskärsklubb	33	1980-2015				
Herring, Landsort	33	1980-2016	1.9 (0.55, 3.2)			
Herring, Utlängan	35	1980-2016	1.8 (0.40, 3.2)			
Herring, Fladen	22	2005-2016				
Herring, Väderöarna	22	2004-2016				
PFOS						
Serum, Uppsala	617	1996-2016	-8.6 (-9.1, -8.0)	2004	<0.001	Plateau/decrease
Serum (pooled), Uppsala	48	1996-2016	-8.1 (-8.8, -7.4)	2002	0.005	Faster decrease
Human milk, Stockholm	50	1972-2016	-1.8 (-3.3, -0.28)	1988	<0.001	Increase/decrease
Human milk, Göteborg	27	2007-2016	-10 (-19, -0.43)			
Guillemot egg	22	1973-2016	4.3 (2.0, 6.7)	1997	>0.001	Increase/decrease
Herring, Harufjärden	22	2005-2016	-4.2 (-8.0, -0.22)			
Herring, Ängskärsklubb	33	1980-2016	5.8 (4.2, 7.5)			
Herring, Landsort	33	1980-2016	6.6 (6.1, 8.1)	2000	<0.001	Slower increase
Herring, Utlängan	35	1980-2016	3.6 (2.6, 4.8)	1994	<0.001	Increase/plateau
Herring, Fladen	22	2005-2016	-8.7 (-12, -4.9)			
Herring, Väderöarna	22	2004-2016				

Decreasing log-linear trends of PFOS were seen in all human matrices, with the slowest average decline for the longest time series from Stockholm (1972-2016, -1.8% per year) and the fastest decline in the shortest series from Göteborg (2007-2016, -10%) (Table 18). In guillemot eggs PFHxS increased on average 4.3% per year from 1973 to 2016. In herring liver an increasing trend was seen in the longest time series (1980-2016), whereas a decline was observed in two of the shorter series 2005-2016 (-4.2% and -8.7%) (Table 18).

Table 19. Statistically significant change-points (CPs) in time-series of PFASs in different matrices from the Swedish environment. The year in cells gives the year of the CP. Green cells show CPs with increases going to suggested decreases. Orange cells show increases that are plateauing after the CPs, and yellow cells show un-changed levels or very slow decreasing levels going to clearly decreasing levels. Empty cells show time series with no significant CPs (p>0.05). NA= not analyzed. SU= human serum individual samples Uppsala, SUP=human serum pooled samples Uppsala, HS=human milk Stockholm, GE=guillemot eggs, C1=herring liver Harufjärden, C2=herring liver Ängskärsklubb, C3=herring liver Landsort, C4=herring liver Utlängan, C6=herring liver Fladen, C7=herring liver Väderöarna. Years in time series given in the heading of each column.

Substance	SU 96-16	SUP 96-16	HS 72-16	GE 73-16 03-16[1]	C1 05/06-16	C2 80-15	C3 80-16	C4 80-16	C6 05-16	C7 04-16
PFOA	2004	2002	2000	NA[1]						
PFNA		2007	2010				1996			
PFDA		2004		2004		2005	2004	2008		
PFUnDA	2000	2001	1984	2007		2005	2006	2006		
PFDoDA	NA	2009	NA	2008		2006	2006	2004		
PFTrDA	NA			2009				2010		
PFHxS	2008	2009	2004	2006	2009					
PFOS	2004	2002	1988	1997			2000	1994		

PFOA showed CPs 2000-2004 in human matrices with increasing levels before the CPs and decreasing levels after the CPs (Table 16 and 19). No CPs were detected in herring liver. For PFNA similar CPs as for PFOA were observed 2007-2010 in human matrices. In herring liver from Landsort, the levels seemed to reach a plateau in 1996. For PFDA, PFUnDA and PFDoDA similar patterns were observed in human and guillemot matrices, with CPs 2004-2009, but levels seemed to reach a plateau instead of decreasing after the CPs in the human matrices. For PFTrDA a CP was observed in 2009 in guillemot eggs, with increasing levels up to the CP and decreasing thereafter, and in herring liver at Utlängan with an increase plateauing in 2010 (Table 19, Appendix 5). For PFHxS levels increased in human and guillemot egg matrices until 2004-2006, and decreased thereafter (Table 19, Appendix 5). In Harufjärden a CP was observed in 2009 going from increasing to decreasing levels. PFOS levels increased in human and guillemot matrices before the CPs detected in 1988-2002, and decreased thereafter. In herring liver a CP was observed with increases plateauing in the period 1994-2000 in two of the longest time series (Table 19, Appendix 5).

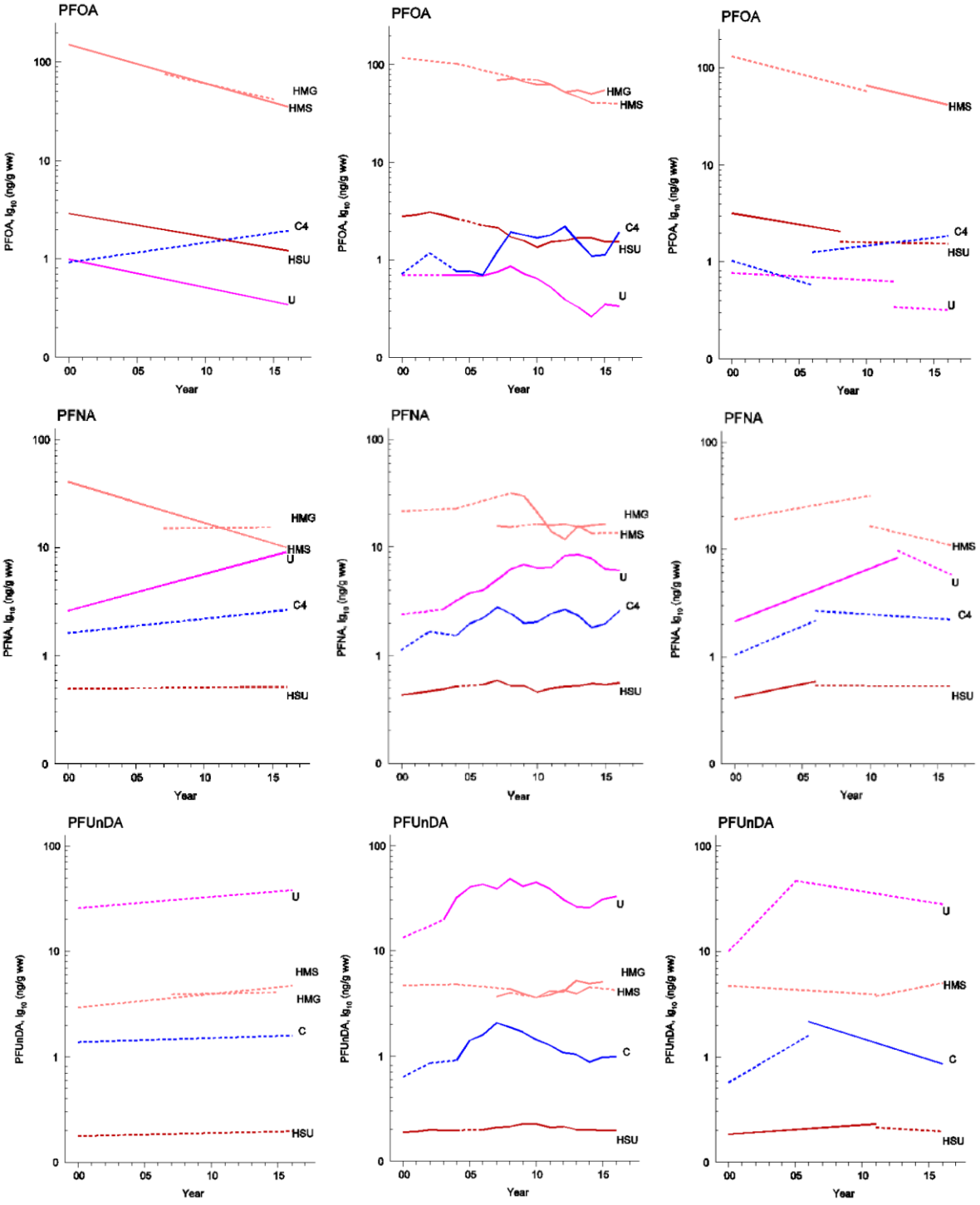


Figure 9. Left figures: log-linear regression lines for temporal trends of PFOA, PFNA and PFUnDA in different matrices sampled in Sweden from year 2000 and later. Middle figures: smoothed lines. Right figures: log-linear regression lines with change point (CP). Dashed lines have non-significant slopes. U= guillemont eggs from Stora Karlsö (south Baltic Proper), C=herring liver Utlängan (south Baltic Sea Proper, autumn), HMS=human milk Stockholm, HMG=human milk Göteborg, HSU=human serum Uppsala. HMS and HMG: pg/g wet weight.

In the period at the end of the time series, from year 2000, decreasing trends of PFOA were observed for human milk from Stockholm, serum from Uppsala and in guillemot eggs, whereas in herring liver from Utlängan no significant trend was observed. No consistent CP pattern was seen (Fig. 8). In human milk from Stockholm PFNA concentrations decreased significantly, whereas no trends could be seen for the other human matrices. PFNA increased in guillemot eggs but not in herring liver from Utlängan (Fig. 8). CPs were observed for all matrices with indicated increases before and decreases after. PFUnDA did not change significantly in any of the studied matrices from year 2000, although a significant decrease was observed in herring liver after a CP in 2007 (Fig. 8).

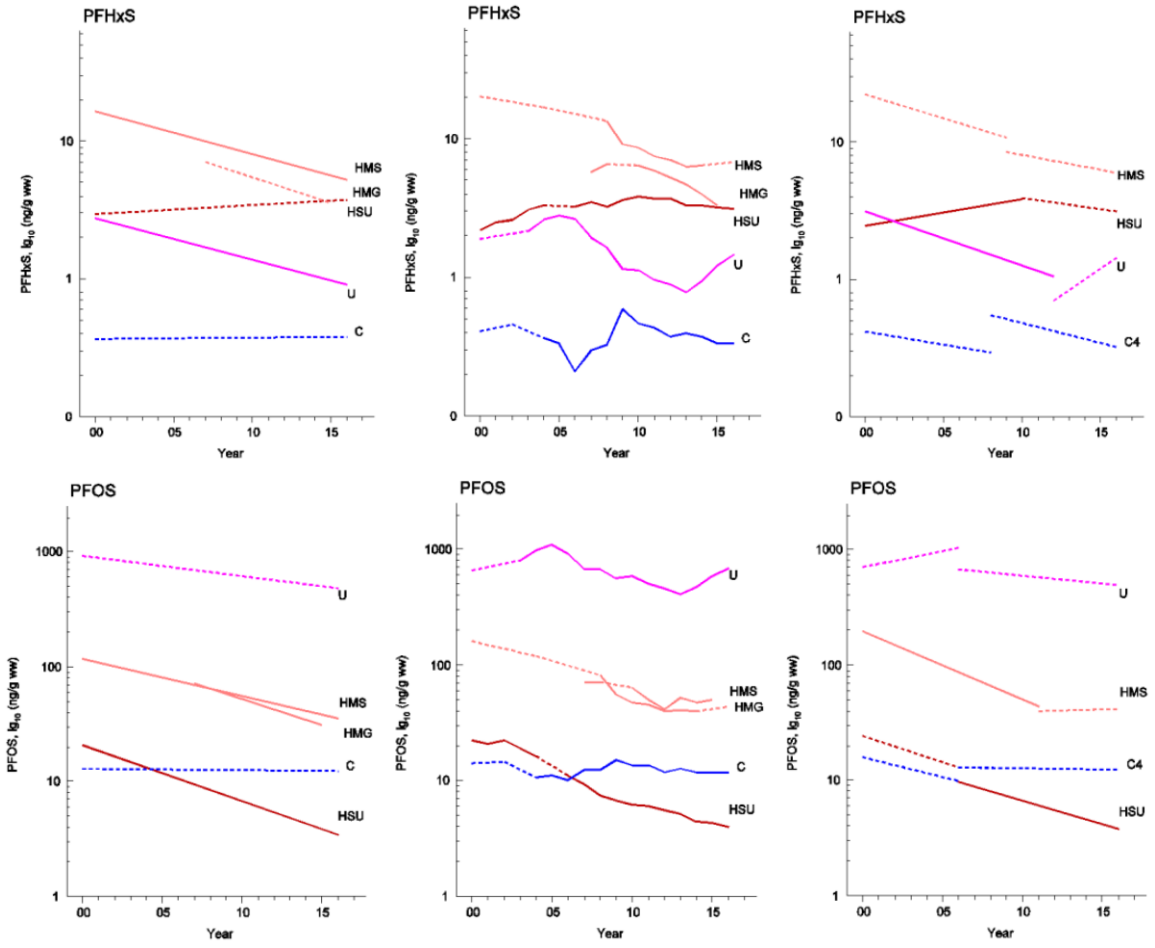


Figure 10. Left figures: log-linear regression lines for temporal trends of PFHxS and PFOS in different matrices sampled in Sweden from year 2000 and later. Middle figures: smoothed lines. Right figures: log-linear regression lines with change point. Dashed lines have non-significant slopes. U= guillemont eggs from Stora Karlsö (south Baltic Sea Proper), C=herring liver Utlängan (south Baltic Sea Proper, autumn), HMS=human milk Stockholm, HMG=human milk Göteborg, HSU=human serum Uppsala. HMS and HMG: pg/g wet weight.

PFHxS declined from year 2000 and onwards in human milk from Stockholm and in guillemot eggs, but no significant trends were apparent for the other matrices (Fig. 10). No consistent CPs in trends were observed. PFOS decreased in all human matrices, but no significant trends were observed in guillemot eggs and herring liver. No consistent CPs could be seen in guillemot eggs and herring liver, whereas the decline in human milk levelled off in 2011, but not in serum (Fig. 10).

Table 20. Actions against PFAS pollution in Sweden and internationally.

Year		National/ International	Comment	Reference
2000	US EPA/3M	International	Phase-out of production and use of PFHxS/PFOS/PFOA and related substances	[87, 88]
2001-2005	EU	International	PFOS nominated to the Stockholm convention by Sweden	[89]
	EU	International	Limitation of PFOS in goods/products in Reach	[86]
2006-2010	US EPA	International	PFOA Stewardship program – Main manufacturers agree on phasing out PFOA to 2015	[90]
	Sweden	National	Proposed environmental quality standards for PFOS	[91]
	EU	International	Ban of use of PFOS and related compounds in the POPs Directive	[86]
	Stockholm Convention	International	PFOS included in Annex B. Restrictions of use	[27]
	UNECE	International	Limiting emissions of PFOS to air	[64]
2011-2019	US FDA	International	Voluntary agreements with the industry to remove certain long-chain PFASs (≥C8) from food contact applications	[92]
	Sweden	National	Swedavia allows use of fluorine-free fire-fighting foams	[93]
	Sweden	National	Discovery of PFAS contamination of drinking water in Tullinge, Uppsala, Halmstad and Ronneby	[94]
	EU	International	Environmental quality standards for PFOS	[95]
	Sweden	National	Information to drinking water producers about risk analysis of PFAS polluting of raw water	[96]
	EU	International	PFOA and APFO harmonised classification under Reg. (EC) No. 1272/2008 (2013); Classification, labelling, packaging of dangerous substances and mixtures	[97]
	Sweden	National	Drinking water guideline values for PFAS	[98]
	Sweden	National	Preliminary guideline values for soil and groundwater - PFOS	[99]
	US FDA	International	FDA revokes approval of long-chain PFASs (≥C8) in FCM	[100]
	Sweden	National	Update of drinking water guideline values for PFAS	[98]
	EU	International	PFDA on the candidate list of toxic substances	[101]
	Stockholm Convention	International	PFOA included in Annex A. Elimination of production and use	[27]

Actions against PFAS pollution nationally and internationally

In 2000, the Environmental Protection Agency in the USA (US EPA) and 3M jointly announced that 3M´s production of PFOS and related compounds would be phased out (Table 20). Soon thereafter, the Swedish authorities started working on the issue, with the Swedish Chemicals Agency as the principal authority, leading to the Swedish nomination of PFOS to the Stockholm Convention in 2005. In 2004 the first regulation within the EU was initiated with restriction of PFOS in products, and in 2008 PFOS was included in the EU POPs regulation banning the use of PFOS and related substances in products (Table 20). In 2009 PFOS was included in the Stockholm Convention. During this initial period the US

EPA agreed with the main North American manufacturers of PFOA that phase-out of production and use would start and be completed 2015. Moreover, the PFAS industry in North America agreed with the Food and Drug Administration in the USA (US FDA) in 2011 to voluntarily remove certain long-chain PFASs from food contact applications. The same year Swedavia, which owns, operates, and develops a network of Swedish airports, gave permission for use of PFAS-free fire-fighting foam at its airports. In 2011, highly PFAS-contaminated drinking water was discovered in Tullinge, south of Stockholm (Table 20). This was followed by Uppsala and in 2013 Ronneby, in the latter case drinking water with PFOS and PFHxS concentrations higher than 1000 ng/L. In Halmstad, high PFAS levels in groundwater were reported to county officials already in 2009, but the drinking water producer did not get the information until 2012.[94] The reported PFAS concentrations in drinking water in Halmstad were similar as those reported from Tullinge and Uppsala.[102] These incidents prompted the SNFA to issue drinking water guide-line values in 2014 for the 7 most commonly found PFASs in drinking water, with an update in 2016 now including 11 PFASs. In 2016 the long-chain PFDA was included in the Reach candidate list and in 2019 PFOA was included in the Stockholm Convention (Table 20).

Discussion

The analyses of temporal trends in human matrices, guillemot eggs and herring muscle included POPs for which risk reducing activities started in the 1970s (PCBs, PCDD/Fs, HCB), in the 1980s (PBDEs) and in the 2000s (PFAS). Thanks to the storage of human milk samples from Stockholm, guillemot eggs (Stora Karlsö, Gotland, south Baltic Sea Proper), and herring (Ängskärsklubb, south Bothnian Sea), in the freezers at the Swedish Museum of Natural History, it has been possible to create time series starting already in the 1970s for all studied POPs, thus enabling follow-up of effects of actions taken against pollution. Moreover, the time series of human milk from Uppsala, starting 1996 and from Göteborg starting 2007 have made it possible to get detailed knowledge about national trends of POPs in human milk during the last 2 decades. Finally, the shorter time series of herring muscle from other sites than Ängskärsklubb in the Baltic gives information about both possible local/regional differences in temporal trends and more general patterns for the whole Baltic Sea area. For PCBs, PCDD/Fs and HCB risk reducing actions influencing production/use and emissions were initiated during the same time period as the temporal trend studies were initiated, making it difficult to evaluate trends before risk reducing actions were initiated. For PBDEs, HBCDD and PFASs it have in some time series of human and biota samples been possible to investigate the temporal trends before the risk-reducing actions were initiated.

PCBs

When looking at the temporal trends of PCBs in the longest time series, human milk from Stockholm, guillemot eggs (Stora Karlsö) from the south Baltic Proper, and herring muscle (Ängskärsklubb) from the south Bothnian Sea, it is obvious that the environmental pollution of both ndl- and dl-PCBs have decreased substantially since the late 1970s-early 1980s. In human milk and guillemot eggs average concentrations have decreased about 10-fold since the 1970s. This shows that the actions against PCB pollution initiated in the 1970s have been successful in limiting PCB pollution of the Swedish environment. The high persistence of PCBs in the environment and the long half-lives in humans have, however, caused a “delay” in improvement of pollution, i.e. although production and use of PCBs have been more or less abolished world-wide the environmental load of PCB still lingers and have decreased at a relatively slow rate (on average about 7% per year) in human milk and guillemot eggs since the 1970s. The first national/international actions restricting production and use of PCBs during the 1970s was followed by a steady decline in levels of several PCB congeners in all

studied matrices. As new national/international actions were initiated during the 1980s, the decline in PCB levels continued. The pathways of contamination differ substantially between humans, and the biota from the Baltic Sea area. The similarities in rates of decline of PCBs in the different long-term matrices show that the measures taken had a general impact on all potential pathways of PCB contamination of the human and Baltic Sea environment. The inclusion of PCBs in the Stockholm convention in 2004 was a milestone, securing the ban of PCB production and new use globally. However, it occurred many decades after national and regional regulation was initiated, but the convention is an instrument for continuous efforts to reduce PCB pollution in the future.

The rate of decline in PCB levels in human milk did not appear to slow down towards the end of the study period, showing that actions against PCB pollution still were effective to result in a steady decline. The positive effects of international efforts to eliminate PCB pollution of the human environment for decades is further illustrated by an almost 7-fold decrease in average total PCB levels in human milk from Germany 1984-2003, and a 6-fold decrease of total PCB in milk from Croatia 1981-2003.[103, 104]

In contrast to human milk, a slower relative rate of decline (% per year) was suggested for several PCB congeners in guillemot eggs during the last two decades. As for guillemot eggs the rate of decline of CB-28, -52 and -101 seemed to slow down in several of the herring time series. However for the other congeners the results were more variable between sampling sites. Although, differences due to chance or time periods of the time series, the overall results suggests that the measures to reduce environmental pollution of PCBs towards the end of the study period have influenced the pathways of human PCB exposure differently than those of guillemot and herring.

A decreased PCB contamination of the Baltic Sea environment, as observed in guillemot eggs and herring muscle since the 1980s, is mirrored by a general decline in atmospheric deposition of the PCB marker CB-153 in the Baltic Sea area between 1990 and 2016, estimated to a 61% decline.[105] Moreover, in Baltic Sea off-shore sediments from five sites covering the whole Baltic Sea area total PCB concentrations peaked in the early 1990s and declined thereafter.[5] However, the Swedish EPA modelling of PCB emissions to air in Sweden suggests unchanged emissions between 1990 and 2018.[106] Moreover, Sobek et al. observed that the reduction of PCB levels in Baltic Sea offshore sediments has been slower during the last two decades, and that the levels of PCBs appear to be at or near a steady-state condition.[107] This corroborates with the indication of a slower decline of PCBs in guillemot eggs and in herring muscle at the end of the study period at some of the sampling sites, but

future updates of the time series are needed in order to draw firm conclusions about slowing down of trends in the two matrices from the Baltic Sea.

As mentioned above, the rate of PCB declines in the shorter time series of human milk from Uppsala (1996-2016) and Göteborg (2008-2015) were similar as those of the longer Stockholm series. This suggests that the decline in PCB body burden of pregnant/nursing women have been similar in different parts of Sweden for several decades. It may be argued that there can be populations in Sweden not following the observed decline in PCB exposure, but the decreasing temporal trends of the most common PCB in Swedish food producing animals (CB-153) on the Swedish market, observed by us, strongly support a general decrease in PCB exposure in the Swedish population.

Food of animal origin is the major source of PCB exposure in Sweden, after the complete ban of use of PCB products in Sweden was introduced more than two decades ago.[108] PCBs enter the food chain in a complicated manner. Wild food-producing animals (wild edible fish, game), can for instance be contaminated from food organisms in the environment. Moreover, both wild and domesticated animals get exposure from ingestion of contaminated soil/soil organisms (grazing animals, free-range (outside) poultry, or via animal feed (farmed fish, farm animals).[22] Components of animal feed may be contaminated directly from the environment, as in the case of PCB-containing fish meal or fish oil. Contamination may also occur due to use of feed components that have been contaminated for instance by accidental/illegal use of feed components contaminated by technical PCB mixtures.[22] Despite these complicated pathways of PCBs contamination of the food chain, the levels of CB-153 have declined during several decades in all types of food producing animals. Declining trends of CB-118 and CB-126 were also observed in some of the matrices from food producing animals, despite the lower statistical power in the time series for these congeners than in the series for CB-153.

Since the Swedish population is consuming a large amount of imported foods, the decreasing trends of PCBs in human milk in Uppsala, Stockholm and Göteborg strongly suggests that the PCB levels in imported foods also have declined. This is supported by a mean decline in per capita intake of CB-153 by 4.5% per year between 1999 and 2015, reported in the market basket study performed by the Swedish Food Agency.[23] In the market basket study, both imported and domestically produced foods with a per capita consumption of 0.5 kg or more per years are sampled.[23] A further support of decreased PCB levels in imported food is the report of declining PCB exposure from food among adults in Europe between 2002 and 2010.[109]

The indicated differences in rates of PCB declines between human and biota matrices towards the end of the study period may be due to the large differences in contamination pathways in the Baltic Sea environment and food. The indicated slower declines in PCB levels in some of the Baltic Sea matrices may illustrate that it more recently has become much more difficult to limit pollution. The bans of use and production of PCBs eliminated the major sources of pollution, and now more diffuse sources are remaining. However, for humans food is the dominating source of exposure, and initiation of regulation of maximum levels of PCBs (and dioxins) in feed and food on the EU market may have caused further decreases in human exposure, starting in 2002.[53] Obviously, these measures did not affect environmental pollution of PCBs. However, reduction of PCB contamination of feeds for food-producing animals have the potential to relatively rapidly decrease the PCB levels in the foods giving the major contribution to PCB exposure of humans.

A support for the importance of the feed as a source of PCB exposure of food producing animals is the higher levels of PCB in organically produced eggs in Sweden compared to those in conventionally produced sputtering and cage eggs (Fig. 1 and 2) during the study period from year 2004. In 2004, it was discovered that organic eggs had high levels of both PCBs and PCDD/Fs in comparison to conventionally produced eggs.[110] The egg producers started a project with the aim to determine the cause of this and it was found that the organic hen feed was a major source of the high PCB/PCDD/F levels, mainly due to the use of fish meal in the feed.[110] After a change in the feed composition with less contaminated fish meal, and a decreased fish meal addition in the feed, the PCB/PCDD/F levels decreased in the organic eggs.[111] However, the consistent higher average PCB levels in the time series of organic eggs than sputtering and cage eggs, show that the PCB levels have not reached down to the levels in conventionally produced eggs. This is most probably both depending of prevailing use of some fish meal in the feed and the fact that the organic hens are, in contrast to cage and sputtering hens, allowed to forage outside.[112]

There was an indication of a faster decline for some dl-PCBs, but not of ndl-PCBs, in human milk from Stockholm, starting during the 1990s. These differences between the two types of PCBs are difficult to explain. The regulation of maximum limits in feed and food would most probably have similar effects on concentrations of the two types of PCBs. Nyberg et al.[31] proposed that the observed faster decline in PCB levels in human milk from Stockholm than in the Swedish marine and freshwater environment may be due to the advice issued by the Swedish Food Agency to girls and women in child-bearing age, with the aim to limit PCB (and dioxin) exposure from highly contaminated fatty fish from the Baltic Sea

area. This would however also have similar effects on the temporal trend of the two types of PCB. It cannot be excluded that the differences in CPs between dl- and ndl-PCBs in human milk from Stockholm could be due to a change in analytical laboratory for dl-PCBs occurring after 1997. Another change of laboratory occurred 2011.[31]

Although there was a general decrease in PCB levels in human milk, guillemot eggs and in herring from certain areas of the Baltic Sea, herring from the Swedish west coast (Väderöarna) showed significant increases in levels of dl-PCBs but not of ndl-PCBs. This observation is hard to explain, but the short sampling period (2007-2016) and the relatively low levels may contribute to the uncertainty of these results.[12] Moreover, the age of the herrings in this time series increased over time and the fat content decreased, adding to the uncertainty of the observed increases in levels of some of the PCB congeners.[113]

PCDD/Fs

Similarly as with PCBs, PCDD/F concentrations decreased substantially in the longest time series, human milk from Stockholm, guillemot eggs from the south Baltic Sea Proper and herring muscle from the southern Bothnian Sea. Initially in the 1970s, the actions against PCB pollution, especially bans of production, also affected PCDD/Fs emissions since PCDD/Fs were present as contaminants in technical PCB mixtures.[34] Moreover, bans of the PCDD/F-contaminated pesticide 2,4,5-T and wood treatment chemical pentachlorophenol (PCP) also had positive effects on PCDD/F emissions. For PCDD/Fs actions against pollution intensified in the 1980s-1990s, with restrictions against PCDD/F in waste incineration and the chlorine industry, and phase-out of chlorine bleaching of pulp and paper. Our results show that a combination of continuous international/national efforts to limit PCB production and use, and restricting PCDD/F emissions more specifically have had positive effects on PCDD/F trends in Swedish human milk, guillemot eggs and herring. The international efforts to limit PCDD/F pollution is further illustrated by the observed more than 3-fold decline in average PCDD/F levels in human milk in Germany in 1989-2003, and 4 fold decrease in Croatia 1981-2000.[103, 104] In 2004 PCDD/F was included in the Stockholm Convention, which is an important instrument for continuous efforts to reduce PCDD/F pollution on a global scale.

Declining trends of most PCDD/F congeners are also observed in the shorter time series of human milk from Uppsala (1996-2017) and Göteborg (2007-2015). However, slower trends were suggested for PCDFs than for PCDDs, with some PCDF congeners showing no

significant trends. Slower trends of PCDFs than of PCDDs were also observed for guillemot eggs and in herring muscle. Miller et al.[114] proposed that the slower decline of PCDFs than of PCDDs in herring muscle could be due to differences in emission reductions between the main PCDD and PCDF sources. Modelling of sources of PCDD/Fs emissions to the Baltic Sea, performed around 2010, suggested that atmospheric deposition was the main source of contamination in the Baltic Sea.[5] Atmospheric PCDD/F seemed to be dominated by non-industrial PCDD/F sources, with a higher contribution of PCDFs than of PCDDs.[5] In a further modelling of sources of PCDD/F contamination of Baltic Sea herring, it was suggested that during the pre-2000 period thermal source type of contamination dominated, whereas in the post-2000 period contribution of tetra-chlorophenol and penta-chlorophenol/atmospheric background sources increased in relation to thermal source type contamination.[115] However, other factors may contribute to the suggested slower decline of PCDFs in herring muscle, such as to congener-specific differences in bioavailability from sediment and resuspension reservoirs.[114] Moreover, slower elimination of some PCDFs than of PCDDs from biota could add to the slower decline.

Despite the observation of slower declines of PCDFs than of PCDDs, the overall results for human milk, guillemot eggs and herring muscle show that the efforts to diminish PCDD/F contamination of the environment have been successful for decades. This is further supported by the decline in PCDD/F levels in off-shore sediments from the Baltic sea since the early 1990s,[5] and in modelled atmospheric emissions in the Baltic Sea (31% decline) between 1990 and 2015.[116] Moreover, as with PCBs, the mean decline in per capita human intake of total PCDD/PCDF/PCB TEQ of 4.5% per year between 1999 and 2015, reported in the Swedish market basket study, strongly suggests a general decline of levels in both domestically produced foods and imported foods.[23] Furthermore, the European Food Safety Authority reported an estimated general decrease in dietary exposure to dioxins and dl-PCBs of 17% to 79% in different European populations between 2002 and 2010.[109] The general decrease in PCDD/F exposure in Europe is further supported by long-term decrease in PCDD/F levels in human milk from Germany (1989-2003) and Croatia (1981-2000).[103, 104]

In human milk from Stockholm an increase in the rate of decline of PCDDs was suggested already in the 1980s-1990s, but not for PCDFs. This may indicate that the actions affecting PCDD/F pollution had “better” effects on PCDD pollution. As mentioned before, changes in food habits may affect trends. However, it may be speculated that changes in food habits causing a lower PCDD/F exposure should have affected trends of PCDD/Fs similarly. As proposed for dl-PCBs a change in analytical laboratory occurring after 1997,[31] may have

played a role in the observed CPs for PCDDs, with a faster decline afterwards. Why this would not affect the PCDF trends similarly is however hard to explain.

When looking at the human milk time series from Uppsala, CPs with slower declines indicated afterwards were observed 2006-2011, both for PCDDs and PCDFs. Although not possible to completely rule out, changes in analytical laboratories are not a likely explanation to this finding, since extensive "calibration studies" showed good agreement between participating laboratories. The more detailed analyses of temporal trends of TCDD, 1,2,3,7,8-PeCDD, and 2,3,4,7,8-PeCDF from 2000 and onwards suggest initiation of slower rates of decline between 2005 and 2010 in human milk from both Uppsala and Stockholm.

For guillemot eggs indications of declines slowing down were observed for several PCDD/Fs, mostly starting in the early 1990s. In herring muscle from Ängksärsklubb (southern Bothnian Sea) 1979-2015 decreases of a few congeners also appeared to slow down although in many cases not for the same congeners and time periods as in guillemot eggs. For the shorter herring muscle series from the other sampling sites, some congeners showed no significant temporal trend, especially among PCDFs. Taken together the results strongly suggests a slowing down of the rate of decline in both guillemot eggs and herring towards the end of the study period. This corroborates with the results of the more detailed analyses described in Bignert et al.,[113]

HCB

Similarly as with PCBs and PCDD/Fs, concentrations of HCB decreased substantially in the longest time series, human milk from Stockholm, guillemot eggs from the southern Baltic Sea proper, and herring muscle from the southern Bothnian Sea. In Stockholm human milk and guillemot eggs the average decrease of HCB has been around 10-fold. The Swedish ban of HCB as a pesticide in 1980 was most certainly an important factor for this positive development. Since HCB is, similarly as PCBs and PCDD/Fs, unintentionally produced in combustion processes and in production of chlorinated products,[7] national/international actions against such pollution in the 1980s also helped with the HCB pollution. This is corroborated by the almost 20-fold decrease in average HCB levels in human milk from Croatia 1981-2000 and the considerable decline in human milk from Germany 1984-2001.[103, 104] The mean decline in per capita intake of HCB by 1.5% per year between 1999 and 2015, reported in the Swedish market basket study, further support the positive impact of the national/international HCB actions on human exposure.[23] The decline in per capita intake was

however much slower than that observed for human milk, especially from Stockholm since 1972, suggesting a reduction in the rate of decline of human HCB exposure during the last 2 decades.

As with PCBs and PCDD/Fs, food the major source of human HCB exposure in Sweden,[23] after the complete ban of use of HCB products in Sweden was introduced more than three decades ago.[47] As with the other chlorinated POPs there are several paths of entry of HCB into food-producing animals. The observed decline of HCB in hen´s eggs, cow´s milk and cattle fat during the 2-3 last decades show that the actions taken to reduce HCB pollution has affected HCB levels in domestic animal foods positively. However, the lack of trends in lamb and swine fat, and the increase in reindeer fat, argues against a general decline in HCB pollution in Swedish animal production. Moreover, the observed CPs with a slower decrease, or even increase, in levels afterwards, in cow´s milk, cattle fat and hen´s eggs corroborates with the conclusion that the decreases in HCB pollution has ceased.

Also in guillemot eggs and in all herring muscle sampling sites, CPs with indicated slower declines or even increases in concentrations were observed, both when looking at the full time series and in the CP analyses starting 2000. Interestingly, in offshore sediments from the Baltic Sea HCB concentrations increased after 2000.[107] Recent increases in HCB levels 2007-2011 in kittiwakes (*Rissa tridactyla*) has been observed on Svalbard.[117]. Moreover, in three Artic air monitoring stations, HCB showed increasing trends at two (Svalbard and Iceland) and slow decreasing trends at one (Canada).[118]

As with PCBs and PCDD/Fs, atmospheric deposition has been estimated to be the major source of HCB contamination of the Baltic Sea area during the last decades.[119] Barber et al.[120] reported that global HCB production exceeded 100 000 tons and primary emissions probably peaked in the 1970s. In general, atmospheric HCB emissions has substantially fallen globally after the more or less global ban of HCB production.[121] After the more or less global ban of HCB as a pesticide other sources of pollution have taken over nationally and internationally, mainly unintentional formation in different industrial processes and during combustion.[7] Currently identified primary sources are among others fuel combustion, waste incineration, metal and cement production, and production and use of chlorinated chemicals.[122] It has also been proposed that secondary sources may contribute as a significant source of contamination of the Swedish environment,[123] mainly from volatilization of "old" HCB in soil from past contamination.[120] In 2017, it was modelled that 60% of the HCB deposition over Europe came from emissions from secondary sources.[124] Due to the high long-range transport potential HCB is now detected in Arctic air, being found at the highest

concentrations of any individual organochlorine.[120] Taken together, these processes of HCB pollution in the northern hemisphere may at least partly explain the recent negative picture of HCB trends in Sweden.

PBDEs and HBCDD

In general, increasing trends of most of the PBDE congeners and HBCDD were initially observed in the longest time series of human milk from Stockholm, guillemot eggs from the southern Baltic Sea Proper and herring muscle from the southern Bothnian Sea. This was due to increased production and use of the chemicals, before pressure was put on the producers to phase out production and use. For instance, it has been estimated that the global consumption of bromine for flame retardant production increased from less than 50 000 tons/year in 1975 to almost 150 000 tons/year in 1995.[125] A Danish estimation of global consumption of commercial pentaBDE mixtures showed an increase from 4500 tons/year in 1994 to 7500 tons/year in 2001.[126] In Sweden the use of PBDEs peaked in year 2000, with close to 100 tons/year, and decreased rapidly thereafter.[127] Import of HBCDD in Sweden peaked in 1997 at approximately 120 tons/per year and decreased to below 10/ year tons in 2004.[128]

After the initial increases in tetra-pentaBDEs (BDE-47, -99 and -100) peaks in temporal trends occurred more than 10 years earlier in the Stockholm time series than in the Uppsala series (1996-2016). The comparison of the results in the two time series are hampered by a sample with very high BDE-47 and -100 in 2013 in the Stockholm series, and a change in laboratory in 2010.[31] However, these late events in the time series should not cause a much earlier CP in the Stockholm series. One factor that could affect the CP analyses is that the Stockholm series was based on pooled samples starting already in 1984 and that the Uppsala series was based on individual samples starting 1996. The time series from Uppsala thus started after the CPs were detected in Stockholm. A visual inspection of the trends in the Stockholm series suggests that the levels of BDE-47 reached a plateau during the late 1990s and started to decline in the early 2000s, which nevertheless is similar as observed in the Uppsala series (Appendix 4).

For BDE-99 there are also similarities in the trend pattern around 2000, with a decline in levels in both Stockholm and Uppsala starting during the end of the 1990s (Appendix 4). BDE-100 similarly reached a plateau or started to decrease from the middle of the 1990s to the middle of the 2000s (Appendix 4). These trend patterns are in accordance with the estimated peaks in global societal PBDE consumption in the late 1990s and the peak in

pentaBDE (technical mixture) use in Sweden in 2000.[126, 127] In the market basket study 1999-2015, per capita intake of BDE-47 and -99 in Sweden decreased with 9-10% per year,[23] supporting a decrease in human exposure to these PBDEs in Sweden during the last decades.

Our search for regulatory actions to mitigate pentaBDE production and use in Europe suggested that legislative bans of PBDE production and use were not initiated within the EU until after the tetra-pentaBDE levels started to decline in human milk. However, already in 1989 we found a reference to voluntary phase out of PBDE production and use by the German plastics industry.[72] Moreover, the Swedish Government started "sending out signals" about future restrictions already in the early 1990s, thus putting pressure on the domestic industry to phase out pentaBDE use. Other more or less national/international voluntary actions to reduce production and use, also commenced during the 1990s.

Guillemot eggs showed peak levels of tetra-pentaBDEs already in the early 1980s and in herring muscle peaks were observed towards the end of the 1980s. This is much earlier than the observed concentration peaks in human milk. It has been suggested that the earlier peak of BDE-47 in guillemot eggs from Stora Karlsö, south Baltic Sea Proper, than that observed in eggs from the terrestrial Swedish peregrine falcon, was due to events that had more pronounced effects on the emissions to the Baltic Sea environment than to the general terrestrial environment in Sweden.[72] Such events was proposed to include voluntary discontinuation in the late 1980s of the use of PBDEs by the Swedish textile industry and phase-out of the production and use of pentaBDE mixtures by German plastics industry.[72] It was speculated that these voluntary measures caused a decreased pollution of the Baltic Sea area due to reduced atmospheric emissions.[72]

In contrast to the tetra-pentaBDE congeners, being components only in the commercial pentaBDE mixtures, the hexaBDE-153 and -154 were components both in commercial pentaBDE and octaBDE mixtures.[129] This could be one reason for the differences in temporal trend patterns between the tetra-pentaBDEs and these hexaBDEs, with concentration peaks of the latter at later stages of the time series of human milk, guillemot eggs and herring muscle. Although the production and use of octaBDE mixtures appears to have peaked at about the same time as the pentaBDE mixtures both globally and in Europe, it has been reported that the European production and consumption of pentaBDE mixtures have been considerably less than that of octaBDE mixtures.[26] The trend analyses starting 2000 showed significantly decreasing BDE-153 levels in human milk, and the decreased human exposure in Sweden during the recent decades is further supported by the decreased per capita intake of BDE-153 in the Swedish market basket study between 2010 and 2015.[23]

DecaBDE (BDE-209) trends were only studied in human milk and decreasing levels were observed 2010-2014 in Stockholm, but not in Uppsala (2009-2016) and Göteborg (2011-2015). The short duration of the time series makes the results uncertain. A decreased per capita intake of BDE-209 from food was observed between 2010 and 2015, suggesting that the human exposure have decreased during the last decade.[23] This corroborates with the modelled peak in BDE-209 production and consumption in Europe and other parts of the world before 2010.[26] This decline started before decaBDE was included in the Stockholm Convention 2017.

In human milk from Stockholm HBCDD levels peaked in the early 2000s and declined rapidly thereafter. In Uppsala, the decline was almost 6% per year between 2003 and 2016. Taken together, the results show that the human exposure to HBCDD has declined during the last two decades, supported by the observed decline in per capita intake in Sweden between 2010 and 2015.[23] A similar trend pattern, although more uncertain, was indicated in guillemot eggs 1969-2016, with a peak in mid-2000. In the analyses of trends starting 2000 declining trends were observed in both guillemot eggs and in human milk from Stockholm and Uppsala. This strongly suggests that both human and guillemot exposure to HBCDD has declined during the most recent decades. In herring muscle from Ängskärsklubb the HBCDD levels seemed to increase up to year 2000, then the trend became more uncertain with a lot of variation in levels between years. In the shorter time series decreasing levels were observed in 3 out of 5 series, indicating that at least some areas of the Baltic Sea have experienced a decline in HBCDD pollution the last decades. When looking at actions to limit HBCDD pollution, the first reference to HBCDD found by us was the closure of a HBCDD-producing facility in the early 2000 in Great Britain. This coincides with the decreasing in HBCDD levels in the studied matrices, but there is no evidence that there is a connection. HBCDD was included in the Stockholm convention in 2013 thus putting pressure on the then still existing production and use HBCDD.

PFASs

In human milk from Stockholm, PFOA levels increased up to around 2000 and thereafter decreased. A similar pattern was observed in human milk and serum samples from Uppsala although the peak in levels occurred slightly later than in Stockholm. The increase in human milk PFOA concentrations up to around 2000 is in agreement with the estimated average annual global production of ammonium perfluorooctanoate increasing from 5-25 tons/year in

1951-1964 to 200-300 tons/year in 1995-2002.[130] Moreover, modelling of global emissions of ammonium perfluorooctanoate projected a 9-fold decrease between 2000 and 2006.[130] In Göteborg, the PFOA concentrations decreased 2007-2016, agreeing with the decreasing trend at the end of the study period in Stockholm and Uppsala. Taken together, the results show that the human exposure to PFOA has decreased during the last 2 decades, after an exponential increase for several decades before that.

The decrease in human exposure coincided with the phase-out of PFOA production by 3M shortly after 2000,[87] and the US EPA agreement in 2006 with major world-wide PFOA producers to almost completely phase out production by 2015.[90] Another action that may have supported the downward trend in human PFOA exposure is the US FDA agreement with the food contact material (FCM) industry to voluntarily phase out use of long-chain PFASs in FCMs in 2011, and the following revoking of approval for use in FCMs in 2016. However, in the Swedish market basket study no significant trend in per capita PFOA intake was observed,[131] which is in contrast with the suggested decreased human exposure in Sweden. This may suggest that there were other PFOA exposure sources than food that were eliminated in the early 2000s. However, the basic foods included in the market basket study were not to a large degree packaged in the type of grease and water repellent packaging that PFAS is used for. Consequently, this FCM-related decrease in exposure may not have been picked up in the market basket study.

In Guillemot eggs PFOA time series started in 2003 and, similarly as in human milk, declining trends were observed up to 2017. This strongly suggest that the actions initiated in North America to eliminate PFOA production and use had similar effects on the exposure of humans and guillemots in Sweden. Modelling of the contribution of historic and contemporary manufacturing sources of PFOA have suggested that the historic and contemporary sources contributed with about 50% each of the PFOA detected in sea water in the Baltic Sea.[132] With this in mind drastic decreases in contemporary production and use of PFOA and related compounds would most probably had a positive effect on the PFOA pollution of the Baltic Sea environment.

However, in contrast to the recent decreasing PFOA trends in human matrices and in guillemot eggs, no clear indication of declining levels after 2000 was observed in the herring time series starting in 1980 at Ängskärsklubb, Landsort and Utlängan. However, in the short time series from Harufjärden and Väderöarna, starting in the mid 2000s declining trends were observed. This suggests regional/local differences in PFOA pollution trends along the Swedish coasts. A survey of PFAS in rivers along the Swedish coasts have shown large

variations in PFOA concentrations in the water indicating large differences in local contamination along the coast.[133] A study of PFASs in water and sediments of the Baltic Sea suggested that diffuse sources of PFASs are important for emissions to the Baltic Sea area, but riverine influence was also clearly indicated.[134]

In contrast to the decreasing levels of PFOA in human milk and guillemot eggs during the 2000s, PFCAs with longer carbon chains, PFNA, PFDA, PFUnDA, PFDoDA and PFTrDA, showed increasing levels well into this decade. This shows that the measures that caused decreasing PFOA levels after year 2000 did not have similar effects on the other long-chain PFCAs in human matrices and in guillemot eggs. The increasing trends of these PFCAs in human milk and guillemots appeared to level off much later than PFOA, at the end of the 2000s and thereafter in some cases levels started to decrease. PFNA has been intentionally manufactured for several purposes, and PFUnDA and PFTrDA have been found as impurities in commercial PFNA products.[28] This could be a reason behind the similarities in temporal trends of these PFCAs. In our search for actions against pollution of PFCAs it was hard to find direct actions focusing on limiting pollution of PFNA-PFTrDA, in contrast to PFOA. The US FDA agreement with the food contact material (FCM) industry to voluntarily phase out use of long-chain PFASs in FCMs in 2011, and the following revoking of approval for use in FCMs in 2016, may have contributed to the observed changes in trends to the better at the end of the study period. However, the lack of action against PFNA-PFTrDA pollution could be one reason behind the differences in trend patterns between PFOA and the other long-chain PFCAs. Moreover, differences in sources, environmental fate and/or elimination half-lives of individual PFASs may have contributed to the observed differences in trend patterns between PFOA and longer-chain PFCAS.[17, 135]

Herring liver from the longest time series from Ängskärsklubb, Landsort and Utlängan showed, similarly as for PFOA, overall increasing trends between 1980 and 2014/2016 for PFNA, PFDA, PFUnDA, PFDoDA and PFTrDA. However, in contrast to PFOA, the increasing levels of some of the longer-chain PFCAs seemed to reach a peak in the middle of the 2000s. Taken together, the herring trends were more similar to the human and guillemot trends when looking at PFNA-PFTrDA, than the trends for PFOA.

PFHxS and PFOS levels increased for several decades in the human milk series from Stockholm, with a peak around year 2000. Similar trends were observed in guillemot eggs. In Uppsala, the peak in PFHxS increase occurred later than in Stockholm, which was due to contamination of the Uppsala drinking water with PFHxS, which was mitigated in 2012.[136] PFOS levels in the Uppsala matrices started decreasing after year 2000, coinciding with the

trend pattern in Stockholm. The exponential increase in PFHxS and PFOS exposure of human and guillemots up in the early period of the time series was due to a drastic increase in production of PFHxS- and PFOS-related substances for several decades before the phase-out of production by the main manufacturer 3M.[87,137] It has been estimated that the total historical production of PFOS-related chemicals before the phase-out was over 100 000 tons.[138] This phase-out of production of the main manufacturer worldwide most probably is the most important reason for the decreased levels observed in human and guillemot egg matrices.

The strong influence of drinking water PFAS contamination on temporal trends in Uppsala shows that local contamination of drinking water sources may have strong influence on human exposure and temporal trends. In the Uppsala time series the increase in PFHxS levels was halted when the pollution of the drinking water was mitigated. Similarly in Ronneby, where drinking water were severely polluted by PFOS and PFHxS, serum concentrations of many of the exposed individuals started decreasing immediately after the mitigation.[139] It has been indicated that low-grade PFHxS, PFOS and PFOA contamination of drinking water, at much lower levels than found in Uppsala and Ronneby, explains a significant portion of the variation in blood serum concentrations of these PFASs.[140, 141] This more general low-grade PFAS contamination of drinking water from both diffuse sources and from hot spots will most likely have a significant effect on future temporal trends of certain PFASs in sweden. Future drinking water legislation with EU maximum limits of PFAS in drinking water, and national action limits against PFAS pollution of drinking water are important signals to the drinking water producers to keep PFAS pollution of drinking water in check.

The pattern in the human matrices and guillemot eggs of an increasing trend of PFHxS and PFOS to a peak and then a decrease thereafter was not as evident for the herring liver. For PFHxS increasing trends with no peaks were observed in the long-term time series starting in 1980. At two of the three sampling sites the PFOS levels plateaued during the 1990s-2000s, but no clear decrease in concentrations could be seen. In the shorter time series no decrease in levels was obvious. This suggests, as with PFOA, that the temporal trend patterns differ between humans/guillemots and herring. The reason behind these differences has still to be determined.

Conclusions

The present study of temporal trends of PCBs and HCB in human matrices from Stockholm, Uppsala and Göteborg, in guillemot eggs from Stora Karlsö (southern Baltic Sea), and herring muscle from the Baltic Sea and the Swedish west coast, clearly shows that banning of production and use of these man-made chemicals have lead to declining levels in the environment already soon after the legislative decisions were taken. This shows that the relatively fast elimination of primary sources of pollution has given desired effects on the environmental load of these persistent POPs. This observation is also valid for PCDD/Fs that have not been produced intentionally. The risk management decisions with the aim to eliminate primary PCB sources initially also had a positive effect on the PCDD/F pollution, since PCDD/Fs were present as contaminants in the technical PCB mixtures produced by the industry.

For PBDEs, HBCDD and PFASs declining temporal trends were in many cases observed already before legislation to limit use and production had been implemented. In the case of PBDEs and HBCDD it was suggested that voluntary elimination of production and use by the industry, in some cases most probably due to non-legislative pressure from the society, had positive effects on the load of the Swedish environment. In the case of the PFASs PFOS, PFOA, PFHxS and related compounds, the more or less voluntary agreements between main producers and the US EPA in the beginning of the 2000s were most probably the initial driver of the declining levels of these PFASs in humans in Sweden.

PCDD/Fs have not been intentionally produced, and it is impossible to totally ban or phase out emissions to the environment. The actions against pollution have nevertheless been successful, as shown by the significant decline in human, guillemot and herring levels since the early 1970. However, as indicated in the present study, and more in detail described in Bignert et al.,[113] there is strong evidence that the relative rate of decline (percent/year) has slowed down during the recent decade, especially for PCDFs. This suggests that the actions against PCDD/F pollution have not been effective enough to ensure a continuous rate of decline in the Swedish environment during the most recent decades. As with the other POPs, actions against primary sources of pollution have been effective to initially reduce pollution. However, it is more difficult and costly to follow up with actions against more diffuse sources, such as atmospheric deposition from long-range transport, which most probably currently gives a large contribution to deposition in the Swedish environment.

As for biota, a decrease of the general environmental pollution often causes a decreased human exposure, due to less contamination of food sources. However, there is one action against pollution that is only relevant for humans, i.e. reduction of contamination of animal feed and drinking water (PFAS) given to food-producing animals. For most POPs, foods originating from animal production are a large source of human exposure. Since animal feed is a significant source of entry into the food chain for most of the studied POPs, actions against POP pollution of animal feed is most probably a cost effective action to further decrease human exposure. Therefore, strict regulation of POP levels in animal feed may be a way to further decrease human exposure, as has been initiated for PCBs and PCDD/Fs within EU. Currently this regulation has however not yet mitigated the slowing down of the rate of decline in human exposure to PCDD/Fs in Sweden, but there is potential for such an effect if PCDD/Fs in the future are more strictly regulated in animal feed than currently is the case.

Among the POPs studied HCB appears to be a special case for which increases in levels were observed in some of the studied matrices during the last decades, in some longer time series after declines for decades. In other matrices the rate of decline has more or less ebbed out. As with the other POPs the decline in trends was initiated close to the period when the HCB use was banned in Sweden and most probably also in other European countries, and the decline continued for an extended period. However, there are large amounts of HCB remaining in soils all over the world, and the volatilization of "old" HCB in soil from past contamination has been modelled to be the currently largest source of HCB deposition over Europe. This process of HCB pollution of the northern hemisphere will most probably be impossible to limit, and follow-up of HCB trends in biota and humans are needed in order to get better predictions of future development of HCB pollution in Sweden.

Differences in patterns of temporal trends between the different matrices studied were observed for some of the studied POP groups, suggesting differences in "environmental responses" after actions to limit pollution. For example, tetra-pentaPBDEs showed a delay in peak levels, with the earliest in guillemot eggs (early 1980s), followed by herring muscle (late 1980s) and human milk (late 1990s/early 2000s). Since EU legislation to eliminate production and use of these PBDEs was not in place until early 2000s, the results suggest that national actions against production and use of these PBDEs occurred in the Baltic Sea area in the 1980s, causing more direct positive effects on the pollution of the Baltic Sea environment than on the human exposure in Sweden.

The reverse was indicated for PFOS, i.e. the "human environment" responded more rapidly than the Baltic Sea environment after the phase-out of production by the main

manufacturer in the US. This to some extent illustrate the possible differences in environmental effects of actions, depending on closeness of the primary pollution source, for the PBDEs most likely regionally in the Baltic Sea area and for PFOS in North America. Moreover, it may be speculated that the rapid response of human exposure after PFOS phase-out was at least partially due to elimination of direct sources of exposure, for instance in food contact materials, whereas the PFOS load of the Baltic Sea environment most likely had a large component of long-range transport which takes longer to respond after phase-out of production in North America.

Our results suggest that the human exposure pattern of tetra-pentaPBDEs more or less followed the overall industrial production/use volumes reported for EU and Sweden, whereas the patterns for guillemots and herring most likely was strongly influenced by regional changes in emissions in the Baltic Sea area. For hexaPBDEs, peak levels occurred more or less simultaneously in human, guillemot and herring matrices around the turn of the millennium. A similar pattern was suggested for HBCDD, showing that the actions that reduced tetra-pentaPBDEs during the 1980s in the Baltic Sea environment did not influence pollution of hexaBDEs and HBCDD. This pattern highlights the problem that actions are usually not simultaneously taken against a whole group of similar POPs. In the BFR example, voluntary/regulatory actions were initially mainly focused on a limited number of PBDEs (tetra-pentaBDEs), most probably because of better knowledge about environmental fate and toxicity for these BFRs than for the others. The lack knowledge about environmental pollution and toxicity of hexaBDEs and HBCDD (and even decaBDE) most probably made it more difficult for the society to take initial actions against pollution. A similar pattern was observed for the PFASs, where actions against PFOS, PFOA and PFHxS occurred in the early 2000s, resulting in a general decline in human exposure. At the same time pollution of the environment with alkyl acids with longer carbon chains than PFOA appeared to continue resulting in increasing human exposure. From the point of view of environmental protection it would have been desirable that POPs such as BFRs and PFASs initially had been regulated as whole groups.

The retrospective trend studies of PBDEs, HBCDD and PFASs clearly show that persistent and bioaccumulating chemicals have the “nasty habit” to increase exponentially in the environment as production and use increase. This is a reminder of the fact that the production and use of these types of chemicals in general always should be kept to a minimum, or not be allowed at all. The industry has an important responsibility not to develop new chemicals with similar properties as the POPs studied in the present report. The

EU chemical legislation is unfortunately not able to “catch” these types of chemicals if the use and production are below certain limits. Our study suggests that this responsibility of the industry has in some cases not been dealt with in an ethical manner, as is shown by the exponential increases of environmental levels for many decades as the main manufacturers increased their production. These industries most probably had knowledge about the problematic properties of the POPs in question, but still continued to produce and sell them in increasing volumes. In near future the chemical industry has to take on the responsibility not to put these types of chemicals on the market before it has been clearly proved that production and use will not lead to accumulation in the environment. Moreover, the legislators should in collaboration with the industry set up more effective legislation to limit the risk of the emergence of new POPs in the future.

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References

1. Naturvårdsverket, Nationell miljöövervakning *https://www.naturvardsverket.se/Miljoarbete-i-samhallet/Miljoarbete-i-Sverige/Miljoovervakning/Vad-ar-miljoovervakning/* **2019**.
2. Naturvårdsverket, Miljöövervakning, forskning och tidiga varningssignaler *https://www.naturvardsverket.se/Miljoarbete-i-samhallet/Miljoarbete-i-Sverige/Miljoovervakning/Miljoovervakning-forskning-och-tidiga-varningssignaler/* **2019**.
3. Naturvårdsverket, Hälsorelaterad miljöövervakning. *https://www.naturvardsverket.se/Miljoarbete-i-samhallet/Miljoarbete-i-Sverige/Miljoovervakning/Miljoovervakning/Halsorelaterad-miljoovervakning/* **2019**.
4. Naturvårdsverket, Miljöfarliga ämnen i vattenmiljön. *https://www.naturvardsverket.se/Sa-mar-miljon/Vatten/Miljofarliga-amnen-i-vattenmiljon/* **2019**.
5. Naturvårdsverket, Managing the dioxin problem in the Baltic region with focus on sources to air and fish. *https://www.naturvardsverket.se/Documents/publikationer6400/978-91-620-6566-9.pdf?pid=8228* **2013**.
6. Bernes, C., *Persistent Organic Pollutants. A Swedish View of an International Problem*. Swedish Environmental Protection Agency: Stockholm, 1998; p 152.
7. Naturvårdsverket, Kartläggning av källor till oavsiktligt bildade ämnen. *https://www.naturvardsverket.se/Documents/publikationer/620-5462-7.pdf?pid=3091* **2005**.
8. Ahrens, L.; Bundschuh, M., Fate and effects of poly- and perfluoroalkyl substances in the aquatic environment: a review. *Environ Toxicol Chem* **2014,** *33*, (9), 1921-9.
9. Livsmedelsverket, Dioxiner och PCB. *https://www.livsmedelsverket.se/livsmedel-och-innehall/oonskade-amnen/miljogifter/dioxiner-och-pcb* **2019**.
10. Ålander, J.; Nilsson, I.; Sundström, B.; Jorhem, L.; Nordlander, I.; Aune, M.; Larsson, L.; Kuivinen, J.; Bergh, A.; Isaksson, M.; Glynn, A., Tidstrender av tungmetaller och organiska klorerade miljöföroreningar i baslivsmedel. *Livsmedelsverkets Rapport 3 - 2012* **2012,** *https://www.livsmedelsverket.se/globalassets/publikationsdatabas/rapporter/2012/2012_livsmedelsverket_3_tidstrender_tungmetaller_organiska_miljofororeningar.pdf*.
11. Glynn, A.; Bignert, A.; Nyberg, E.; Lignell, S.; Aune, M.; Darnerud, P. O., Trenderna för svårnedbrytbara halogenerade föroreningar varierar. *Gifter & Miljö. 2013. Om påverkan på yttre miljö och människor* **2013,** *Naturvårdsverket*.
12. Bignert, A.; Danielsson, S.; Ek, C.; Faxneld, S.; Nyberg, E., Comments Concerning the National Swedish Contaminant Monitoring Programme in Marine Biota, 2017. *http://nrm.diva-portal.org/smash/record.jsf?pid=diva2%3A1090746&dswid=4686* **2017**.
13. Faxneld, S.; Danielsson, S.; Nyberg, E., Distribution of PFAS in liver and muscle of herring, perch, cod, eelpout, arctic char, and pike from limnic and marine environments in Sweden. *Report to the Swedish EPA* **2014,** *https://www.diva-portal.org/smash/get/diva2:767385/FULLTEXT01.pdf*.
14. Bignert, A.; Helander, B. O., Monitoring of contaminants and their effects on the common Guillemot and the White-tailed sea eagle. *Journal of Ornithology* **2015,** *156*, 173-185.
15. Eriksson, U.; Roos, A.; Lind, Y.; Hope, K.; Ekblad, A.; Karrman, A., Comparison of PFASs contamination in the freshwater and terrestrial environments by analysis of eggs from osprey (Pandion haliaetus), tawny owl (Strix aluco), and common kestrel (Falco tinnunculus). *Environ Res* **2016,** *149*, 40-47.
16. Glynn, A.; Lignell, S.; Aune, M.; Darnerud, P. O.; Törnkvist, A., Temporal trends of organohalogen compounds in mother´s milk from Sweden. In *Global contamination trends of persistent organic chemicals*, Loganathan, B. G.; Lam, P. K. S., Eds. CRC Press: Boca Raton, 2012.
17. Nyberg, E.; Awad, R.; Bignert, A.; Ek, C.; Sallsten, G.; Benskin, J. P., Inter-individual, inter-city, and temporal trends of per- and polyfluoroalkyl substances in human milk from Swedish mothers between 1972 and 2016. *Environ Sci Process Impacts* **2018,** *20*, (8), 1136-1147.
18. Lignell, S.; Aune, M.; Darnerud, P. O.; Soeria-Atmadja, D.; Hanberg, A.; Larsson, S.; Glynn, A., Large variation in breast milk levels of organohalogenated compounds is dependent on mother's age, changes in body composition and exposures early in life. *J Environ Monit* **2011,** *13*, (6), 1607-16.

19. van den Berg, M.; Kypke, K.; Kotz, A.; Tritscher, A.; Lee, S. Y.; Magulova, K.; Fiedler, H.; Malisch, R., WHO/UNEP global surveys of PCDDs, PCDFs, PCBs and DDTs in human milk and benefit-risk evaluation of breastfeeding. *Arch Toxicol* **2017,** *91*, (1), 83-96.
20. Liu, J.; Li, J.; Liu, Y.; Chan, H. M.; Zhao, Y.; Cai, Z.; Wu, Y., Comparison on gestation and lactation exposure of perfluorinated compounds for newborns. *Environ Int* **2011,** *37*, (7), 1206-12.
21. Tornkvist, A.; Glynn, A.; Aune, M.; Darnerud, P. O.; Ankarberg, E. H., PCDD/F, PCB, PBDE, HBCD and chlorinated pesticides in a Swedish market basket from 2005--levels and dietary intake estimations. *Chemosphere* **2011,** *83*, (2), 193-9.
22. Malisch, R.; Kotz, A., Dioxins and PCBs in feed and food--review from European perspective. *Sci Total Environ* **2014,** *491-492*, 2-10.
23. Livsmedelsverket, Swedish Market Basket Survey 2015. *https://www.livsmedelsverket.se/globalassets/publikationsdatabas/rapporter/2017/swedish-market-basket-survey-2015-livsmedelsverkets-rapportserie-nr-26-20172.pdf* **2017**.
24. Van den Berg, M.; Birnbaum, L. S.; Denison, M.; De Vito, M.; Farland, W.; Feeley, M.; Fiedler, H.; Hakansson, H.; Hanberg, A.; Haws, L.; Rose, M.; Safe, S.; Schrenk, D.; Tohyama, C.; Tritscher, A.; Tuomisto, J.; Tysklind, M.; Walker, N.; Peterson, R. E., The 2005 World Health Organization reevaluation of human and Mammalian toxic equivalency factors for dioxins and dioxin-like compounds. *Toxicol Sci* **2006,** *93*, (2), 223-41.
25. Naturvårdsverket, National Implementation Plan for the Stockholm Convention, Sweden 2017. *https://www.naturvardsverket.se/Documents/publikationer6400/978-91-620-6794-6.pdf?pid=21458* **2017**.
26. Abbasi, G.; Li, L.; Breivik, K., Global Historical Stocks and Emissions of PBDEs. *Environ Sci Technol* **2019,** *53*, (11), 6330-6340.
27. Convention, S., The new POPs under the Stockholm Convention. *http://www.pops.int/TheConvention/ThePOPs/TheNewPOPs/tabid/2511/Default.aspx* **2019**.
28. Buck, R. C.; Franklin, J.; Berger, U.; Conder, J. M.; Cousins, I. T.; de Voogt, P.; Jensen, A. A.; Kannan, K.; Mabury, S. A.; van Leeuwen, S. P., Perfluoroalkyl and polyfluoralkyl substances (PFASs) in the environment: terminology, classification, and origins. *Integr Environ Assess Manag* **2011**.
29. KEMI, Occurrence and uses of highly fluorinated substances and alternatives (in Swedish). *Rapport 6/15* **2015,** *http://www.kemi.se/global/rapporter/2015/rapport-6-15-forekomst-och-anvandning-av-hogfluorerade-amnen-och-alternativ.pdf*.
30. Lignell, S.; Aune, M.; Darnerud, P. O.; Cnattingius, S.; Glynn, A., Persistent organochlorine and organobromine compounds in mother's milk from Sweden 1996-2006: compound-specific temporal trends. *Environ Res* **2009,** *109*, (6), 760-7.
31. Nyberg, E.; Aune, M.; Awad, R.; Benskin, J. P.; Bergh, A.; Bignert, A.; Dahlgren, H.; Danielsson, S.; de Wit, C.; Egebäck, A. L.; Ek, C.; Eriksson, U.; Kruså, M.; Näslund, M.; Sällsten, G., Monitoring of POPs in human milk from Stockholm and Gothenburg, 1972-2015. *http://www.diva-portal.org/smash/record.jsf?pid=diva2%3A1138755&dswid=-6722* **2017**.
32. Glynn, A.; Berger, U.; Bignert, A.; Ullah, S.; Aune, M.; Lignell, S.; Darnerud, P. O., Perfluorinated alkyl acids in blood serum from primiparous women in Sweden: serial sampling during pregnancy and nursing, and temporal trends 1996-2010. *Environ Sci Technol* **2012,** *46*, (16), 9071-9.
33. Sturludottir, E.; Gunnlaugsdottir, H.; Nielsen, O. K.; Stefansson, G., Detection of a changepoint, a mean-shift accompanied with a trend change, in short time-series with autocorrelation. *Commun Stat Simul Comput* **2017,** *46*, 5808-5818.
34. SNV *Survey of unintentionally formed contaminants*; Naturvårdsverket: Stockholm, Sweden, 2005; pp 3-78 (in Swedish). http://www.naturvardsverket.se/Documents/publikationer/620-5462-7.pdf.
35. Polder, A.; Skaare, J. U.; Skjerve, E.; Loken, K. B.; Eggesbo, M., Levels of chlorinated pesticides and polychlorinated biphenyls in Norwegian breast milk (2002-2006), and factors that may predict the level of contamination. *Sci Total Environ* **2009,** *407*, (16), 4584-90.
36. Jensen, S., The PCB Story. *Ambio* **1972,** *1*, (4), 123-131.
37. Naturvårdsverket, PCB-lagen. *SFS 1971:385* **1971**.

38. OSPAR, Convention for the prevention of marine pollution by dumping from ships and aircraft (with annexes). Signed at Oslo on 15 February 1972. *https://treaties.un.org/doc/Publication/UNTS/Volume%20932/volume-932-I-13269-English.pdf* **1974**.
39. Naturvårdsverket, PCB-kungörelsen. *https://data.riksdagen.se/fil/76A99B3E-FAC7-45E8-A218-BB1A576E515E* **1972**.
40. OECD, OECD action to restrict use of a hazardous substance. *The OECD Observer* **1973,** *https://www.oecd-ilibrary.org/docserver/observer-v1973-2-en.pdf?expires=1581933771&id=id&accname=oid053050&checksum=C01B904C21B969E86E9972631795176C*.
41. OSPAR, About OSPAR. *https://www.ospar.org/about* **1974**.
42. Naturvårdsverket, Lagen om hälsofarliga varor. *SFS 1973:329* **1973,** *https://www.riksdagen.se/sv/dokument-lagar/dokument/proposition/om-andring-i-lagen-1973329-om-haso--och_G20374*.
43. Livsmedelsverket, SLV SFS 1974:2. **1974**.
44. EU, Council Directive 76/403/EEC of 6 April 1976 on the disposal of polychorinated biphenyls and polychlorinated terphenyls. *https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A31976L0403* **1976**.
45. Naturvårdsverket, PCB i miljön. *https://www.naturvardsverket.se/Sa-mar-miljon/Manniska/Miljogifter/Organiska-miljogifter/PCB/* **2019**.
46. OSPAR, Polychlorinated Biphenyls. *https://www.ospar.org/documents?v=6918* **2004**.
47. KEMI, National Implementation Plan for the Stockholm Convention on Persistent Organic Pollutants for Sweden. *https://www.kemi.se/global/rapporter/2006/rapport-4-06.pdf* **2006**.
48. HELCOM, Convention. *https://helcom.fi/about-us/convention/* **1992**.
49. EU, Rådets direktiv 96/59/EG av den 16 september 1996 om bortskaffande av polyklorerade bifenyler och polyklorerade terfenyler (PCB/PCT). *https://eur-lex.europa.eu/legal-content/SV/TXT/?uri=CELEX%3A31996L0059* **1996**.
50. UNECE, The 1998 Aarhus Protocol on Persistent Organic Pollutants (POPs) *https://www.unece.org/env/lrtap/pops_h1.html* **1998**.
51. Naturvårdsverket, Inventering och sanering av PCB i byggnader och anläggningar. *https://www.naturvardsverket.se/Documents/publikationer6400/978-91-620-6884-4.pdf?pid=24454* **2019**.
52. Naturvårdsverket, Miljöbalk. *https://www.riksdagen.se/sv/dokument-lagar/dokument/svensk-forfattningssamling/miljobalk-1998808_sfs-1998-808* **1998**.
53. EU, Limits on presence of dioxin in food and feed enter into force on 1 July. *https://ec.europa.eu/commission/presscorner/detail/en/IP_02_959* **2002**.
54. Larsson, S., Den svenska avfallsförbränningen. Praktisk eller problematisk? *http://www.diva-portal.org/smash/get/diva2:1192953/FULLTEXT01.pdf* **2016**.
55. Convention, S., History of the negotiations of the Stockholm Convention. *http://www.pops.int/TheConvention/Overview/History/Overview/tabid/3549/Default.aspx* **2019**.
56. Naturvårdsverket, Naturvårdsverkets föreskrifter om yrkesmässig förbehandling av avfall som utgörs av elektriska eller elektroniska produkter;. *https://www.naturvardsverket.se/Documents/foreskrifter/nfs2005/nfs_2005_10.pdf* **2005**.
57. EU, KOMMISSIONENS FÖRORDNING (EG) nr 1881/2006 av den 19 december 2006 om fastställande av gränsvärden för vissa främmande ämnen i livsmedel *https://eur-lex.europa.eu/legal-content/SV/TXT/PDF/?uri=CELEX:02006R1881-20140701&from=EN* **2006**.
58. Naturvårdsverket, Förordning (2007:19) om PCB. *https://www.riksdagen.se/sv/dokument-lagar/dokument/svensk-forfattningssamling/forordning-200719-om-pcb-mm_sfs-2007-19* **2007**.
59. Livsmedelsverket, Fisk och skaldjur - råd. *https://www.livsmedelsverket.se/matvanor-halsa--miljo/kostrad-och-matvanor/rad-om-bra-mat-hitta-ditt-satt/fisk#Barn, unga, kvinnor i barnafödande ålder, gravida och ammande* **2008**.
60. Kimmig, J.; Schulz, K. H., [Occupational acne (so-called chloracne) due to chlorinated aromatic cyclic ethers]. *Dermatologica* **1957,** *115*, (4), 540-6.

61. Enander, K.-G., Skogsbruk på samhällets villkor. Skogsskötsel och skogspolitik under 150 år. *https://pub.epsilon.slu.se/8483/1/Enander_K-G_111130.pdf* **2007**.
62. Naturvårdsverket, Betydelse av pentaklorfenolbehandlat trä för spridning av dioxiner i miljön. *https://www.naturvardsverket.se/Documents/publikationer/978-91-620-5911-8.pdf* **2009**.
63. Andersson, L. E.; Bergquist, A.-C., Effekter av miljöpolitiska styrmedel i skogsindustrin *https://www.tillvaxtanalys.se/download/18.201965214d8715afd169d82/1432802733989/Effekten+av+milj%C3%B6politiska+styrmedel+i+skogsindustrin.pdf* **2015**.
64. UNECE, Protocol on Persistent Organic Pollutants (POPs). *http://www.unece.org/fileadmin//DAM/env/lrtap/pops_h1.htm* **2020**.
65. Weber, R.; Tysklind, M.; Gaus, C., Dioxin--contemporary and future challenges of historical legacies. Dedicated to Prof. Dr. Otto Hutzinger, the founder of the DIOXIN Conference Series. *Environ Sci Pollut Res Int* **2008,** *15*, (2), 96-100.
66. EFSA, Opinion of the Scientific Panel on Contaminants in the Food Chain on a request from the Commission related to the presence of non-dioxin-like polychlorinated biphenyls (PCB) in feed and food. *The EFSA Journal* **2005,** *284*, 1-137.
67. Ramstad, T.; Mahle, N. H.; Matalon, R., Automated cleanup of herbicides by adsorption chromatography for the determination of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Anal Chem* **1977,** *49*, (3), 386-90.
68. KEMI, Stockholmskonventionen – ämnen och genomförandeplan. *https://www.kemi.se/internationellt-samarbete/internationella-konventioner-och-overenskommelser/stockholmskonventionen-amnen-och-genomforandeplan* **2019**.
69. KEMI, Förbud mot klorerade lösningsmedel. *https://www.kemi.se/lagar-och-regler/regler-som-endast-galler-i-sverige/nationella-begransningar-och-forbud/svenska-regler-om-klorerade-losningsmedel* **2019**.
70. Skåne, L., Nya regler om trikloretylen *https://www.lansstyrelsen.se/download/18.4df86bcd164893b7cd93619a/1535032535941/TVL-info%202014:2%20Nya%20regler%20om%20trikloretylen.pdf* **2014**.
71. Andersson, Ö.; Blomkvist, G., Polybrominated aromatic pollutants found in fish in Sweden. *Chemosphere* **1981,** *10*, 1051-1060.
72. Johansson, A. K.; Sellstrom, U.; Lindberg, P.; Bignert, A.; de Wit, C. A., Temporal trends of polybrominated diphenyl ethers and hexabromocyclododecane in Swedish Peregrine Falcon (Falco peregrinus peregrinus) eggs. *Environ Int* **2011,** *37*, (4), 678-86.
73. Regeringen, En god livsmiljö. Proposition 1990/91:90. *https://www.riksdagen.se/sv/dokument-lagar/dokument/proposition/en-god-livsmiljo_GE0390* **1991**.
74. TCO, TCO´95 – Addition of hazardous content criteria, focusing on flame retardants and heavy metals; lead, cadmium and mercury. *https://tcocertified.com/the-story-of-tco-certified/* **2019**.
75. KEMI, Bromerade flamskyddsmedel– förutsättningar för ett nationellt förbud. Rapport från ett regeringsuppdrag. *https://www.google.se/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=2ahUKEwiC9qvNleLnAhVB5KYKHV65CA4QFjAAegQIAxAC&url=https%3A%2F%2Fwww.kemi.se%2Fglobal%2Frapporter%2F2003%2Frapport-4-03.pdf&usg=AOvVaw1bIzgN98j04Yq21kkiNCOD* **2003**.
76. Regeringen, Regeringens proposition 1997/98:145. Svenska miljömål. Miljöpolitik för ett hållbart Sverige. *https://www.google.se/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=2ahUKEwiwmebFmOLnAhXlzMQBHWprA4gQFjAAegQIARAC&url=https%3A%2F%2Fwww.regeringen.se%2F49bba3%2Fcontentassets%2Fc887c3695078405aa08d48990deec32e%2Fdel-1&usg=AOvVaw0JnKa6z6Ck9R9mEP9h8fPR* **1998**.
77. Norén, K.; Meironyte, D. In *Contaminants in Swedish human milk. Decreasing levels of organochlorine and increasing levels of organobromine compounds*, Organohalogen compounds, 1998; Organohalogen compounds: 1998; pp 1-4.
78. KEMI, Avveckling av PBB och PBDE. Rapport från ett regeringsuppdrag. *KemI Rapport 3/99* **1999**.
79. EU, 2455/2001/EC: Decision N0 2455/2001/EC of the European Parliament and of the Council of 20 November 2001. establishing the list of priority substances in the field of water policy

and amending Directive 2000/60/EC *http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:331:0001:0005:EN:PDF* **2001**.
80. OECD, Brominated Flame Retardants (BFRs): Hazard/Risk Information Sheets. PENTABROMODIPHENYLETHER (pentaBDE). *http://www.oecd.org/chemicalsafety/risk-management/42073463.pdf* **2008**.
81. Johansson, A. K.; Sellstrom, U.; Lindberg, P.; Bignert, A.; De Witt, C. A., Polybrominated diphenyl ether congener patterns, hexabromocyclododecane, and brominated biphenyl 153 in eggs of peregrine falcons (Falco peregrinus) breeding in Sweden. *Environ Toxicol Chem* **2009,** *28*, (1), 9-17.
82. EU, DIRECTIVE 2008/105/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL. *https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008L0105&from=EN* **2008**.
83. ECHA, Allmän rapport 2009. *https://echa.europa.eu/documents/10162/13560/echa_general_report_2009_sv.pdf* **2009**.
84. ECHA, Substance Infocard. Hexabromocyclododecane. *https://echa.europa.eu/sv/substance-information/-/substanceinfo/100.042.848* **2019**.
85. KEMI, Handlingsplan för en giftfri vardag 2011 – 2014. Delredovisning 2011 – 2013. **2014**.
86. KEMI, Långlivade organiska föroreningar - POP. *https://www.kemi.se/lagar-och-regler/ytterligare-eu-regler/langlivade-organiska-fororeningar-pop* **2019**.
87. EPA, EPA and 3M announce phase out of PFOS. *https://archive.epa.gov/epapages/newsroom_archive/newsreleases/33aa946e6cb11f35852568e1005246b4.html* **2000**.
88. Olsen, G. W.; Mair, D. C.; Lange, C. C.; Harrington, L. M.; Church, T. R.; Goldberg, C. L.; Herron, R. M.; Hanna, H.; Nobiletti, J. B.; Rios, J. A.; Reagen, W. K.; Ley, C. A., Per- and polyfluoroalkyl substances (PFAS) in American Red Cross adult blood donors, 2000-2015. *Environ Res* **2017,** *157*, 87-95.
89. KEMI, Perfluorerade ämnen - användningen i Sverige. *KEMI Rapport 6/06*. **2006**, 4-56.
90. EPA, 2010/2015 PFOA Stewardship Program. *https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/20102015-pfoa-stewardship-program* **2015**.
91. Naturvårdsverket, Förslag till gränsvärden för särskilda förorenande ämnen. *https://www.naturvardsverket.se/Documents/publikationer/620-5799-2.pdf* **2008**.
92. FDA, Update on Perfluorinated Grease-proofing Agents. *http://wayback.archive-it.org/7993/20171115164049/https://www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/Notifications/ucm308462.htm* **2017**.
93. IVL, Årsrapport 2011 för projektet RE-PATH. Mätningar av PFAS i närområdet till Stockholm Arlanda Airport och Göteborg Landvetter Airport. *https://www.ivl.se/download/18.343dc99d14e8bb0f58b7639/1454339598438/B2060.pdf* **2012**.
94. Regeringskansliet, Utredningen om spridning av PFASföroreningar i dricksvatten (M 2015:B). *https://www.regeringen.se/492d3a/contentassets/014c3e70e27c4ecf8d5b91553dd34559/utredningen-om-spridning-av-pfas-fororeningar-i-dricksvatten.pdf* **2015**.
95. EU, DIRECTIVE 2013/39/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 12 August 2013 amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. *https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:226:0001:0017:EN:PDF* **2013**.
96. Livsmedelsverket/KEMI, Brandskum som möjlig förorenare av dricksvattentäkter. *https://www.kemi.se/global/pm/2013/pm-5-13.pdf* **2013**.
97. OECD, Portal on Per and Polyfluorinated compounds. European Union. *https://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals/countryinformation/european-union.htm* **2020**.
98. Livsmedelsverket, Risk management of PFAS in drinking water and fish (in Swedish). *http://www.livsmedelsverket.se/livsmedel-och-innehall/oonskade-amnen/miljogifter/pfas-poly-och-perfluorerade-alkylsubstanser/riskhantering-pfaa-i-dricksvatten/* **2016**.
99. SGI, Riskbedömning PFAS. *https://www.swedgeo.se/sv/vagledning-i-arbetet/fororenade-omraden/hogfluorerade-amnen-pfas/riskbedomning-pfas* **2019**.

100. FDA, FDA Revokes Food Additive Approval for the Use of Long-Chain Perfluorinated Compounds as Oil and Water Repellents for Paper Used in Food Packaging. *http://wayback.archive-it.org/7993/20171114120118/https:/www.fda.gov/Food/NewsEvents/ConstituentUpdates/ucm479465.htm* **2015**.
101. KEMI, EU listar bisfenol A och PFDA som särskilt farliga ämnen. *https://www.kemi.se/nyheter-fran-kemikalieinspektionen/2016/eu-listar-bisfenol-a-och-pfda-som-sarskilt-farliga-amnen/* **2016**.
102. LaholmsbuktensVA, Perfluorerade ämnen i centrala Halmstad. *https://www.lbva.se/dricksvatten/vattnetikranen/pfas.4.1f7204ab16a69460ec4147f5.html* **2020**.
103. Furst, P., Dioxins, polychlorinated biphenyls and other organohalogen compounds in human milk. Levels, correlations, trends and exposure through breastfeeding. *Mol Nutr Food Res* **2006,** *50*, (10), 922-33.
104. Krauthacker, B.; Votava-Raic, A.; Herceg Romanic, S.; Tjesic-Drinkovic, D.; Reiner, E., Persistent organochlorine compounds in human milk collected in Croatia over two decades. *Arch Environ Contam Toxicol* **2009,** *57*, (3), 616-22.
105. HELCOM, Atmospheric Deposition of PCB-153 on the Baltic Sea. *https://helcom.fi/baltic-sea-trends/environment-fact-sheets/hazardous-substances/atmospheric-deposition-of-pcb-153/* **2018**.
106. Naturvårdsverket, Utsläpp av PCB till luft. *https://www.naturvardsverket.se/Sa-mar-miljon/Statistik-A-O/PCB-utslapp-till-luft/* **2019**.
107. Sobek, A.; Sundqvist, K. L.; Assefa, A. T.; Wiberg, K., Baltic Sea sediment records: Unlikely near-future declines in PCBs and HCB. *Science of the Total Environment* **2015,** *518-19*, 8-15.
108. Darnerud, P. O.; Atuma, S.; Aune, M.; Bjerselius, R.; Glynn, A.; Grawe, K. P.; Becker, W., Dietary intake estimations of organohalogen contaminants (dioxins, PCB, PBDE and chlorinated pesticides, e.g. DDT) based on Swedish market basket data. *Food Chem Toxicol* **2006,** *44*, (9), 1597-606.
109. EFSA, Update of the monitoring of levels of dioxins and PCBs in food and feed. *EFSA Journal* **2012,** *https://www.efsa.europa.eu/en/efsajournal/pub/2832*.
110. Bergkvist, P.; Ankarberg, E.; Aune, M. Källor till dioxiner i hönsägg 2004.
111. Broman, F.; Halldin Ankarberg, E.; Bergkvist, P., Hanteringsrapport gällande dioxin och dioxinlika PCB i ägg. *https://www.google.se/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=2ahUKEwj-7femwPbnAhUUBBAIHVbDDhkQFjAAegQIBhAC&url=https%3A%2F%2Fwww.livsmedelsverket.se%2Fglobalassets%2Fpublikationsdatabas%2Frapporter%2F2016%2Fhanteringsrapport-dioxin-och-dioxinlika-pcb-i-agg-2016.pdf&usg=AOvVaw1wD84fTX56kuKRGaoqZwru* **2016**.
112. Weber, R.; Herold, C.; Hollert, H.; Kamphues, J.; Blepp, M.; Ballschmiter, K., Reviewing the relevance of dioxin and PCB sources for food from animal origin and the need for their inventory, control and management. *Environ Sci Eur* **2018,** *30*, (1), 42.
113. Bignert, A.; Aune, M.; Gyllenhammar, I.; Lignell, A.; Nyberg, E.; Glynn, A., Temporal trends of Swedish environmental and human milk concentrations of dioxins, furans and dioxin-like PCBs, with forecasts to 2040. *Report to the Swedish EPA* **2020**.
114. Miller, A.; Hedman, J. E.; Nyberg, E.; Haglund, P.; Cousins, I. T.; Wiberg, K.; Bignert, A., Temporal trends in dioxins (polychlorinated dibenzo-p-dioxin and dibenzofurans) and dioxin-like polychlorinated biphenyls in Baltic herring (Clupea harengus). *Mar Pollut Bull* **2013,** *73*, (1), 220-30.
115. Assefa, A.; Tysklind, M.; Bignert, A.; Josefsson, S.; Wiberg, K., Sources of polychlorinated dibenzo-p-dioxins and dibenzofurans to Baltic Sea herring. *Chemosphere* **2019,** *218*, 493-500.
116. HELCOM, Atmospheric Emissions of PCDD/FS in the Baltic Sea Region. *https://helcom.fi/baltic-sea-trends/environment-fact-sheets/hazardous-substances/atmospheric-emissions-of-pcdd-fs/* **2018**.
117. Bustnes, J. O.; Bardsen, B. J.; Moe, B.; Herzke, D.; Hanssen, S. A.; Sagerup, K.; Bech, C.; Nordstad, T.; Chastel, O.; Tartu, S.; Gabrielsen, G. W., Temporal variation in circulating concentrations of organochlorine pollutants in a pelagic seabird breeding in the high Arctic. *Environ Toxicol Chem* **2017,** *36*, (2), 442-448.

118. AMAP, AMAP Assessment 2015: Temporal Trends in Persistent Organic Pollutants in the Arctic. *https://www.amap.no/documents/doc/amap-assessment-2015-temporal-trends-in-persistent-organic-pollutants-in-the-arctic/1521* **2015**.
119. Naturvårdsverket, Sources, transport, reservoirs and fate of dioxins, PCBs and HCB in the Baltic Sea environment. *http://www.naturvardsverket.se/Documents/publikationer/978-91-620-5912-5.pdf* **2009**.
120. Barber, J. L.; Sweetman, A. J.; van Wijk, D.; Jones, K. C., Hexachlorobenzene in the global environment: emissions, levels, distribution, trends and processes. *Sci Total Environ* **2005,** *349*, (1-3), 1-44.
121. Pacyna, J. M.; Breivik, K.; Munch, J.; Fudala, J., European atmospheric emissions of selected persistent organic pollutants, 1970–1995. *Atmospheric Environment* **2003,** *37, Supplement No. 1*, S119-S131.
122. Agency, E. E., Sources of HCB emmissions. *https://www.google.se/url?sa=t&rct=j&q=&esrc=s&source=web&cd=3&ved=2ahUKEwiw3uq3_N3nAhVO1qYKHW5KANsQFjACegQICxAG&url=https%3A%2F%2Fwww.eea.europa.eu%2Fpublications%2FEMEPCORINAIR5%2FSources_of_HCB_emissions.pdf&usg=AOvVaw3OojfBq-fLWoPbuQhhq5hy* **2005**.
123. Josefson, S., Hexaklorbensen i svenska sediment 1986–2015. *https://resource.sgu.se/produkter/sgurapp/s1823-rapport.pdf* **2018**.
124. EMEP, Assessment of transboundary pollution by toxic substances: Heavy metals and POPs. *http://en.msceast.org/reports/2_2019.pdf* **2019**.
125. Morf, L.; Smutny, R.; Taverna, R.; Daxbeck, H., Selected polybrominated flame retardants PBDE and TBBPA. Substance flow analysis. *ENVIRONMENTAL SERIES No. 338* **2002,** *http://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=12&cad=rja&uact=8&ved=2ahUKEwiMmYnj7_HnAhXyAxAIHUY6Dsw4ChAWMAF6BAgCEAE&url=http%3A%2F%2Fchm.pops.int%2FPortals%2F0%2Fdocs%2Ffrom_old_website%2Fdocuments%2Fmeetings%2Fpoprc%2Fsubmissions%2FComments_2006%2FSelected.brominated.flame.retardants.pdf&usg=AOvVaw2lP9x6KQJkj76XO1JHqj2L*.
126. Lassen, C.; Jensen, A. A.; Crookes, M.; Christensen, F.; Jeppesen, C. N.; Clausen, A. J.; Mikkelsen, S. H., Survey of brominated flame retardants. *https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=28&ved=2ahUKEwi3q5CE7fHnAhVipYsKHeUZBAIQFjAbegQIBxAB&url=https%3A%2F%2Fwww2.mst.dk%2FUdgiv%2Fpublications%2F2014%2F01%2F978-87-93026-90-2.pdf&usg=AOvVaw34us9JW7hBBdTu8FT1SNKR* **2014**.
127. KEMI, Omsättning av några bromerade flamskyddsmedel. *https://www.kemi.se/statistik/kortstatistik/produkter-och-branscher/flamskyddsmedel* **2010**.
128. KEMI, Hexabromocyklododekan (HBCDD) and tetrabrombisfenol-A (TBBPA). *https://www.google.se/url?sa=t&rct=j&q=&esrc=s&source=web&cd=3&ved=2ahUKEwiugJH7w_nnAhWxk4sKHWmvBjQQFjACegQIBxAC&url=https%3A%2F%2Fwww.kemi.se%2Fglobal%2Frapporter%2F2006%2Frapport-3-06.pdf&usg=AOvVaw1jczxrALajCY9sMhv10l9r* **2006**.
129. ECHA, European Union Risk Assessment Report. Diphenyl ether, pentabromo deriv. *https://www.google.se/url?sa=t&rct=j&q=&esrc=s&source=web&cd=3&cad=rja&uact=8&ved=2ahUKEwiQqMaF3vnnAhWixaYKHUYuBnUQFjACegQIAxAC&url=https%3A%2F%2Fecha.europa.eu%2Fdocuments%2F10162%2F781ee1e9-6c90-467e-998b-8910ca2793e5&usg=AOvVaw2luPh75zkHbuPPh-nApC6w* **2001**.
130. Prevedouros, K.; Cousins, I. T.; Buck, R. C.; Korzeniowski, S. H., Sources, fate and transport of perfluorocarboxylates. *Environ Sci Technol* **2006,** *40*, 32-44.
131. Livsmedelsverket, Swedish Market Basket Survey 2015. *https://www.livsmedelsverket.se/globalassets/publikationsdatabas/rapporter/2017/swedish-market-basket-survey-2015-livsmedelsverkets-rapportserie-nr-26-20172.pdf* **2015**.
132. Benskin, J. P.; Ahrens, L.; Muir, D. C.; Scott, B. F.; Spencer, C.; Rosenberg, B.; Tomy, G.; Kylin, H.; Lohmann, R.; Martin, J. W., Manufacturing origin of perfluorooctanoate (PFOA) in Atlantic and Canadian Arctic seawater. *Environ Sci Technol* **2012,** *46*, (2), 677-85.

133. Ahrens, L.; Ribell, E.; Josefsson, S.; Gustavsson, J.; Nguyen, M. A.; Wiberg, K., Screening av perfluoralkylerade ämnen och flamskyddsmedel i svenska vattendrag. *https://pub.epsilon.slu.se/11593/13/ahrens_l_etal_141017.pdf* **2014**.
134. Joerss, H.; Apel, C.; Ebinghaus, R., Emerging per- and polyfluoroalkyl substances (PFASs) in surface water and sediment of the North and Baltic Seas. *Sci Total Environ* **2019,** *686*, 360-369.
135. Wang, Z.; Cousins, I. T.; Scheringer, M.; Buck, R. C.; Hungerbuhler, K., Global emission inventories for C4-C14 perfluoroalkyl carboxylic acid (PFCA) homologues from 1951 to 2030, part II: the remaining pieces of the puzzle. *Environ Int* **2014,** *69*, 166-76.
136. Gyllenhammar, I.; Berger, U.; Sundstrom, M.; McCleaf, P.; Euren, K.; Eriksson, S.; Ahlgren, S.; Lignell, S.; Aune, M.; Kotova, N.; Glynn, A., Influence of contaminated drinking water on perfluoroalkyl acid levels in human serum--A case study from Uppsala, Sweden. *Environ Res* **2015,** *140*, 673-83.
137. Armitage, J. M.; Schenker, U.; Scheringer, M.; Martin, J. W.; Macleod, M.; Cousins, I. T., Modeling the global fate and transport of perfluorooctane sulfonate (PFOS) and precursor compounds in relation to temporal trends in wildlife exposure. *Environ Sci Technol* **2009,** *43*, (24), 9274-80.
138. Paul, A. G.; Jones, K. C.; Sweetman, A. J., A first global production, emission, and environmental inventory for perfluorooctane sulfonate. *Environ Sci Technol* **2009,** *43*, (2), 386-92.
139. Li, Y.; Fletcher, T.; Mucs, D.; Scott, K.; Lindh, C. H.; Tallving, P.; Jakobsson, K., Half-lives of PFOS, PFHxS and PFOA after end of exposure to contaminated drinking water. *Occup Environ Med* **2018,** *75*, (1), 46-51.
140. Glynn, A.; Kotova, N.; Dahlgren, E.; Lindh, C.; Jakobsson, K.; Gyllenhammar, I.; Lignell, S.; Nalsen, C., Determinants of serum concentrations of perfluoroalkyl acids (PFAAs) in school children and the contribution of low-level PFAA-contaminated drinking water. *Environ Sci Process Impacts* **2020**.
141. Glynn, A.; Nyström, J.; Benskin, J. P.; Plassmann, M. M.; Lignell, S.; Gyllenhammar, I.; Lindroos, A. K.; Ahrens, L., Koppling mellan halter av per- och polyfluorerade alkylsubstanser i dricksvatten och blodserum bland deltagarna i Riksmaten ungdom 2016-17. **2020**.