Ministry of Environment and Food of Denmark
Environmental Protection Agency

Risk assessment of fluorinated substances in cosmetic products

Survey of chemical substances in consumer products No. 169

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Sources must be acknowledged.

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Preface

This project is part of the Danish Environmental Protection Agency's chemical initiative, with the aim of assessing consumers' exposure to problematic chemistry. The purpose of the project is to build knowledge of PFAS in cosmetic products and to clarify whether using cosmetic products containing PFAS poses a risk to consumers.

The project was carried out from September to December 2017 by COWI and NIPSECT. The chemical analyses were performed by Eurofins.

The project has been followed by a steering committee composed of the following members:

- Toke Winther, Environmental Protection Agency
- Bettina Ørsnes Larsen, Environmental Protection Agency
- Anna Brinch, COWI
- Frans Christensen, COWI
- Allan Astrup Jensen, NIPSECT.

Summary and conclusion

The purpose of this project is to build knowledge of fluorinated substances in cosmetic products and to clarify whether the use of cosmetic products containing certain fluorinated substances presents a health risk to consumers. The project focuses on perfluoroalkyl and polyfluoroalkyl substances (PFAS), which are also denoted fluoroalkyl substances. PFAS and other fluorinated compounds are used in a variety of cosmetic products such as foundation, moisturizer, eyeshadow, powder, lipstick and shaving cream. PFAS occurs both as desired ingredients in cosmetic products and as unintentional degradation products and impurities from the production of the PFAS precursors used in certain cosmetic products.

The project consists of three phases:
1. Survey of PFAS in cosmetic products
2. Chemical analyses of PFAS and total organic fluorine content in selected cosmetic products
3. Health hazard and risk assessment

It should be noted that perfluoroalkyl substances are considered to be problematic as they are very persistent (vP) in the environment, some may accumulate in humans or the environment (bioaccumulative (B) or very bioaccumulative (vB)) and because some of the substances are known to be toxic (T).
For PBT/vPvB substances it is not possible to establish a safe level of exposure and emissions are to be minimised.

Survey of PFAS in cosmetic products
The purpose of the survey is to provide an overview of PFAS used in cosmetic products on the Danish market. This overview provides the basis for the selection of cosmetic products for chemical analysis in the second phase of the project. In the survey, various data sources have been identified - databases addressing cosmetic products and their ingredients, as well as a literature search on PFAS in cosmetic products - and reviewed. One of the main sources for the survey is an app from the Danish Consumer Council Tænk Kemi called 'Kemiluppen', which contains information about ingredients in a wide range of cosmetic products, reported by Danish consumers. In addition, two Danish trade associations have been contacted; however, this did not result in any additional information relevant to this project.

The results from the survey show that a variety of fluoroalkyl substances and other fluorinated compounds are present in cosmetic products. As already mentioned, this project only focuses on a part of these, namely fluoroalkyl substances. According to the databases reviewed, Polytetrafluoroethylene (PTFE) was found in most different product types, followed by $C_{9\text{-}15}$ fluoroalcohol phosphate. Generally, fluoroalkyl substances are used in a wide range of products, with emphasis on foundations, BB/CC[1] cream, creams/lotions and powders.

The concentration of PFAS in cosmetic products has been studied in two previous projects. Here the results showed that there was a large variation in the concentration of PFAS depending on the product type being analysed and the product brand. With the exception of sunscreens, the highest measured concentrations were found in foundations; the highest measured value was 2,160 ng/g for perfluorooctanoic acid (PFOA).

[1] BB can stand for both Beauty Balm and Blemish Balm. CC stands for Color Corrector.

The results from the survey also indicate that cosmetic products containing fluoroalkyl substances and other fluorinated compounds on the Danish market typically have women and, in a few cases, men as target groups. The survey has not identified cosmetic products containing PFAS-related substances distinctly targeting children.

Based on the results of the survey, 22 products, as well as two control products, were selected for chemical analysis. Only products with a declared content of PFAS in the product itself or with declared ingredients where there was knowledge of possible PFAS degradation products/impurities were selected. The constituents of the products were identified based on information from the product's International Nomenclature of Cosmetic Ingredients (INCI) list. Products with the following ingredients (INCI names) were prioritized:

- C_{9-15} fluoroalcohol phosphate
- Perfluorononylethyl carboxydecyl PEG-10 dimethicone
- Perfluorononyl dimethicone
- Perfluorooctyl triethoxysilane
- PTFE
- Polyperfluoroethoxymethoxy difluoroethyl PEG phosphate
- Ammonium C_{6-16} perfluoroalkyl ethyl phosphate

Actual products were then selected on the basis of a number of criteria, including the number of scans of the product in the 'Kemiluppen' app, product type, position of the ingredient name on the product ingredient list (where earlier listing indicate higher concentration), product target group and product price. In addition, the products' immediate availability in stores was taken into account.

Chemical analysis of PFAS and total organic fluorine content in selected cosmetic products

Of the 22 selected products, only 18 products were analysed, as three of the products no longer indicated declared content of the selected PFAS or other fluorinated compounds and the last product was not possible to purchase. The selected products were analysed for a number of single PFAS where analytical standards were available, as well as for total organic fluorine (TOrF) content.

One or more PFAS substances was identified in 17 products[2] (for hair spray and eyeliner, the substances were found only in one of the duplicate determinations). The highest concentration of a single substance was 3,340 ng/g PFHxA (perfluorohexanoic acid) found in a foundation, while the highest concentration of total PFAS (10,700 ng/g) was found in a concealer.

In addition, for two of the products (both foundations) perfluorooctanoic acid (PFOA) was found in concentrations above the forthcoming EU limit value of 25 ng/g. In six of the products, the proposed REACH EU sum limit value for C_9 -C_{14} perfluoroalkyl acids or perfluorocarboxylic acids (PFCAs) was also exceeded.

Using the TOrF method, fluorine was found in all analysed products, except for a single product (hair spray). There was a relatively large difference between the content of the individual

[2] The number of products is reduced from 18 to 17, as review of the INCI list of products revealed that one product (No. 13) has a declared content of synthetic fluoroplogopite instead of C_{9-15} fluorophosphate (the presence of which was the reason for this product's selection for analysis. Therefore, in practice, the number of analysed products, based on information on ingredients from the INCI list assumed to contain PFAS, was reduced to 17 in total.

PFASs and the concentration of organic fluorine in the products. This is because, in the absence of standards and analytical methods, it has not been possible to analyse for all of the PFAS-relevant substances listed in the INCI list of individual products. The relatively simple fluorinated alkyls, which were determined quantitatively, are probably derived primarily from impurities from the production and degradation products, as the free acids themselves are rarely used in cosmetic products. Examples of the substances used are listed in Table 4 and in Appendix 1.

Based on the results from the chemical analyses, following substances were selected for the hazard and risk assessment:

- Perfluorooctanoic acid (PFOA)
- Perfluorobutanoic acid (PFBA)
- Perfluoropentanoic acid (PFPeA)
- Perfluorohexanoic acid (PFHxA)
- Perfluorheptanoic acid (PFHpA)

The last four substances were selected as they were identified in the largest number of different cosmetic products and in relatively high concentrations. PFOA was chosen as a reference substance, against which the other selected perfluoroalkanoic acids can be evaluated and compared to. PFOA is the most well-known PFCA and is considered to be one of the most potent PFAS substances. In addition, PFOA was found in a relatively high concentration in a single product.

Hazard and risk assessment

The purpose of the risk assessment was to assess whether the measured content of fluoroalkyl substances in the analysed cosmetic products could pose a risk to consumers.
Exposure scenarios and risk assessment were prepared for the following product types:

- Body lotion
- CC cream/foundation
- Concealer

These product types were selected primarily because they contain the highest concentrations of the selected substances, and secondly based on consideration of the products' use, e.g. body lotion is used in larger amounts on the entire body while foundation and CC cream are used largely on the face. All three products are also "leave-on" products, i.e. they are intended to stay on the skin all day, with a consequently greater exposure expected compared to other product types that are intended to be washed off immediately after application ("rinse-off" products).

Hazard Assessment

The hazard assessment is based primarily on previous assessments of the selected substances where available within the EU framework, in other countries' assessments and/or in the Danish Environmental Agency's previous publications on PFAS, as well as IARC's recent assessment of PFOA. The hazard assessment is supplemented with new data from the literature as well as information on physicochemical properties from different databases.

In the hazard assessment, PFOA was used as a reference substance against which the four other selected PFCAs were evaluated with respect to toxicological properties, half-life in animals and humans, and distribution of the substances in animals and/or humans.

PFOA and its salts was used as a reference substance as they are relatively well-researched substances relative to the four other selected PFCAs (PFBA, PFPeA, PFHxA and PFHpA).

Among these, PFBA and PFHxA are reasonably well studied, while limited information is available for PFPeA and PFHpA.

In general, it was found that:

- In cases where No Observed Adverse Effect (NOAEL) values were available from comparable studies for the selected PFCAs, PFOA in all cases had the lowest NOAEL (0.06 mg/kg bw/day).
- Based on existing data, PFOA is apparently the only PFCA selected which: i) has an estrogenic effect in animal experiments and *in vitro* test systems; ii) is potentially carcinogenic, and iii) has an effect on the mammary gland.
- For the selected PFAS, there were major differences in the serum/plasma half-life of the perfluoroalkyl acids in different animals and humans as well as between the sexes. PFOA has the longest half-life of the selected PFCA (2-8.5 years in humans).
- PFOA is detected in the highest concentrations in bone and bone marrow in humans. The substance is also detected in high concentrations in human blood, lungs, and liver, as well as in the liver, bones and kidneys of mice. For humans, occurrence of PFOA in the brain has not been detected; however, it has been detected for PFBA and PFHxA. However, there is no data on potential toxicity associated with this occurrence.
- PFOA has the most effective binding to the protein TTR and thus the greatest effect on the thyroid gland out of the selected PFCA.
- PFOA has the strongest binding to albumin in the blood relative to the other PFCA under consideration in this report.

Selection of NOAEL for use in the calculation of risk

PFOA is therefore considered the most potent of the selected PFCA. Therefore, the exposure and risk assessment was initially based on PFOA, assuming that all measured PFAS content in the product is PFOA. As there are different approaches for NOAEL selection for PFOA, MoS calculations were made for three scenarios:

- ***Scenario 1 (dose approach):*** External oral NOAEL = 0.06 mg/kg bw/day (Perkins *et al*. 2004), which is the lowest NOAEL value from animal studies. Assuming that the oral absorption is 93%, an internal NOAEL was calculated at: 0.056 mg/kg bw/day.
- ***Scenario 2 (dose approach):*** External oral NOAEL = 1 mg/kg bw/day (Lau *et al*. 2006). As above, an internal NOAEL of 0.93 mg/kg bw/day was calculated.
- ***Scenario 3 (serum concentration approach):*** As discussed above, elimination of PFOA in humans is different from that in experimental animals. In order to take into account the difference in elimination of PFOA between humans and animals, a risk assessment was also performed which compares internal serum concentration values. As NOAEL, 20,000 ng/mL (equivalent to the external NOAEL of 1 mg/kg bw/day reproduced above) is used, as determined in Lau *et al*. (2006).

The above data originates from the two studies that the European Food Agency (EFSA) and the European Chemicals Agency (ECHA) use in regulatory assessments of PFOA and its salts.

Exposure assessment

The exposure assessment was carried out in accordance with the principles from the guidance for safety assessment of chemical substances in cosmetic products from the Scientific Committee for Consumer Safety (SCCS) (Notes of Guidance for the Testing of Cosmetic Products and Their Safety Evaluation). The Systemic Exposure Dosage (SED) was determined in scenarios using the default parameters specified in Notes of Guidance for adult consumers.

In the exposure assessment data for the total PFAS content (calculated as the sum of individual PFASs) for the selected product types was initially used. The highest measured total PFAS concentration within each product type was used in the calculation.

Two different situations are considered; one with 2% dermal absorption, which is expected to be a conservative assumption of how much of the PFAS salts would be absorbed, and one with 70% dermal absorption, based on data from a recent study on PFOA as acid. 70 % dermal absorption is considered to be conservative for the PFOA acid, as it is assumed that the total amount measured in the human epidermis (45%) would be systemically available. The study itself showed that 23-25% of PFOA as acid was absorbed. Furthermore, it is conservative to assume that all PFAS will occur as acids.

Table 1 Daily Systemic Exposure Dosage (SED) for the three selected product types assuming 2 and 70% dermal absorption, respectively (mg/kg bw/day).

Product type	2 % dermal absorption (for APFO)	70% dermal absorption (PFOA as acid)
Body lotion	2.05×10^{-7}	7.16×10^{-6}
Concealer	8.45×10^{-7}	2.96×10^{-5}
Liquid foundation	7.85×10^{-7}	2.75×10^{-5}

The highest estimated daily exposure (SED) for total PFAS was found using the concealer, unsurprising given the relatively high content of PFAS in the specific product found during the chemical analyses.

In the third scenario (serum concentration approach), the estimated external exposure dose was converted to an internal concentration. The highest SED values for PFOA as salt and as acid, respectively, were used (i.e. the SED values for the concealer). The calculated internal concentrations are shown in Table 2 below.

Table 2 Internal total PFOS-concentration calculated as PFOA as salt (2% dermal absorption) and acid (70% dermal absorption), respectively, calculated for concealer (in mg/ml).

Product type	2 % dermal absorption (for APFO)	70% dermal absorption (PFOA as acid)
Concealer	1.66×10^{-5}	5.80×10^{-4}

The calculated internal concentration at 70% dermal absorption is high compared to the serum/plasma concentrations of PFOA listed in the background document for REACH Annex XV restriction proposals for PFOA (ECHA, 2015b). This also applies when taking into account the real content of PFOA in the concealer and not the total PFAS concentration.

Risk assessment

The risk assessment follows the principles of "Notes of Guidance" (SCCS, 2016), and involves the calculation of a Margin of Safety (MoS). Margin of Safety (MoS) is a safety margin that expresses the relationship between NOAEL and the estimated exposure. In order to conclude that there is little or no risk, MoS must be greater than the assessment factor that would be used if a risk assessment, for instance as under REACH, was performed. The “Notes of Guidance” sets a default value of 100 (covering default factors of 10 for intraspecies differences

and 10 for interspecies differences) as assessment factor. Therefore, as a rule of thumb: if the calculated margin of safety is less than 100, this basically indicates a risk to consumers[3].

The risk assessment is done stepwise/iteratively, which means that initially the total content of PFAS is used and the potency of the individual PFAS substances is not taken into account, thus assuming that all identified PFAS substances are as potent as the most potent PFAS (worst case consideration in relation to the hazard assessment). Thus, the highest calculated exposure values for total PFAS content are held against the NOAEL value for PFOA, as the most potent of the selected PFAS. If no risk is identified in the first step, it is not necessary to proceed. If a risk is identified in the first step, the risk assessment is expanded, taking into account the content and potency of the individual PFAS substances, in order to clarify whether the risk identified in the first step is real.

Table 3 Calculated MoS values for the three different scenarios assuming 2 and 70% dermal absorption, respectively. The calculations are made for the concealer as it has the highest daily exposure (SED).

Scenario	2 % dermal absorption (for APFO)	70% dermal absorption (PFOA as acid)
Scenario 1	66,012	1,886
Scenario 2	1,100,201	31,434
Scenario 3	1,207	34

As seen, the calculated MoS for the individual cosmetic product (based on the concealer as worst case) are well above 100 in the scenarios based on NOAEL and exposure expressed as dose (Scenario 1 and 2) when assuming both 2 and 70% dermal absorption. The same is true for scenario 3 if 2% absorption is considered, whereas in scenario 3 with an assumption of 70% absorption, the estimated MoS is 34, which is below the default assessment factor of 100. However, according to the principles of Notes of Guidance described above, deviations from the use of this default factor is possible, depending on the data base. The Chemical Assessment Agency (ECHA) Risk Assessment Committee (RAC) recommends an assessment factor of 25 for the general population using the same NOAEL as in scenario 3 (NOAEL expressed as serum concentration). Applying the same assumption as RAC – i.e. that a part of the interspecies differences has been accounted for in scenario 3, MoS should be above 25 to conclude that there are no indications of consumer risk. It is seen that the calculated MoS of 34 is higher than 25, which indicates that there is no risk for consumers in scenario 3 when using the individual cosmetic product.
A MoS below 25 and thus a risk in the most conservative (extreme worst case scenario) scenario cannot be ruled out if a consumer uses the three cosmetic products at the same time. This is the case if the concealer is used in more than 1/10 of the face and body lotion and foundation is used as assumed in Notes of Guidance.
The assessment is conservative/extreme worst case for the following reasons:

- Dermal absorption is set conservatively at 70%. As mentioned earlier, the value is based on a study (Franko *et al*., 2012) which showed that approximately 25% PFOA (as acid) was absorbed through the skin and that 45% of the substance was retained in the epidermis. If using the situation of 70% dermal absorption, it is assumed that the proportion of PFOA retained in the epidermis would be systemically available, which is a highly conservative assumption. If instead 25% dermal absorption is assumed, MoS for the individual cosmetic product would be 97 in scenario 3. If the concealer is used in 1/10 of the face and body lo-

[3] Notes of Guidance, however, prescribe that these default factors may be deviated from when the specific data gives rise to it or otherwise taking into account differences between humans or between humans and animals. This is assessed on a case by case basis.

tion and foundation is used as assumed in Notes of Guidance while 25% dermal absorption is considered, MoS will be 70 in scenario 3.
- It is assumed that all PFAS measured in the chemical analyses would occur as PFOA, which, on the basis of the available data, is assumed to be the most toxic PFAS and the PFAS which is eliminated slowest from the human body. Again, this is a highly conservative assumption. If the calculations instead are conducted for PFOA concentration alone or using an 'average' NOAEL for the selected substances (which would be higher than that for PFOA alone), MoS would be significantly larger.

All in all, based on highly conservative scenarios and the no-effect values used by the regulatory authorities within the EU, it is assessed that the measured concentrations of PFCA in cosmetic products themselves do not pose a risk to consumers. However, in the most conservative scenario a risk cannot be completely ruled out if several cosmetic products containing PFAS are used at the same time - this very conservative scenario is, however, not considered to be particularly realistic.

Still, the above conclusion must be seen in light of the following uncertainties:
- The conclusion is based on studies which are currently considered relevant for quantitative risk assessment in the EU. It should be mentioned that a number of studies of PFOA and its salts indicate that there may be effects at lower levels, but these studies were not considered suitable for quantitative risk assessment in the RAC opinion.
- Data show that PFOA and other PFCA is eliminated much more slowly from serum in humans than from serum in experimental animals. It has been attempted to take this issue into account in scenario 3. This scenario is uncertain because i) the external dose is theoretically converted to an internal concentration, and ii) the scenario does not directly account for differences in deposition in human or animal organs.
- Cosmetic products may contain lipophilic precursors, which may be absorbed through the skin and which, after exposure, could be metabolised to PFAS to an unknown extent. These precursors are not quantified in the chemical analyses. The analysis of total organic fluorine (TOrF) may provide an indication of the amount of total organic fluorine in the cosmetic products, but it is unknown as to how much of the measured content consists of lipophilic precursors that could be metabolised to PFAS in the body after dermal uptake. Therefore, from the chemical analyses it cannot be determined the extent to which lipophilic precursors could contribute to the PFAS blood concentration of the consumer using the cosmetic products.
- It is assumed that PFOA is the most toxic PFCA. At the present time, too little is known about other PFCAs to rule out that these substances may be as hazardous to health or more so than PFOA in some cases.
- Most toxicity studies are based on the PFCA salts, which cannot be assumed to have the same toxicological profile as the acids, thus adding further uncertainty to the conclusions. The risk assessment only takes PFCA exposure from the cosmetic products into account. Thus, eventual exposure of PFCA from other sources or other substances with the same mode of action is not considered.

Despite the fact that the risk assessment, based on the measured concentrations of PFCA, shows that the individual cosmetic product in itself is unlikely to pose a risk for consumers, the concentrations in products 4 and 17 exceed both the upcoming EU limit value of 25 ng/g for PFOA and the proposed EU sum limit for C_9-C_{14} PFCA of 25 ng/g. Product No. 10, 16, 21 and 23 also exceeds the proposed sum limit value for C_9-C_{14} PFCA. PFOA, its salts and PFOA-related substances are banned from 4 July 2020. On 6 October 2017, a proposal has been submitted to ECHA to ban the manufacture and use of C_9-C_{14} PFCA, salts thereof and C_9-C_{14} PFCA-related substances.

C_9-C_{14} PFCA, PFOA, PFHpA, PFHxA, PFPeA, PFBA and other perfluoroalkyl acids are extremely persistent substances. Any emission of these substances or their precursors will contribute to an accumulation in the environment and thus potentially also to an increased exposure of humans via the environment

1. Introduction

1.1 Background and purpose of the project

Perfluoroalkyl and polyfluoroalkyl substances (PFAS), also known as fluoroalkyl substances (or the short term 'fluorinated substances'), are a large group of substances used in a wide range of consumer products to make them water-, grease- and dirt-repellent. Perfluoroalkyl substances are considered to be problematic as they are very persistent (vP) in the environment, some may accumulate in humans or the environment (bioaccumulative (B) or very bioaccumulative (vB)) and because some of the substances are known to be toxic (T).
For PBT/vPvB substances it is not possible to establish a safe level of exposure and emissions are to be minimised[4].
PFAS and other fluorinated compounds are used in cosmetic products because they are surfactants and therefore make creams etc. penetrate the skin more easily, make the skin brighter, make the skin absorb more oxygen, or make the makeup more durable and weather resistant. Fluoroalkyl substances and other fluorinated compounds are used, for example, in foundation, moisturizer, eyeshadow, powder and lipstick, shaving cream etc.

PFAS are used as cosmetic ingredients in themselves, but are also found in cosmetic products as degradation products of larger fluorinated molecules or as residues from production.

In this report, “fluoroalkyl substances” is used as term for PFAS, whereas “other fluorinated compounds” denote substances that do not comply with the PFAS definition (i.e. which do not have a functional group).

1.1.1 Purpose and delimitations

The purpose of the project is to build knowledge of fluoroalkyl substances in cosmetic products and to clarify whether the use of cosmetic products containing certain fluoroalkyl substances presents a health risk to consumers.

This project has chosen to focus on cosmetic products with declared PFAS or other fluorinated compounds wherein there is the potential to find residues of PFAS from production, and which are available to consumers in the Danish market.

The project consists of three different parts:
1. Survey of PFAS in cosmetic products
2. Chemical analysis of PFAS and total organic fluorine content in selected cosmetic products
3. Health hazard and risk assessment

The project focuses on perfluoroalkyl and polyfluoroalkyl substances (PFAS), which are also known as fluoroalkyl substances or fluorinated substances. These fluorinated substances should not be confused with the water-soluble inorganic fluoride salts used in, for example, toothpaste to strengthen the dental enamel (e.g. sodium fluoride (NaF) or sodium fluorophosphate (Na_2PO_3F)), substances not covered by this report. In addition, a number of organic fluorinated compounds that do not meet the definition of PFAS are also not covered by this report.

[4] REACH Annex I, paragraph 6.5

1.2 Regulation of cosmetic products

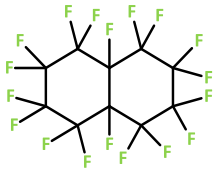
Cosmetic products are defined in Article 2 part 1 (a) of the Cosmetics Regulation as: "*any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours*".

The Cosmetics Regulation contains a number of provisions regarding the content of chemical substances in cosmetic products and labelling of the products. According to Article 3 of the Cosmetic Regulation, a cosmetic product made available on the market in the EU must be safe for human health when used under normal conditions or under conditions reasonably foreseeable.

The Cosmetics Regulation also contains a number of restrictions on various chemical substances; for example, only certain preservatives are permitted. A safety assessment of the cosmetic products (Article 10) must be made before the products can be placed on the market. According to the Cosmetics Regulation, cosmetic products must be labelled with a full declaration of contents (Article 19). It is therefore possible to identify which substances have been used in the products from the product's packaging. In the ingredient list, the ingredients must be indicated by their INCI name. INCI is an abbreviation for "International Nomenclature Cosmetic Ingredients" and is a common nomenclature that must be used to declare the content of cosmetic products in the EU.

1.3 Description of the substances concerned

Various types of fluoroalkyl substances and compounds are used in cosmetic products, i.e. both substances that fall within the definition of PFAS, which are therefore included in this project, as well as other substances, e.g. certain organic fluorinated compounds, such as perfluorodecalin, which does not fall under the definition of PFAS. As already mentioned, inorganic fluorinated compounds are also outside the scope of the project.



Perfluorodecalin

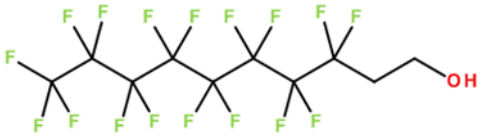
This project focuses on the use of perfluoroalkyl and polyfluoroalkyl substances (PFAS) in cosmetic products, which are used, *inter alia*, to reduce surface tension. In many cases, these are mixtures of fluoroalkyl substances with different lengths of the polyfluoroalkyl chain.

The commonly used, often complex, fluorinated substances and other fluorinated compounds may also contain residues of the basic perfluoroalkyl acids or perfluorocarboxylic acids (PFCA).

The most important PFCA is perfluorooctanoic acid (PFOA) with a perfluoroalkyl chain of seven carbon atoms:

PFOA

On 13 June 2017, the European Commission published: "Regulation (EU) 2017/1000 the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards perfluorooctanoic acid (PFOA), its salts and PFOA-related substances". The restriction will enter into force on 4 July 2020. The restriction includes 8:2 fluorotelomers and related substances (precursors) that can be broken down into, for example, PFOA. The restriction proposal lists more than 50 PFOA-related substances (ECHA, 2015a).



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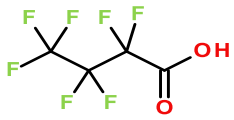
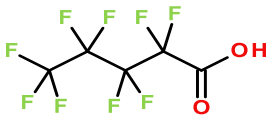
PFOA and its salts and related substances are not normally used in cosmetic products, but precursors of PFOA and salts have previously been used in various cosmetic products. These have been replaced by precursors to perfluorocarboxylic acids with shorter or longer perfluoroalkyl chains.

Fluoroalkyl substances with longer perfluoroalkyl chains than PFOA are, however, also on their way to become phased out and prohibited because they are considered to be both very persistent, highly bioaccumulative and toxic (PBT/vPvB substances). Therefore, on 6 October 2017, Germany in cooperation with Sweden submitted a proposal for restriction to ban production, use and marketing in the EU of C_9-C_{14} perfluoroalkanoic acids (PFCAs) and their salts and precursors (ECHA, 2017). The substances concerned are perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA), perfluorododecane acid (PFDoDA), perfluorotridecanoic acid (PFTrDA) and perfluorotetradecanoic acid (PFTeDA) and their salts and precursors.

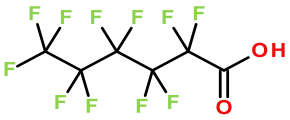
The following short-chain PFCA and their precursors, which are currently among the most used, are not (yet) regulated. These include, for example, PFBA, PFPeA, PFHxA and PFHpA, where PFBA and PFHxA are the most important:



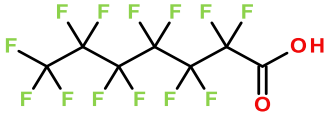
PFBA



PFPeA



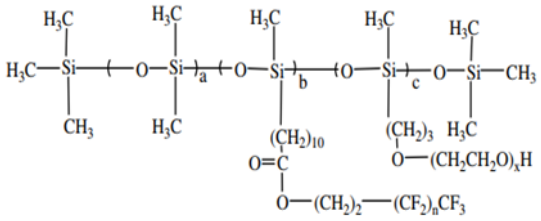
PFHxA



PFHpA

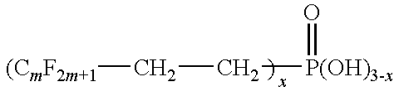
In some cases, the polyfluoroalkyl group is bound to a siloxane, a phosphorus compound, an ether or other group from which it can be cleaved again, either during use of the product or after absorption into the body. This process is illustrated for perfluoroalkylethyl carboxydecyl

peg-10 dimethicone from which one side chain can be hydrolysed to release fluorotelomer alcohols (FTOH).



Perfluoroalkylethyl carboxydecyl peg-10-dimethicone

Another example is fluorotelomer phosphates of different chain lengths, which can also degrade to FTOH. As mentioned above, FTOH can be degraded to PFCA, e.g. PFOA.



Fluorotelomer phosphates

1.3.1 Limit values for the substances concerned

In the EU restriction of PFOA, its salts and related substances, it is stated that PFOA and its salts should not be used in articles and chemical mixtures in terms of production, sales and imports at concentrations above 25 ng/g and that related substances may not be used in concentrations above 1000 ng/g (ECHA, 2015a).

In the proposal for EU restriction of C_9-C_{14} perfluoroalkanoic acids, their salts and precursors, a limit value of 25 ng/g and 260 ng/g is suggested for the sum of C_9-C_{14} PFCA and their salts and the sum of C_9-C_{14} PFCA precursors, respectively (ECHA, 2017). It should be noted that the PFOA limit values and the proposed C_9-C_{14} PFCA levels are not risk-based (not based on a risk to humans) as for PBT/vPvB substances it is not possible to establish a safe level of exposure with sufficient reliability under REACH[5]. The limit values are therefore set as low as technically possible, so that it is still possible to market raw materials based on short-chain PFAS containing residues of the long chain PFAS (PFOA, C_9-C14 PFCA and their related substances) up to the respective limit values.

[5] In REACH Guidance R11, 2017 (page 11) it is stated that "*A conventional hazard assessment of the long-term effects and the estimation of the long-term exposure cannot be carried out with sufficient reliability for the purpose of assessing the safety of sub-stances satisfying the PBT and vPvB criteria in Annex XIII"*. REACH Guidance R11, 2017 (page 11) furthermore states that "*experience with PBT/vPvB substances has shown that they can give rise to specific concerns that may arise due to their potential to accumulate in parts of the environment and i) that the effects of such accumulation are unpredictable in the long-term; and ii) such accumulation is in practice difficult to reverse as cessation of emission will not necessarily result in a reduction in substance concentration"*

In addition, Denmark has established a sum criterion for drinking water, groundwater and soil for 12 specific PFAS compounds (PFBS, PFHxS, PFOS, PFOSA, 6: 2 FTS, PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA and PFDA). The limit value is 0.1 µg/L for drinking and groundwater and 0.4 mg/kg soil (dry matter) for soil. The criterion is administratively established, as there are only sufficient data available for a health assessment for two of the PFAS compounds (PFOS and PFOA) (Danish EPA, 2015). Other EU countries and the United States have also established limit values for PFAS in drinking water.

2. Survey of PFAS in cosmetic products

2.1 Method

The purpose of the survey was to provide an overview of which PFAS are found in cosmetic products in the Danish market. This overview formed the background for the selection of cosmetic products for chemical analysis in the second phase of the project.

The survey consisted of:

- A review of survey data from Tænk Kemi and other databases on the use of PFAS and other fluorinated compounds in cosmetic products
- A review of known literature describing the use of PFAS in cosmetic products. The literature search was done by searching the terms "PFAS" or "PFCA" in combination with "cosmetics" on the Web of Science, as well as a general Google search of these terms. Therefore, no extensive literature search has been made in relation to this project.

In addition, the Danish Environmental Protection Agency contacted the following Danish trade associations:

- VKH (The Association of Danish Detergents and Cosmetics Industries)
- The Danish Association of Cosmetics and Detergents (formerly known as SPT, Association of Danish Cosmetics, Toiletries, Soap and Detergent Industries)

VKH has informed the Danish Environmental Protection Agency that none of their members uses fluorinated substances in cosmetic products.

2.2 Survey

2.2.1 Databases

2.2.1.1 Kemiluppen (TÆNK Kemi)

The Danish Consumer Council, Tænk Kemi, launched a free app, "Kemiluppen"[6], in December 2015, whereby consumers can scan the barcode for cosmetic products with their smartphone. Based on its constituents, the product is subsequently evaluated by Tænk Kemi, resulting in a classification in category A, B or C. Tænk Kemi's assessment is based on existing lists and knowledge of problematic substances, which means that the classification is solely based on a hazard assessment and not an actual risk assessment of the products.

Kemiluppen had approx. 223,000 downloads as of September 2017 (Tænk Kemi, personal comm., 2017).

In June 2017, Tænk Kemi provided an extract of all scanned products containing fluoroalkyl substances and other fluorinated compounds from the app. At the time of data extraction, there were a total of 11,108 evaluated cosmetic products (entered as separate barcodes) in Kemiluppen's database, and 78 products had declared contents of fluoroalkyl substance and other fluorinated compounds (Tænk Kemi, personal comm., 2017). These products were identified by Tænk Kemi by comparing the ingredient lists of the products found in the database with a list of identified fluoroalkyl substances and other fluorinated compounds prepared by

[6] http://kemi.taenk.dk/bliv-groennere/kemiluppen-tjek-din-personlige-pleje-uoensket-kemi

Tænk Kemi. This list was primarily compiled on the basis of information from the European Commission's Cosmetics and Ingredients Database (CosIng) (Tænk Kemi, personal comm., 2017).

The data extraction also includes information about how many times the individual product has been scanned by consumers, providing an indication of the market for the individual product. According to Tænk Kemi, the most popular products in Kemiluppen have been scanned more than 10,000 times each (Tænk Kemi, personal comm., 2017).

As shown in Table 4, PTFE is found in most product types (13 in total), followed by C_{9-15} fluorophosphate, found in four different product types. The other fluoroalkyl substances and fluorinated compounds are found in one or two different product types. Looking at the product types, most different fluoroalkyl substances and fluorinated compounds have been found in creams/lotions (six different substances), followed by foundation, as well as BB/CC cream[7] (three different substances in each). PTFE is the only fluorinated compound found in shaving cream, blush/highlighter, brow products, mascara/lash products, wax, eye cream and eyeshadow.

[7] BB can stand for both Beauty Balm and Blemish Balm. CC stands for Color Corrector. Both BB and CC cream are moisturising creams with color that are used in the same way as foundation, but they provide a lighter coverage.

Table 4 Overview of the presence of fluoroalkyl substances and other fluorinated compounds in cosmetic products as well as number of product scans within the specified product types, cf. the app 'Kemiluppen' from Tænk Kemi (data from Tænk Kemi, Pers. comm, 2017).

INCI name	Shaving foam/ shave gel	BB/CC cream	Blush/ highlighter	Body lotion/ body cream	Brows	Concealer/ corrector	Cream/lotion	Foundation	Hair spray/ heat spray	Hair mousse	Mascara// lashes	Nail polish/ nail care	Primer/fixer	Powder	Cleansing wipes	Scrub/peeling	Wax/cream/ gel/oil	Eye Pencil/ eyeliner	Eye cream	Eyeshadow	Total number of scans
Acetyl trifluoromethylphenyl valylglycine		55					1,533														1,588
C_{9-15} Fluoroalcohol phosphate		3,303				198		3,714						611							7,826
Methyl perfluorobutyl ether, Methyl perfluoroisobutyl ether													216								216
Perfluorodecalin												118			30						148
Perfluorodecalin, Polyperfluoromethylisopropyl ether							83														83
Perfluorononyl dimethicone																		14			14
Perfluorononylethyl carboxydecyl peg-10 dimethicone																997					997
Perfluorooctyl triethoxysilane		1,826						1,847													3,673
Polyperfluoroethoxymethoxy difluoroethyl peg phosphate									7	3											10
Polyperfluoroisopropyl ether							230														230
Polyperfluoromethylisopropyl ether							1,584														1,584
PTFE (polytetrafluoroethylene)	6,809		1,640	280	300	76	980	404			2,280			211			181		91	3,361	16,614
Tetradecyl aminobutyroylvalylaminobutyric urea trifluoroacetate				622			852														1,474

2.2.1.2 Skin Deep Database

Skin Deep Database is a database of cosmetic products developed by the US Non-Profit Organization Environmental Working Group. The database was launched in 2004 and contains information about cosmetic products and their ingredients. The Skin Deep database currently contains information about 70,806 products from 2,117 different brands. Information about ingredients comes mainly from the product's own ingredient list, but also from the scientific literature or from industry (EWG, n.d.). The database divides the products into recent products (products found on the market in the last 3 years) and old products (products found on the market between 3 and 6 years ago).

To find relevant products, the search box was used to search for "fluoro" in the database. This search resulted in 40 hits, after which potential fluoroalkyl substances and other fluorinated compounds were selected (21 in total). The database was hereafter examined more thoroughly as to the types of products the substances were found in. Substances found only in old products were excluded, as for these products it is highly likely that the composition has changed such that the products no longer contain the relevant fluorinated substances. Subsequently, a Google search was carried out for the specific product names identified in the Skin Deep database, to investigate whether Danish consumers can buy the product. This selection resulted in 11 substances found in product types sold in Denmark as well as one substance for which it is uncertain whether it is found in products sold in Denmark (see Table 5) (see also the table in Appendix 1). In some cases there was an overlap with the products identified through the Kemiluppen database.

Table 5 Data from the Skin Deep database for selected fluoroalkyl substances and other fluorinated substances

INCI name	Product type (number of products)	Comment
C_{9-15} Fluoroalcohol phosphate	Makeup with SPF (21), foundation (21), concealer (11), BB cream (4), sunscreen med SPF >30 (4), eyeliner (2), facial cream (2), Anti-aging cream (1), skin lightening product (1)	Several of the products are also sold in DK.
Octafluoropentyl methacrylate	Hairspray (4), conditioner (3), shampoo (3), hair care/serum (2), mask (1), hair styling	All products are from the same brand, which is also sold in DK.
C_{4-18} Perfluoroalkylethyl thiohydroxypropyltrimonium chloride	Conditioner (1)	The product is sold online via a Danish retailer.
Polytetrafluoroethylene acetoxypropyl betaine	Shaving cream (1)	The product is sold online via a Danish retailer.
Perfluorononyl octyldodecyl glycol meadowfoamate	Blush (1)	The product is sold online via a Danish retailer.
Perfluorononylethyl carboxydecyl peg-10 dimethicone	Conditioner (1), serum (1)	The serum is sold online via a Danish retailer.
Perfluorononyl dimethicone	Eyeliner (60), eyeshadow (8), lip balm (1), shaving cream (1), hairspray (1)	Uncertain whether products are sold in DK, but some of the brands are
Polyperfluoroethoxymethoxy difluoroethyl peg phosphate	Sunscreen SPF >30 (1), Sunscreen SPF 15-30 (3)	The products are not immediately sold in DK
Perfluorodecalin	Facial cream (11), sunscreen (6), anti-aging product (6), eye cream (5), CC cream (5), facial cleansing (4), acne treatment (3), mask (2), shampoo (1), conditioner (1), facial gel (1), lip	One of the brands is sold in several places in DK.

INCI name	Product type (number of products)	Comment
	plumber (1), scrub (1), nail polish (1), hair styling (1)	
Perfluorooctyl triethoxysilane	CC cream (2)	The product is sold online via a Danish retailer.
Methyl perfluorobutyl ether	Lip product (1), mask (1)	The products are sold online via a Danish retailer.
PTFE (polytetrafluoroethylene))	Foundation (17), eyeshadow (14), makeup with SPF (11), moisturizer with SPF (9), mascara (9), facial powder (8), blush (7), anti-aging product (6), bronzer/highlighter (6), moisturising cream (3), shaving foam (2), shaving foam for men (2), eye cream (2), facial cream (1), brow product (1), other eye makeup (1)	Few of the products are sold in DK.

2.2.1.3 Green Science Policy database

The Green Science Policy (GSP) Institute is a US NGO institute aiming to facilitate knowledge and awareness raising of responsible use of chemicals to researchers, politicians and other stakeholders. In 2014, the GSP Institute has prepared an overview of fluoroalkyl substances and other fluorinated compounds in cosmetic products (GSP, 2014). This overview is based on data from the Skin Deep database (see section 2.2.1.2) and the GoodGuide® database, another US database that evaluates different consumer products based on different parameters depending on what the consumer product is (the database contains information about cosmetic products, food, household products (cleaning) and cosmetic products for children). The cosmetic products are evaluated based on their ingredients, corresponding to the products in the Skin Deep database. Relevant substances and product types from GSP's overview not already included in data from the Skin Deep database are included in Appendix 1.

2.2.2 Literature data

Fujii *et al*. (2013) conducted a study of PFCA concentrations in different types of cosmetic products. The study selected 24 different cosmetic products for face and nails, including nine different sunscreens, for which the ingredient list indicated that the product contained either polyfluoroalkyl phosphate esters (PAP) or other fluorinated substances. The study was conducted on cosmetic products purchased in Japan. The country of origin for the products was mainly Japan, but two of the analysed products originated in France and one originated in the United States.

The results showed that 87% (13 out of 15) of cosmetic products (excluding sunscreen), where PAP or other types of fluorinated substances were listed in the ingredients, contained concentrations of PFCA. For sunscreens alone, this result was 89% (8 out of 9). The highest concentrations of PFCA were found in sunscreens; 19 µg/g total PFCA was the highest (Table 6).

Table 6 Content of PFCA measured in sunscreens (Fujii *et al.*, 2013)

Substance	Concentrations [ng/g]
PFHxA (C_6)	180-6,500
PFHpA (C_7)	53-670
PFOA (C_8)	3.7-5,700

Substance	Concentrations [ng/g]
PFNA (C_9)	7.3-670
PFDA (C_{10})	1.9-2,900
PFUnDA (C_{11})	47-330
PFDoDA (C_{12})	78-1,400
PFTrDA (C_{13})	28-140
PFTeDA (C_{14})	28-600

Among the cosmetic products (excluding sunscreen), the highest concentrations were found in foundations - both solid (i.e. powder) and liquid products, see Table 7. The lowest PFCA concentrations were found in lipstick. The total concentrations of PFCA, in cases where all nine PFCAs were found in the same product, ranged between 140 ng/g (makeup base coats) and 5.9 µg/g (solid powder foundation).

Table 7 Content of PFCA measured in other cosmetic products (Fujii *et al*. 2013)

Substance	Concentrations [ng/g]	Product types
PFHxA (C6)	4.7 – 2,100	Foundation (liquid and solid), manicure product, manicure base coat[8], liquid makeup base[9]
PFHpA (C7)	13-290	Foundation (liquid and solid), manicure product, liquid makeup base
PFOA (C8)	4.1-1,700	Foundation (liquid and solid), manicure product, manicure base coat, liquid makeup base, lipstick
PFNA (C9)	1.0-380	Foundation (liquid and solid), manicure product, manicure base coat, liquid makeup base, lipstick
PFDA (C10)	2.8-1,000	Foundation (liquid and solid), manicure product, manicure base coat, liquid makeup base, lipstick
PFUnDA (C11)	0.76-180	Foundation (liquid and solid), manicure product, manicure base coat, liquid makeup base, lipstick
PFDoDA (C12)	2.4-940	Foundation (liquid and solid), manicure product, manicure base coat, liquid makeup base, lipstick
PFTrDA (C13)	0.91-71	Foundation (liquid and solid), manicure product, liquid makeup base
PFTeDA (C14)	0.75	Foundation (liquid and solid), manicure product, manicure base coat, liquid makeup base, lipstick

As shown in the above table, concentrations of the different PFCAs vary widely depending on the specific cosmetic product analysed.

As a control, two products (a nail product and a sunscreen) that were manufactured by the same manufacturers, but where PAP or other fluorinated substances were not included in the ingredients list, were analysed. These products contained no detectable levels of PFCA; according to the authors of the study, this fact indicates that PAP may be an important source of PFCA in cosmetic products (Fujii *et al*., 2013). To investigate this idea further, two commercially available raw materials (mica and talc) treated with PAPs were also analysed for PFCA

[8] A nail polish is laid as a base under ordinary nail polish as a ridge-filler and in order to achieve a more uniform surface

[9] Typically a so-called "primer" laid under foundation, to make it last longer and to create a more even surface

content. In mica, the concentration of individual PFCA was 1.1-8.4 µg/g and the total amount of PFCA was 35 µg/g. In talc, the concentration of individual PFCA was 0.06-0.6 µg/g and total PFCA 2.5 µg/g. The authors estimated, based on information about the content of PAP in the raw materials, that the total amount of PFCA in raw materials containing PAP was 700 µg/g PAP and 50 µg/g PAP for mica and talc, respectively. This investigation suggests that raw materials with PAP may be an important source of PFCA in cosmetic products (Fujii *et al*., 2013).

In Sweden, Naturskyddsföreningen (Nature Conservation Association) analysed 22 cosmetic products from nine different brands for PFAS content. The products come from well-known brands and were randomly selected. All products had declared contents of fluorine.

The PFAS and other fluorinated compounds listed in the ingredients of the products were (INCI names):

- C_{9-15} Fluoroalcohol Phosphate
- Ammonium c_{6-16} perfluoroalkylethyl phosphate
- Polyperfluoroethoxymethoxy difluoroethyl peg phosphate
- Polyperfluoromethylisopropyl ether
- Perfluorononyl dimethicone
- Perfluorooctyl triethoxysilane
- Polytef
- Polytefum
- PTFE

A total of 16 different PFAS were analysed: (PFBS, PFHxS, PFOS, PFDS, PFOSA, 6:2 FTS, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTriDA, PFTeDA, and PFHxDA). Of the 22 products, PFAS was found in 20 of the products, and as shown in Table 8 below, there was a large variation in total PFAS content depending on which product was analysed (from 0.13 ng/g to 7,730 ng/g). One product in particular contained large amounts of different PFAS. 17 products contained PFOA, 12 contained PFNA and 10 contained PFDA (Naturskyddsföreningen, 2017a). Naturskyddsföreningen did not report results for PFAS other than the three mentioned above.

Table 8 Analysis of PFAS in cosmetic products in Sweden (Naturskyddsföreningen, 2017b)

Product	PFAS declared	PFOA [ng/g]	PFNA [ng/g)	PFDA [ng/g]	Total content of PFAS [ng/g]
Lumene Nude perfection fluid foundation (Soft honey 2)	C9-15 Fluoroalcohol phosphate	2160	659	891	7730
The Body Shop Fresh Nude Foundation (Bali Vanilla 020)	Ammonium C6-16 Perfluoroalkylethyl Phosphate	8.05	2.75	6.78	7490
The Body Shop Shade adjusting drops (Darkening)	Ammonium C6-16 Perfluoroalkylethyl Phosphate	2.5	-	-	4810
Lumene BLUR Foundation longwear (6 golden light)	Perfluorooctyl triethoxysilane	-	-	-	1290
Lumene Luminous matt (Soft honey 2)	Perfluorooctyl triethoxysilane	-	-	-	384
Lumene Longwear blur (Soft Honey 2)	Perfluorooctyl triethoxysilane	0.37	0.11	-	364
Lumene CC color correcting powder 6 in 1 (light/medium	Perfluorooctyl triethoxysilane	-	-	-	348

Product	PFAS declared	PFOA [ng/g]	PFNA [ng/g)	PFDA [ng/g]	Total content of PFAS [ng/g]
Eylure Brow Palette, brow trio	PTFE	42	43.1	34.8	243
H&M Face Palette (3 colours)	Polytef (PTFE)	9.49	7.47	8.98	51.3
H&M Face Palette (4 colours)	Polytefum (PTFE), Polytef (PTFE)	6.08	4.44	4.84	27.5
H&M Highlight Palette	Polytef (PTFE), Polytefum (PTFE)	2.96	3.22	3.38	20.3
IsaDora Eye color bar	PTFE	1.34	1.44	1.29	8.62
L'oreal SkinPerfection (Correcting Day Moisturiser)	PTFE	1.2	0.97	0.93	4.68
Biotherm Skin-best (cream spf 15)	PTFE	0.72	0.74	0.42	3.75
IsaDora Ultra Cover compact powder (22 camouflage classic)	Polyperfluoroethoxymethoxy Difluoroethyl Peg Phosphate	3.3	0.11	-	3.56
IsaDora Hydralight (57 fair beige)	Polyperfluoroethoxymethoxy Difluoroethyl Peg Phosphate	3	-	-	3.00
Garnier The Miracle Cream (Anti-wrinkle skin beautifier)	PTFE	0.95	0.53	0.37	2.51
Gillette Satin Care, Pure & Delicate	[*not specified in the report*]	0.6	-	-	0.60
IsaDora Anti-Shine Mattifying Powder (Matte bonde 30)	Polyperfluoroethoxymethoxy Difluoroethyl PEG Phosphate	0.34	-	-	0.34
Biotherm Aquasource (Rich Cream, dry skin)	Polyperfluoromethylisopropyl ether	0.13	-	-	0.13
H&M Color Essence Eye Pencil (celestial)	Perfluorononyl dimethicone	-	-	-	Not found
Biotherm Homme Aquapower	Polyperfluoromethylisopropyl ether	-	-	-	Not found

Based on information from the two above-mentioned studies, a Lund University thesis (Henricsson, 2017) examined the presence of PFAS in cosmetic products on the Swedish market. In the survey, 30 brands were selected for examination, where ingredients lists for a total of 1,354 products in the categories sunscreen, foundation, powder, moisturizer, eyeliner and eye shadow were reviewed.

The presence of PFAS in the products was identified based on the substances' INCI names (Henricsson, 2017). The report does not show which specific INCI names were screened for the product ingredient lists, but the following PFAS were identified in the products studied:

- Perfluorooctyl triethoxysilane
- Polyperfluoroethoxymethoxy difluoroethyl PEG phosphate
- Ammonium C_6-C_{16} perfluoroalkylethyl phosphate
- Perfluorononyl dimethicone
- Polyperfluoromethyl isopropyl ether.

Of the 1,354 products examined, 59 (4.4%) of the products had declared contents of PFAS. The 59 products were divided into six different brands. These six brands account for 29% of total sales in Sweden (Henricsson, 2017). Table 9 shows an overview of which product types have declared contents of PFAS. It was found that foundations and powders are the product types that most often contain PFAS.

Table 9 Overview of the number of products with declared contents of PFAS, as well as information about the proportion of products within the product type with a declared content of PFAS (Henricsson, 2017)

Product type	Number of products containing PFAS	Proportion of products containing PFAS out of total number of products
Moisturizing cream	1	1.7
Foundation	23	39.0
BB/CC cream	11	18.6
Powder	18	30.5
Eyeliner	6	10.5

2.3 Summary of the survey

The results from the survey show that there was a large variation in the concentration of PFAS in different products. Apart from sunscreens, the highest concentrations were found in foundations (both liquid and solid). PFAS is found in many different types of cosmetic products, but most often in cream/lotion, foundation, BB/CC cream and powder. There are also major differences in the PFAS concentration between brands. The results from the survey also indicate that cosmetic products containing fluoroalkyl substances and other fluorinated compounds on the Danish market typically have women and, in a few cases, men as target groups. It can, though, not be ruled out that more women than men are using “Kemiluppen”. The survey has not identified cosmetic products containing PFAS-related substances distinctly targeting children.

The results from the survey also show that, although there are many INCI names related to fluorinated substances in cosmetics, it is not all substances which are PFAS or which can be degraded to PFAS.

Data from the survey are summarized in Appendix 1. In addition, the table contains information on the chemical structure of the substances and on possible degradation products.

2.4 Criteria for selection of products for chemical analysis

Products for chemical analyses were selected on the basis of the following criteria and considerations.

Only products with declared PFAS content in the product itself (i.e. PFAS ingredient) or with ingredients where there is the potential for PFAS degradation products/impurities were selected (see table in Appendix 1 for further information). In addition, substances for which it was considered possible to carry out a hazard assessment for the substance itself or potential degradation products/impurities (PFCA) were selected. Products with the following ingredients (INCI names) have therefore been prioritized:

- $C_{9\text{-}15}$ fluoroalcohol phosphate
- Perfluorononylethyl carboxydecyl PEG-10 dimethicone

- Perfluorononyl dimethicone
- Perfluorooctyl triethoxysilane
- PTFE
- Polyperfluoroethoxymethoxy difluoroethyl PEG phosphate
- Ammonium C_{6-16} perfluoroalkyl ethyl phosphate.

The actual products were then selected according to following criteria (in order of priority):

1. How many scans the product has had in the Kemiluppen App
2. Product type (different product types with different exposure are selected)
3. Position of the relevant substance on the ingredient list (products where the fluoroalkyl substance stated in the beginning of the list (indicating high concentrations) are prioritized)
4. Whether the product has different target groups (products for men included) and
5. Whether the product is expensive/cheap (different price ranges are selected).

The immediate availability of the products in the stores was also taken into account. In the event that a product was not available, it was replaced with the next product on the list.

Application of the above procedure resulted in the selection of 22 different products for chemical analysis.

In addition, two control products were selected according to two different criteria. Both products have no declared content of PFAS on the ingredient list; one product (a body lotion) from a manufacturer known for not using fluorinated substances (a manufacturer of eco-labelled products), and one product similar to one of the 22 selected products, but without the declared content of PFAS[10].

[10] However, it has subsequently been found that foundation No. 11 (Control Product) has a declared content of synthetic fluoroplogopite, which was not detected before the product has been analysed. This means that, in fact, there has been only a single, completely fluorine-free control product included in the analyses, a fact further discussed in section 3.3.

3. Chemical analysis

3.1 Introduction

A great variety of fluoroalkyl substances and other fluorinated compounds exist and are in use; it would be prohibitive to make a complete analysis and determination of all of these possible substances, and standard analysis methods exist only for a few of the substances. It is often the basic perfluoroalkyl acids listed below as well as some fluorotelomers for which there are standard analytical methods. It is likewise these acids that are expected to occur as degradation products and impurities in cosmetic products. Thus, not all fluorinated substances are determined by the analysis of the substances listed below, and analyses of the content of total organic fluorine (TOrF) is therefore included. Since it has not been possible to analyse for the fluoroalkyl substances and other fluorinated compounds indicated on the products' INCI list in a commercial laboratory, TOrF can be used as a measure for fluorinated compounds other than PFCA in the products. The majority of the fluorine identified by the TOrF method may be assumed to originate from the fluoroalkyl substances and other organic fluorinated compounds that are declared on the products.

3.2 Method

Twenty-two products (as well as two control products) were selected for chemical analysis. Out of the 22 selected products, only 18 products were analysed, as three of the products no longer had declared content of the selected PFAS and the last product was not possible to purchase.

The selected products were all analysed for the following single PFAS for which there are analytical standards (analytical package available in a commercial laboratory) and for total organic fluorine (TOrF) content:

- Perfluorobutanoic acid (PFBA)
- Perfluoropentanoic acid (PFPeA)
- Perfluorohexanoic acid (PFHxA)
- Perfluoroheptanoic acid (PFHpA)
- Perfluorooctanoic acid (PFOA)
- Perfluorononanoic acid (PFNA)
- Perfluorodecanoic acid (PFDA)
- Perfluoroundecanoic acid (PFUnA)
- Perfluorododecane acid (PFDoA)
- Perfluorotridecanoic acid (PFTrA)
- Perfluorotetradecanoic acid (PFTeA)
- Perfluoro-3,7-dimethyloctanoic acid (PF-3,7-DMOA)
- 7*H*-Dodecafluoroheptanoic acid (HPFHpA)
- Perfluorobutane sulfonate (PFBS)
- Perfluorohexane sulfonate (PFHxS)
- Perfluoroheptane sulfonate (PFHpS)
- Perfluorooctane sulfonate (PFOS)
- Perfluorooctane sulfonamide (PFOSA)
- Perfluorodecane sulfonate (PFDS)
- 4:2 Fluorotelomer sulfonate (4:2 FTS)
- 6:2 Fluorotelomer sulfonate (6:2 FTS)
- 8:2 Fluorotelomer sulfonate (8:2 FTS).

For the samples that were analysed, duplicate determinations were made for per-/polyfluoroalkyl substances (PFAS) and single determinations for TOrF.

3.2.1 Analytical method

3.2.1.1 Principle of analysis of perfluorinated substances (PFAS)

The sub-samples of 0.1 g were homogenised and extracted in an ultrasonic bath with methanol for 30 min. Several selected per- or polyfluorinated compounds (PFAS) were added as internal standards to the sample material. The samples were then concentrated to dryness, acetonitrile was added and the samples were shaken with hexane. In the subsequent purification step, activated carbon was added to the sample extract to eliminate interfering sample matrix components. The analyses were performed by liquid chromatography coupled with mass spectrometry (LC-MS/MS).

The single PFAS were identified using retention time and molecule or fragment ions and the quantification of the native PFAS were calculated using internal isotope-labelled standards.

Some of the samples had to be reanalysed due to challenges with the matrix, and these were additionally purified by solid-phase extraction (SPE).

3.2.1.2 Principle of analysis for total organic fluorine (TOrF)

The subsamples of 1 gram were homogenised by milling with a Retsch ZM 200 Ultra-centrifugal mill or homogenised, depending on the matrix. Tablets were firmly pressed to prevent blowing of the sample in the gas stream. By combustion in an oxygen flow of 8-10 tablets at 900 °C, following a certain program for the temperature, the perfluorinated substances (and other organic fluorinated substances) degrades to hydrogen fluoride which is collected quantitatively in an impinge with a buffer solution. The amount of hydrogen fluoride collected is determined by ion chromatography.

3.3 Results

The results of the chemical analyses are summarized for those products with identified PFAS content in Table 10 below. Detailed results for all products are shown in Appendix 2.

Two control products (Product nos. 18 and 11) without declared contents of PFAS were selected for analysis. However, as shown in the results, fluoride content was identified in product No. 11 using the TOrF method. After purchase of the product and review of its INCI list, synthetic fluoroplogopite was identified as a constituent, and although this is an inorganic fluorine substance, it cannot be excluded (based on the chemical structure) that the substance contributes to the content of fluoride in the control product. In addition, review of the INCI list of products revealed that one product (No. 13) has a declared content of synthetic fluoroplogopite instead of $C_{9\text{-}15}$ fluorophosphate (the presence of which was the reason for this product's selection for analysis (based on data from Kemiluppen)). Therefore, in practice, the number of analysed products, based on information on ingredients from the INCI list assumed to contain PFAS, was reduced to 17 in total.

One or more PFAS substances were identified in all 17 products (for hair spray (sample no. 12a) and eyeliner (sample no. 6), however, they were found only in one of the duplicate determinations). The highest concentration of a single substance was 3,340 ng/g PFHxA, found in a foundation (no. 14). The highest concentration of total PFAS was found in product no. 4 (a concealer) (10,700 ng/g). In addition, it is notable that PFOA was found in products no. 4 and 17 in concentrations above the 25 ng/g limit. PFNA, PFDA, PFUnA, PFDoA, PFTrA and PFTeA (C_9-C_{14} PFCA) were identified in 6-9 of the 17 tested products with declared contents of PFAS or other organic fluorinated compounds. In six of these (nos. 4, 10, 16, 17, 21 and

23), the proposed sum limit value for C_9-C_{14} PFCAs of 25 ng/g was exceeded. In product no. 4, the sum of these substances is approx. 180 times above the proposed limit value.

Using the TOrF method, fluorine was found in all analysed products, except control product no. 18 and the hair spray (product no. 12). There was a relatively large difference between the content of the individual PFAS and the concentration of organic fluorine in the products. This is assumed to happen because, in the absence of standards and analytical methods, it has not been possible to analyse for all of the PFAS-relevant substances listed in the INCI list of the individual product. The relatively simple fluoroalkyl substances, which were determined quantitatively, are probably derived primarily from impurities from production and degradation of precursors, as the free acids themselves are rarely (if at all) used in cosmetic products. It should be further noted that since the TOrF method does not provide information on the organic fluorine substances from which the fluorine content originates, the method cannot be used for risk assessment of the cosmetic products.

Comparison of the results of the analyses in this project with the results from the study by Naturskyddsföreningen from earlier in the year shows that the concentrations of PFOA and PFNA in cosmetic products are comparable, whereas higher concentrations of PFDA is found in this study (891 ng/g found in the Swedish study as compared to 1,710 ng/g in a concealer in this study). Compared to the Japanese study (Fujii *et al*. 2013), the concentrations are also comparable. However, in general, slightly higher concentrations of all PFAS were found in this study as compared to Japanese data.

The following analysed substances were not found in any of the selected product types:

- Perfluorohexane sulfonate (PFHxS)
- Perfluoroheptane sulfonate (PFHpS)
- Perfluorooctane sulfonate (PFOS)
- Perfluorooctane sulfonamide (PFOSA)
- Perfluorodecane sulfonate (PFDS).

However, it should be emphasized that although the substances have not been found in certain product types as part of the chemical analyses of this project, it cannot be excluded that these substances are present in cosmetic products on the Danish market.

Table 10 Overview of PFAS concentrations identified in the analysed products (ng/g) as well as total organic fluorine content (TOrF). The analysed products are divided by product type and number. "a" is used as the term for the double determination.

Product type	Declared substance on INCI list (INCI name)	PFUnA	PFDoA	PFTeA	PF-3.7-DMOA	HPFHpA	6:2 FTS	PFBA	PFPeA	PFTrA	6:2 FTS	H4PFHxS	PFBS	PFHxA	PFHpA	PFOA	PFNA	PFDA	Total PFAS	TOrF
Facial scrub no. 5	Perfluorononylethyl carboxydecyl peg-10 dimethicone	-	-	-	-	-	-	2.4	3.1	-	-	-	-	5.4	1.3	-	-	-	12	3,300
Facial scrub no. 5a	Perfluorononylethyl carboxydecyl peg-10 dimethicone	-	-	-	-	-	-	2.6	4	-	-	-	-	6.3	1.2	-	-	-	14	
BB cream no. 7	Perfluorooctyl triethoxysilane	-	-	-	-	-	-	51	9.2	-	-	-	-	15	-	-	-	-	76	37,000
BB cream no. 7a	Perfluorooctyl triethoxysilane	-	-	-	-	-	-	16	8.7	-	-	-	-	18	-	-	-	-	43	
Body lotion no. 21	PTFE	8.6	10	12	-	-	-	4.8	4.2	13	-	-	-	4.5	4.6	5.2	6.4	7.5	81	280,000
Body lotion no. 21a	PTFE	9.1	9.8	12	-	-	0.78	4.9	4.2	14	-	-	-	4.5	4.8	5.4	6.2	7.8	83	
Body lotion no. 19	Perfluorononylethyl carboxydecyl peg-10 dimethicone	0.86	1.5	0.5	-	-	-	3.4	3.2	-	1.1	-	-	24	5.1	20	1.4	6.3	68	8,600
Body lotion no. 19a	Perfluorononylethyl carboxydecyl peg-10 dimethicone	0.83	1.4	0.48	-	-	-	3.4	2.7	-	0.93	-	-	24	5.1	22	1.3	6.1	68	
CC cream no. 2	Perfluorooctyl triethoxysilane	-	-	-	-	-	-	35	8.2	-	-	-	-	-	0.93	-	-	-	45	33,000
CC cream no. 20	Perfluorooctyl triethoxysilane	-	-	-	-	-	-	146	39	-	-	-	-	383	35	-	-	-	602	69,000

Product type	Declared substance on INCI list (INCI name)	PFUnA	PFDoA	PFTeA	PF-3.7-DMOA	HPFHpA	6:2 FTS	PFBA	PFPeA	PFTrA	6:2 FTS	H4PFHxS	PFBS	PFHxA	PFHpA	PFOA	PFNA	PFDA	Total PFAS	TOrF
CC cream no. 20a	Perfluorooctyl triethoxysilane	-	-	-	-	-	-	149	40	-	-	-	-	397	34	-	-	-	619	
CC cream no. 2a	Perfluorooctyl triethoxysilane	-	-	-	-	-	-	35	7.7	-	-	-	-	12	-	-	-	-	56	
Concealer no. 4	C_{9-15} fluoroalcohol phosphate	440	842	369	-	4	270	180	190	470	240	4.6	2	1,930	860	2,300	830	1,640	10,600	230,000
Concealer no. 4a	C_{9-15} fluoroalcohol phosphate	440	840	330	-	3.9	260	180	190	450	260	4.1	2	1,940	860	2,370	820	1710	10,700	
Cream/lotion no. 22	PTFE	1	0.75	0.72	-	-	-	1.5	1.2	0.63	-	-	-	1.1	0.96	1.1	1.1	1	11	740,000
Cream/lotion no. 22a	PTFE	0.91	0.53	0.51	-	-	-	2.3	1.6	0.46	-	-	-	1.5	1	1.1	0.87	0.85	12	
Cream/lotion no. 23	PTFE	6.4	7.2	8.2	-	-	-	4.2	2.9	10	-	-	-	2.6	2.6	3.1	3.9	5	56	130,000
Cream/lotion no. 23a	PTFE	6.2	6.5	7.8	-	-	-	4.3	2.8	10	-	-	-	2.8	2.6	3.2	3.7	4.9	55	
Eyeliner no. 6	Perfluorononyl dimethicone	-	-	0.7	-	-	-	-	1.2	-	-	-	-	-	-	-	-	-	1.9	200,000
Eyeliner no. 6a	Perfluorononyl dimethicone	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	ND	
Foundation no. 13	Synthetic fluorphlogopite.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	ND	69,000
Foundation no. 13a	Synthetic fluorphlogopite.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	ND	
Foundation no. 14	Ammonium $_{C6-16}$ perfluoroalkyl ethyl phosphate	-	0.78	-	-	-	24	280	450	-	-	-	-	3,220	830	3.9	0.53	1.8	4,820	160,000

Product type	Declared substance on INCI list (INCI name)	PFUnA	PFDoA	PFTeA	PF-3.7-DMOA	HPFHpA	6:2 FTS	PFBA	PFPeA	PFTrA	6:2 FTS	H4PFHxS	PFBS	PFHxA	PFHpA	PFOA	PFNA	PFDA	Total PFAS	TOrF
Foundation no. 14a	Ammonium C_{6-16} perfluoroalkyl ethyl phosphate	0.49	0.51	-	13	-	23	290	470	-	-	-	-	3,340	827	4.3	0.58	1.8	4,970	
Foundation no. 17	C_{9-15} fluoroalcohol phosphate	17	17	NA	-	-	43	22	20	NA	NA	-	-	80	48	64	35	43	390	79,000
Foundation no. 17a	C_{9-15} fluoroalcohol phosphate	17	18	NA	-	-	42	21	20	NA	NA	-	-	81	44	66	33	40	380	69,000
Foundation no. 8	Perfluorooctyl triethoxysilane	-	-	-	-	-	-	86	30	-	-	-	-	276	16	-	-	-	409	59,000
Foundation no. 8a	Perfluorooctyl triethoxysilane	-	-	-	-	-	-	89	32	-	-	-	-	284	18	-	-	-	423	
Highlighter no. 10	PTFE	25	29	43	-	-	-	36	20	47	-	-	-	18	17	17	22	23	300	310,000
Highlighter no. 10a	PTFE	24	26	39	-	-	-	35	20	40	-	-	-	17	18	17	21	22	280	59,000
Hair spray no. 12	Polyperfluoroethoxymethoxy difluoroethyl peg phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	ND	-
Hair spray no. 12a	Polyperfluoroethoxymethoxy difluoroethyl peg phosphate	-	-	-	-	-	0.69	-	-	-	-	-	-	-	-	-	-	-	0.69	
Powder no. 3	C_{9-15} fluoroalcohol phosphate	-	-	-	#	#	-	84	32	-	-	#	-	34	4.6	NA	-	NA	155	180,000
Powder no. 3a	C_{9-15} fluoroalcohol phosphate	-	-	-	-	-	-	87	29	-	-	-	-	30	2.7	NA	-	NA	150	
Eye shadow no. 16	PTFE	8	9.2	9.9	-	-	-	8.3	4.9	11	-	-	-	5.4	5.3	6	7.1	7.8	83	190,000
Eye shadow no.	PTFE	8.2	8.1	9.2	-	-	-	8.3	5.4	8.9	-	-	-	5.5	4.6	6	6.6	7.6	12	180,000

Product type	Declared substance on INCI list (INCI name)	PFUnA	PFDoA	PFTeA	PF-3.7-DMOA	HPFHpA	6:2 FTS	PFBA	PFPeA	PFTrA	6:2 FTS	H4PFHxS	PFBS	PFHxA	PFHpA	PFOA	PFNA	PFDA	Total PFAS	TOrF
16a																				
Control products																				
Body lotion no. 18	None	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	ND	-
Body lotion no. 18a	None	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.7*	-	-	0.696	
Foundation no. 11	Synthetic fluorphlogopite.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	ND	67,000
Foundation no. 11a	Synthetic fluorphlogopite.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	ND	

-: Below "Limit of Quantification" (LOQ)

#: Unable to report. LOQ was increased due to disturbances from the matrix.

NA: It was not possible to analyse for this substance due to various interferences and matrix disorders.

ND: Not detected.

* 0.7 ng/g is identical to LOQ for this product. It cannot be excluded that the product contains PFOA as background contamination. However, the average of the double determinations gives a concentration below LOQ.

3.3.1 Selection of substances for hazard and risk assessment

The following substances have been selected for health hazard and risk assessment:

- Perfluorooctanoic acid (PFOA)
- Perfluorobutanoic acid (PFBA)
- Perfluoropentanoic acid (PFPeA)
- Perfluorohexanoic acid (PFHxA)
- Perfluoroheptanoic acid (PFHpA).

The last four substances on the list were selected as they were identified in the largest number of cosmetic products (14-16 of a total of 17 products) and in relatively high concentrations. PFOA is chosen as a reference substance against which other selected perfluoroalkanoic acids can be evaluated and compared. PFOA is the most well-known PFCA and is considered to be one of the most potent PFAS substances. PFOA was found in nine out of 17 products, of which the concentration was above the forthcoming 25 ng/g limit value in two of the products. In one of these products (product no. 4) the concentration was almost 100 times the limit value.

Exposure scenarios and risk assessments were prepared for the following product types:

- Body Lotion
- CC cream/foundation
- Concealer.

These product types were primarily selected as they contain the highest concentrations of the selected substances (the concealer - product no. 4 contains the highest concentrations out of all tested product types). In addition, the product types were selected based on consideration of their use, as body lotion is widely used in large quantities (whole body) and foundation/CC cream are used all over the face. All three products are also "leave-on" products, i.e. they are meant to stay on the skin all day.

4. Hazard assessment

4.1 Introduction

The purpose of the health hazard and risk assessment is to assess whether the measured content of PFAS substances in the analysed cosmetic products could pose a risk to consumers.

The hazard assessment will be conducted for the following substances:

- Perfluorooctanoic acid (PFOA)
- Perfluorobutanoic acid (PFBA)
- Perfluoropentanoic acid (PFPeA)
- Perfluorohexanoic acid (PFHxA)
- Perfluoroheptanoic acid (PFHpA).

Therefore, no hazard assessment will be conducted for PFNA, PFDA, PFUnA, PFDoA, PFTUA, and PFTeA (C_9-C_{14} PFCA) despite the fact that these substances have been identified in 6-9 of the 17 tested products with declared contents of PFAS or other organic fluorinated compounds. This is in line with the fact that it is generally not possible with sufficient certainty to establish a safe exposure level for PBT/vPvB substances under REACH[11].

As described in more detail in section 6.1, the risk assessment will be done stepwise/iteratively, meaning that initially, the total content of PFAS is used and the potency of the individual PFAS substances is not taken into account, assuming that all identified PFAS substances are as potent as the most potent PFAS (i.e. PFOA). Like the other identified PFAS substances, C_9-C_{14} PFCA is therefore included in the risk assessment in this way.
It should be mentioned that PFNA (C_9) and PFDA (C_{10}) both have harmonised classifications as Repr 1B (may damage fertility or the unborn child), and that these classifications are partially based on read-across to PFOA. There are no harmonized classifications for the remaining C_{11}-C_{14} PFCA; there are currently few toxicological studies performed for these substances.

4.2 Method

The hazard assessment was preferentially based on previous assessments of the selected substances where available within the EU framework (ECHA 2013abc; ECHA 2015b; EFSA, 2008, 2012), in other countries' assessments (US EPA 2005, 2009) or in the Danish Environmental Protection Agency's previous publications on PFAS (Lassen *et al*., 2013; Kjølholt *et al*., 2015; Lassen *et al*., 2015), and the IARC's recent assessment of PFOA (IARC, 2017). In addition, the authors' literature collections were used. The literature review was supplemented by searches in Google Scholar.

Data for physicochemical properties were also sought in PubChem, Comptox[12], Guidechem, Molbase, ECHA's database of registered substances and similar databases.

[11] According to REACH Guideline R11, 2017 (page 32) it is, however, possible to make a quantitative risk assessment for humans directly exposed to a PBT/vPvB substance. For example for direct exposed workers. In the RAC assessment of PFOA (ECHA, 2015a), quantitative risk assessment has been prepared for several exposure scenarios.

[12] Data from https://comptox.epa.gov are often modelled.

4.2.1 Perfluorooctanoic acid (PFOA)

4.2.1.1 Database

Apart from PFOS, PFOA is the most well-studied PFAS and the most commonly evaluated PFAS. However, most toxicological studies have been performed with the ammonium salt APFO, which is more water soluble and more stable than the acid and not volatile like the acid. It is common practice to evaluate PFOA based on data for APFO.

PFOA is a substance of very high concern (SVHC) included in the REACH Candidate List. It has been decided in the EU, as of May 2020, to ban most uses of PFOA, its salts and related substances that can be converted into PFOA. In the decision-making process, thorough assessments were prepared which *inter alia* form the basis for this assessment, where PFOA is a type of model/reference substance for the four PFCA with shorter perfluoroalkyl chains to be evaluated in this report (ECHA, 2013abc; ECHA, 2015b, US EPA, 2005).

4.2.1.2 Identification

CAS no. 335-67-1
EC no. 206-397-9
Index no. 607-704-00-2

Molecular formula

$C_8HF_{15}O_2$

Structural formula

Synonyms

Pentadecafluorooctanoic acid, 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluoro-1-octanoic acid, perfluorooctanoic acid.

Isomers and salts

	Ammonium perfluorooctanoate (APFO)	Sodium perfluorooctanoate (NaPFO)	Potassium perfluorooctanoate	Silver perfluorooctanoate
CAS no.	3825-26-1	335-95-5	2395-00-8	335-93-3
EC no.	223-320-4	206-404-5	219-248-8	206-402-4
Molecular formula	$C_8H_4F_{15}NO_2$	$C_8F_{15}NaO_2$	$C_8F_{15}KO_2$	$C_8AgF_{15}O_2$

There are 10 branched PFOA isomers with individual CAS numbers and as a group they represent CAS no. 90480-55-0.

4.2.1.3 Physical-chemical properties

	PFOA	APFO	NaPFO
Molecular weight	414.07	431.101	436.052
Boiling point °C (at 101,3 kPa)	[ab]188; 189	[a]Decomposes;190; [c]decomposes; 130	[e]188

	PFOA	APFO	NaPFO
Melting point °C	[ab]54.3; [be]52-54	[b]157-165; [e]164; [c]Decomposes >105 °C	[e]52.1
Solubility in water (at 25 °C)	[b]9.5 g/L = 0.023 mol/L; [d]3.30 g/L	[bc]500 g/L; [e]0.284 mol/L = 122 g/L	[e]0.853 mol/L = 372 g/L
Density (at 20 °C), g/cm^3,	[d]1.792	[e]1.73	
Vapour pressure (at 25 °C)	[ab]4.2 Pa = [d]0.032 mm Hg;	[c]0.0028 Pa =2.2 x 10^{-5} mm Hg; [f]7 x 10^{-5} mm Hg = 0.0093 Pa at 20°C	[e]0.254 mm Hg
Partition coefficient Log P_{ow}	[b]2.69 at pH 7 ; [e]5.68	[e]5.53	[e]3.79

[a]Washburn *et al.* 2005; [b]ECHA (2013a); [c]ECHA (2013b); [d]PubChem; [e]Comptox; [f]Griffith & Long 1980.

Both PFOA as acid and salts are solid colourless substances. However, their properties are very different. The acid has a relatively low melting point and a high boiling point, while the salts decompose as organic salts normally do. The acid has a low vapour pressure, while the salts are not volatile. The acid is moderately soluble in water, where it dissociates as a medium strength acid. As expected, the salts are much more water soluble, e.g. APFO is 50 times more water soluble than the acid. In an aqueous solution there is a pH-dependent equilibrium between acid and acid residue ion.

4.2.1.4 CLP classification

Both PFOA and APFO have the same harmonised classification and labelling (ECHA C&L Inventory, 2017).

Hazard class and category for PFOA	Hazard Statement Codes	Hazard Statements
Acute Tox. 4	H302	Harmful if swallowed
Eye dam. 1	H318	Causes serious eye damage
Acute Tox. 4	H332	Harmful if inhaled
Carc. 2	H351	Suspected of causing cancer
Lact	H362	May cause harm to breast-fed children
STOT RE 1	H372	Causes damage to the liver through prolonged or repeated exposure
Repr. 1B	H360D	May damage fertility or the unborn child

4.2.1.5 Toxicokinetics and metabolism

Absorption in the gastrointestinal tract

In a clinical study, the absorption of an oral dose of the ammonium salt of PFOA (APFO) was very rapid and effective. PFOA concentration in blood was maximal after approximately 1½ hours. Repeated weekly dosing of APFO resulted in continued absorption and accumulation. There was no age or gender difference in the results (Patent, cit. from IARC, 2017).

The absorption of APFO in the gastrointestinal tract in rats is almost complete. In male rats exposed to a single oral dose of 11 mg/kg of ^{14}C-labeled APFO, 93% of the dose was absorbed over a 24-hour period (Laboratory Report 1979, cit. from IARC, 2017). The dermal absorption was assessed to be significant in another study with rats, but was not further quantified. The conclusion in the article was that the oral and dermal uptake were relatively similar (Kennedy, 1985).

Dermal absorption

The dermal absorption of APFO (100 µL/cm^2 of 20% APFO dissolved in water) was investigated *in vitro* with skin preparations on rat and human skin with an exposure area of 0.64 cm^2. In steady state, 190 ± 57 ng APFO x cm^2/h was absorbed through human skin and 6,500 ± 3,000 ng APFO x cm^2/h through rat skin. After 48 hours, the dermal absorption through human skin was calculated at <0.05%, while the absorption was about 34 times greater (<1.5%) through rat skin (Fasano *et al*. 2005). The permeability coefficient was calculated at 9.49 ± 2.86 × 10^{-7} cm/h for human skin and 3.25 ± 1.51 x 10^{-5} cm/h for rat skin. It should be noted that dermal absorption of a water-soluble salt is usually minimal. The dermal absorption of the acid itself or lipophilic precursors, which may occur in cosmetic products, is expected to be much greater.

The dermal permeability of the acid itself, as ^{14}C-labeled PFOA dissolved in acetone in a pH-adjusted saline solution, was later investigated *in vivo* in mice and *in vitro* with mice and human skin (Franko *et al*., 2012). In the *in vivo* experiment, 0.5%, 1% and 2% solutions of PFOA (as acid) in acetone were applied to mice on ears and their shaved back – in total 100 µL. A dose-related increase in PFOA concentration in blood serum of 152 to 226 µg/mL was observed after four days. A doubling of the administered dose did not result in a doubling of the concentration in the blood. Dermal absorption was not further quantified. In the experiment with mouse skin, 38.6% of the amount of PFOA used penetrated through the skin over 25 hours while 11% was retained in the skin. For human skin, only 23-25% penetrated the skin, but almost half (45%) was retained in the skin layer itself.

The study showed that dermal absorption was highly dependent on whether or not PFOA was dissociated. The non-dissociated lipophilic perfluorooctanoic acid at pH 2.25 (median permeability coefficient: 5.5 × 10^{-2} cm/h) was approximately 1,000 times more skin-permeable than the dissociated acid at pH 5.5 (median permeability coefficient: 4.4 × 10^{-5} cm/h), which releases the perfluorooctanoate ion that occurs in salts. The permeability coefficient at pH 5.5 corresponds to the above results for rat skin in Fasano *et al*. (2005).

Washburn *et al*. (2005) used data from the study of Fasano *et al*. (2005) to estimate the transfer of PFO (anion of PFOA) from liquid consumer goods (e.g. carpet care) over the skin and into the bloodstream. The amount of transferred PFO depends, according to the authors of the article, on the concentration of PFO in the product, the exposed area of the skin, the duration of contact and the permeability of the substance (data from Fasano *et al*. (2005). Washburn *et al*. (2005) results in an estimated dermal absorption coefficient of 1.0 × 10^{-5}/h, indicating very low skin permeability.

In previous studies of PFAS in textiles performed for the Danish Environmental Protection Agency (Lassen *et al*., 2015), 2% dermal absorption was reported as a very conservative estimate of PFAS absorption through human skin (also based on data from Fasano *et al*. (2005).

Distribution and accumulation

The distribution in the body of an oral dose of 10 mg/kg of ^{14}C-labeled APFO administered by stomach tube was examined in rats, mice, hamsters and rabbits (Hundley *et al*., 2006). Rabbits were sacrificed and analysed after 168 hours, the other animals after 120 hours. Female rats, rabbits and male hamsters had eliminated most of the substance (74-90% of the radioac-

tivity) via the urine. Mice eliminated only 3-7% in the urine and male rats 26%. Female rats had a surprisingly large distribution of 28% in faeces, as compared to 8-9% in faeces of male rats, male mice and of hamsters of both sexes. In female mice and rabbits of both sexes, the distribution was only 4-6%. Mice, male rats and female hamsters had most of the substance in tissues. For male rats most of the substance occurred in blood, liver and kidneys; for mice in the liver and for hamsters the substance was spread through several tissues and organs.

Of the absorbed PFOA,> 90% is bound to the plasma protein albumin in the blood (Han *et al*., 2003). The half-time for elimination of PFOA from human blood was 2-4 years for more heavily exposed humans, while half-life was twice that in the normal, less exposed, population (Seals *et al*., 2011; Russell *et al*., 2015; Wang *et al*., 2015).

In an earlier 28-day study, rats were administered 3, 10 and 30 mg PFOA/kg daily as acid via stomach tube and the distribution of PFOA in the body was determined (Ylinen *et al*., 1990). Usually each test group consisted of six animals (in some cases only three animals were used). The mean concentrations in different organs are shown in Table 11.

Table 11 Distribution of PFOA into different tissues from rats after daily administration of 3, 10 and 30 mg/kg bw (mean concentration ± standard deviation) respectively (Ylinen *et al*. 1990)

Tissue/organ	Sex	3 mg/kg bw/day	10 mg/kg bw/day	30 mg/kg bw/day
Blood serum (µg/mL)	Female	2.40 (3 animals)	12.47 ± 4.07	13.92 ± 6.06
	Male	48.60 ± 10.30	87.27 ± 20.09	51.56 ± 11.47
Liver (µg/g)	Female	1.81 ± 0.49	3.45 ± 1.36	6.64 ± 2.64
	Male	39.90 ± 7.25	51.71 ± 11.18	49.77 ± 10.76
Kidney (µg/g)	Female	0.06 ± 0.02	7.36 ± 3.19	12.54 ± 8.24
	Male	1.55 ± 0.71	40.56 ±14.94	39.81 ± 17.67
Spleen (µg/g)	Female	0.15 ± 0.04	0.38 ± 0.17	1.59 ± 0.49
	Male	4.75 ± 1.66	7.59 ± 3.50	4.10 ± 1.57
Lungs (µg/g)	Female	0.24 (3 animals)	0.22 ± 0.15	0.75 ± 0.26
	Male	2.95 ± 0.54	22.58 ± 4.59	23.71 ± 5.42
Brain (µg/g)	Female	<LOQ	0.029 ± 0.019	0.044 ± 0.018
	Male	0.398 ± 0.144	1.464 ± 0.211	0.710 ± 0.320
Ovary (µg/g)	Female	<LOQ	0.41 ± 0.27	1.16 ± 0.58
Testicles (µg/g)	Male	6.24 ± 2.04	9.35 ± 4.02	7.22 ± 3.17

The results from Ylinen *et al*. (1990) showed that:

- There was less accumulation of PFOA in female rats than in male rats because of faster excretion in the urine in female rats;
- There was a kind of saturation of PFOA concentrations in most tissues after the middle dose;
- The highest concentrations of PFOA occurred in blood, liver, kidneys and lungs;
- PFOA concentrations in the brain were small, but increased significantly with the dose.
- The half-life of PFOA in the blood was 24 hours in female rats and 105 hours in males, and
- The half-life of PFOA in the liver was 60 hours in females and 210 hours in males, respectively.

In a study of autopsy tissue from 20 deceased humans, the highest concentrations of PFOA were found in the bones, lungs and liver (Perez *et al*., 2013). Bones contained the highest concentration of PFOA of all PFAS examined.

Toxicokinetics in humans of 11 PFAS substances - including PFOA, PFHxA and PFHpA - was studied by Fábrega *et al*. (2015) with a validated physiologically-based pharmacokinetic (PBPK) model. The distribution in the body was described by a distribution coefficient between the concentration in a particular tissue and the concentration in the blood. There was no significant correlation between this distribution and the chain length. Apart from PFOS, PFOA had a relatively larger proportion distributed in the blood among the 11 PFAS investigated, and PFOA also had the highest PFAS concentration found in blood, bone marrow and lungs.

The highest concentration of PFOA in rats is measured in blood, liver, kidneys and lungs. In a recent study, the distribution of low exposures of PFOA, PFHxA and PFBA in mice was investigated by intravenous injection of 7.22 MBq ^{18}F-labeled radioactive compounds (Burkemper *et al*., 2017). Four hours post-injection, radioactivity was measured in 15 tissues/organs as percent of dose per gram of tissue. The highest content of PFOA was found in the liver (7 ± 2%) and in the thigh bone (4 ± 1%).

Metabolism

PFOA can be formed by metabolism/degradation of related complex derivatives, but it is commonly known that the perfluoroalkyl chain cannot be further degraded in the environment, animals and humans because of the very strong carbon-to-fluorine bond. Perfluoroalkyl compounds can generally not be degraded microbiologically (Ochoa-Herrera *et al*., 2016).

There are many more studies that confirm this stability, e.g. in a 28-day study with rats exposed to PFOA intraperitoneally, fluoride could not be measured in blood or urine (Van den Heuvel *et al*.1991). If the perfluoroalkyl chain had been degraded, fluoride should have been detected in blood and urine.

Elimination

The primary excretion of PFOA pathway is in urine, and in mice, rats and monkeys, the half-life for elimination of a dose was 20-30 days. The urinary excretion of PFOA in humans is less effective because of effective re-absorption in the kidneys (IARC, 2017). The elimination of perfluoroalkanoic acids through the kidneys and reabsorption is thoroughly described by Han *et al*. (2012). Therefore, PFCA can accumulate in human tissues and organs, even though the substances are rapidly excreted in animals.

4.2.1.6 Irritation and allergy

PFOA as an acid causes severe irritation to skin and mucous membranes, while the salts are more neutral and do not have the same effect (Franko *et al*., 2012). Thus, APFO was only very mildly irritating to rabbit skin (Griffith & Long 1980; Kennedy 1985). APFO was less irritating to rat skin than rabbit skin (Kennedy, 1985). APFO seems mildly irritating to rabbit eyes (Griffith & Long 1980). Neither PFOA nor APFO is classified as an irritant.

There is no information on any potential allergenic effects for these substances, and neither PFOA nor APFO are classified as sensitizing.

4.2.1.7 Acute and chronic effects

Acute exposure

The acute skin toxicity (LD_{50}) of APFO was determined at 4,300 mg/kg bw in male rabbits, 7,000 mg/kg bw in male rats and > 7,500 mg/kg bw in female rats (Kennedy, 1985).

Repeated exposure

In a 14-day study with mice and rats exposed to 0.3 mg to 30 mg branched or straight-chain APFO/kg bw daily via stomach tube, the lowest exposure to linear APFO of 0.3 mg/kg bw had an effect (LOAEL) in both mice and rats, while the branched isomers had a slightly lesser effect, primarily consisting of lipid changes in serum (Loveless *et al*., 2006). In the EU RAC

report (ECHA, 2015b), it is erroneously stated on page 104 that the exposure of 0.3 mg/kg bw/day is NOAEL for rats, although it is made clear in Table 6 of the article by Loveless *et al*. (2006) that for linear isomers in rats, the 0.3 mg/kg bw is a LOAEL, and the same for all isomers in mice.

In a 28-day study, rats were exposed to 0, 30, 100, 300, 1,000 and 3,000 ppm APFO in the feed. Male rats exposed to 30 ppm APFO and female rats exposed to 300 ppm had enlarged livers and histopathological changes in liver cells (Griffith & Long 1980). Therefore, the 'No Observed Adverse Effect' level (NOAEL) for female rats was 100 ppm, and LOAEL for male rats was 30 ppm.

For male rats exposed to APFO in the feed for 13 weeks (90 days), the lowest intake, which did not produce undesired liver effects (i.e. NOAEL), was 0.06 mg/kg bw/day and the lowest exposure which had an effect (LOAEL) was 0.64 mg/kg bw/day (Perkins *et al*., 2004).

In a 90-day study with monkeys exposed to 0, 3, 10, 30 and 100 mg of APFO/kg bw/day via stomach tube, there were strong organ effects and deaths in the two highest dose groups. In the lowest dose group (3 mg/kg bw/day) there were no effects (NOAEL). Unlike rats, there were effects on the immune system (reticuloendothelial system) and gastrointestinal tract, characteristic of monkeys (Griffith & Long 1980).

In a two-year long-term animal study with rats (also discussed under "Carcinogenicity") exposed to APFO concentrations in the feed of 0, 30 and 300 ppm, effects such as altered blood values and effects on liver, kidneys, testicles and pancreas could be observed at 300 ppm. There were less significant effects at the second dose of 30 ppm, equivalent to 1.3 mg/kg bw/day for male rats and 1.6 mg/kg bw/day for female rats. In the absence of even lower exposure levels, these intakes were considered NOAEL (Butenhoff *et al*., 2012), but they should probably be referred to as LOAEL.

The effect of dermal exposure to repeated doses of APFO was investigated in male rats exposed to 20, 200 or 2,000 mg/kg bw dissolved or suspended in 0.5 mL of water on a shaved area of the back, corresponding to 15% of the rats' body surface area and covered by a collar. APFO was applied 2x5 times with 2 days of rest in between. Exposure time was 6 hours per day (Kennedy, 1985). All treated animals had increased liver weight; i.e. LOAEL for skin exposure of APFO in this short-term study was <20 mg/kg bw (Kennedy 1985).

Toxicological mechanisms

Perfluoroalkanoic acids (PFCA) and their salts with different chain lengths can *inter alia* activate "peroxisome proliferator-activated receptor α" (PPARα) in liver cells, and therefore they may cause peroxisome proliferation, enlarged liver and increased fatty acid oxidation, etc. (Ikeda *et al*., 1985). PFCA with medium fluoroalkyl chain length, such as PFHpA and PFOA, are the most potent PPARα activators, while longer or shorter chains of PFCA exhibit less activity. PPARα is the best-studied liver toxicological mechanism for PFOA, but there are other mechanisms such as oxidative stress, activation of "liver X receptor α (LXRα)", "constitutive androstane receptor (CAR)" and "pregnane X receptor (PXR)" (IARC, 2017).

Mutagenicity/genotoxicity

PFOA/APFO was not genotoxic in various test systems. It does not have mutagenic effects in the Ames test with *Salmonella typhimurium* bacteria, or induce chromosome changes in cellular systems (IARC, 2017). Negative results in the Ames Test of APFO were already published in 1980 (Griffith & Long, 1980).

Carcinogenicity
The text in this section is, unless otherwise stated, based on the IARC (2017) and references therein.

Carcinogenicity in animals
There are two older long-term studies available with rats exposed to the ammonium salt APFO in the feed for 2 years.

In one of the studies, male and female rats were exposed to concentrations of APFO corresponding to 0, 30 or 300 ppm in the feed or an average daily dose of 0, 1.3 and 14.2 mg PFOA/kg bw in male rats and 0, 1.6 and 15.1 mg/kg bw in female rats. After 2 years, male rats exposed to the highest exposure had a significantly increased incidence of tumours in the testicles ("Leydig cell adenomas") and damage to the pancreas. In comparison, the female rats had a significantly increased frequency of tumours in the breasts (fibroadenomas) (Butenhoff *et al*., 2012).

In the other study, male rats were exposed to 300 ppm APFO in the feed (13.6 mg/kg bw). After 2 years, among the exposed male rats, there was an increased incidence of tumours in the liver, testicles and pancreas (Biegel *et al*., 2001).

Carcinogenicity in humans
There are epidemiological studies of PFOA-exposed workers in the United States, which may indicate increased risk of dying from renal and bladder cancer.

Studies of particularly vulnerable populations with homes near a major fluoro-chemical industry in the United States that polluted the Ohio River with PFOA, resulting in contamination of drinking water and wells, showed a doubling or more of renal and testicular cancer, as well as a dose-dependent increased frequency of renal-, prostate- and breast cancer.

There are also epidemiological studies of the general population, including the Danish population, reporting a small excess incidence of cancer in the prostate and pancreas. Here, however, the problem is that, at the same time, the normal population is exposed to PFOS in higher concentrations and other PFCAs in lower concentrations as well as many other factors. As it is a matter of exposure to a cocktail of substances where PFOA is not even the most common, the probability of PFOA causing these effects alone becomes unlikely.

Overall assessment according to IARC
The IARC (2017) assessed that there was limited evidence that PFOA was carcinogenic in humans and experimental animals. Therefore, the overall assessment was that PFOA was possibly carcinogenic in humans (group 2B).

Reproductive toxicity
Many animal studies, especially with mice, have shown that exposure of pregnant females to PFOA/APFO can harm the foetuses (Lau *et al*., 2007).

In one of the studies, pregnant mice were exposed to APFO on days 1-17 via stomach tube, corresponding to 1, 3, 5, 10, 20 or 40 mg PFOA/kg (Lau *et al*. 2006). The number of live born pups was significantly reduced in groups exposed to 10 mg/kg bw or more. Survival after birth was affected and opening of the eyes was delayed at 5 mg/kg bw. In all dose groups, except for the lowest at 1 mg/kg bw, there was an effect on the growth of the offspring. Thus, NOAEL in this study for reproductive toxicity was 1 mg/kg bw.

In a later study of the same research group, it was shown that the effects after birth were due to PFOA being transmitted via placenta and breast milk (Wolf *et al*., 2007).

Steady-state concentrations of PFOA in rat milk are 10 times lower than in the blood of the mother animal (Hinderliter *et al*., 2005). It is the opposite of the lipophilic persistent contaminants such as PCB and PBDE. Therefore, breast milk analysis is a less suitable monitoring method for PFAS. However, many studies have been conducted on breast milk in particular to assess the infants' intake of PFOA (e.g. Antignac *et al*., 2013; Mondal *et al*., 2014; Lorenzo *et al*., 2016; Kang *et al*., 2016; Lee *et al*. 2018).

In another study of the same research group, other and more sensitive mice strains were similarly exposed at days 1-17 during the gestation period to 0.1, 0.3, 0.6, 1, 3, 5, 10 and 20 mg APFO/kg bw/day (Abbott *et al*., 2007). In the most sensitive mice strain, survival of neonates decreased at an exposure of 0.6 mg/kg bw/day, i.e. NOAEL was 0.3 mg/kg bw/day.

Macon *et al*. (2011) studied low dose effects of PFOA with the purpose of investigating mammary gland development in mice following prenatal exposure and determining the corresponding internal dose metric associated with these effects. It was observed that the development of the mammary gland was inhibited up to 84 days after birth at exposures of 0.3 mg/kg bw/day. In addition, impaired mammary gland development was observed, even at lower doses of APFO (0.01 mg/kg bw/day). The absolute and relative liver weight increased in the highest treatment group (1 mg/kg bw/day), but the effect was not as sustained (up to 14 days after birth) compared with changes in the mammary gland (Macon *et al*., 2011)

In a 3-generation study with mice, exposure of the mother animal to 1-3 mg PFOA/kg bw/day as APFO in drinking water resulted in a delay of, *inter alia*, breast development in the offspring with delayed milk production after the pup was full-grown (White *et al*., 2011).

Hormone-disruptive effects
PFOA is in many ways hormone-disruptive (White *et al*., 2011) and affects the function of thyroid hormones by binding to thyroxin (T4) plasma transport protein and transthyretin (TTR), thus reducing the T4 concentration in the blood (Weiss *et al*., 2009).

Exposure of adult rats to PFOA (25 mg APFO/kg bw with stomach tube) lowered testosterone levels in the testicles, increased estradiol levels in blood serum and reduced the relative weight of the accessory genitalia (Biegel *et al*., 1995). This could be explained by the fact that PFOA induces enzyme liver aromatase, which converts testosterone into estradiol.

4.2.1.8 Critical effect

Impact on the blood profile and liver is the most critical effect with the lowest experimentally determined NOAEL value of 0.06 mg/kg PFOA bw/day (equivalent to 60 µg PFOA/kg bw/day) in a 90-day study of male rats exposed to APFO in the feed (Perkins *et al*., 2004).

These are older studies of shorter duration, and the NOAEL values are highly uncertain because there are too few low-dose groups in the studies. It is surprising that NOAEL is higher for long-term studies, where they should be logically be lower, possibly indicating that the long-term study values should be regarded as LOAEL instead. There are also other studies that report higher NOAEL values than in the cited 90-day study. The experiments are made with APFO and not PFOA, adding additional uncertainty to the data.

In the study of developmental toxicity (Lau *et al*. 2006), a NOAEL of 1 mg APFO/kg bw in mice was determined for effects on the growth of the offspring. This NOAEL has been used in the EU RAC assessment (ECHA 2015b); see below for an in-depth review of this assessment. In another more sensitive mouse strain exposed to a broader dose regimen, there was decreased survival of neonates at an exposure of 0.6 mg/kg bw/day, i.e. that NOAEL was 0.3 mg/kg bw/day (Abbott *et al*., 2007).

For a number of years, the European Food Agency (EFSA) recommended a tolerable daily intake (TDI) for PFOA of 1.5 µg/kg bw per day. This TDI was calculated on the basis of the lowest NOAEL identified at 0.06 mg/kg bw/day (from the Perkins *et al*. 2004 study) and a calculated benchmark dose for a 10% effect ($BMDL_{10}$)[13] of 0.3 mg/kg bw/day. An assessment factor of 100 was used to compensate for differences between and within animal species and an assessment factor of 2 was used for toxicokinetic uncertainty (EFSA, 2008).

The TDI value was criticized later for being too high and insufficiently considering the large difference between the excretion in the urine of PFOA in animals and humans, where excretion in humans may be 1000 times less than in rats (Harada *et al*., 2005). It has also not taken into account that the few available animal experiments are old, not published in open literature, and therefore may be of limited quality. In addition, studies of PFOA itself and the ammonium salt APFO have not been assessed separately, but rather mixed together, adding further uncertainty to the TDI value. The population is furthermore exposed to PFOA precursors, often more lipophilic and assumed to be more easily absorbed through the skin, after which the precursor inside the body is broken down into PFOA and bound to albumin in the blood.

Adults' average daily intake of PFOA with food in the EU has been assessed to be 0.08-4.3 ng/kg bw (EFSA, 2012). Therefore, the intake is far less than the established TDI, but using a safety factor of 1000 (worst case) instead of 10 for extrapolation from rats to humans, due to the much more effective resorption in the kidneys in humans relative to rats mentioned above, the TDI would be 0.15 ng/kg bw/day and thus exceeded for a smaller proportion of the population. This would be the case even without including the contributions of drinking water, indoor climate and dermal contact.

In the background document for REACH Annex XV restriction proposals for PFOA (ECHA, 2015b), several DNEL ("derived no-effect level") values are calculated based on NOAELs from animal experiments determined from intake, measured serum concentrations and from epidemiological studies in humans based on measured serum concentrations and of these calculated "NOAEL" values. The background document suggests different DNEL values for various critical effects, including decreased weights in pups for mice (Lau *et al*. 2006), neonatal survival in mice (Abbott *et al*. 2007) and delayed development of the mammary gland (Marcon *et al*. 2011). Based on the epidemiological studies, the background document also proposes DNEL values for elevated total cholesterol and LDL in human serum (Stenland *et al*. 2009) and reduced birth weight in humans (Fei *et al*. 2007) (ECHA, 2015b).

In the final opinion from RAC (ECHA, 2015a) it was concluded that, although there is concern about the effects on the mammary gland, it is currently not possible to determine a robust NOAEL value that can be used for the DNEL calculations based on these effects. Similar conclusions are made for the NOAEL values from epidemiological studies by RAC. Therefore, it was proposed to calculate DNEL based on the study from Lau at al. (2006), supported by data from Abbott *et al*. (2007). Therefore, in the final opinion of RAC, DNEL is calculated on the basis of a NOAEL of 20,000 ng/mL serum (equivalent to an external NOAEL of 1 mg/kg/day). For serum concentration, an assessment factor of 25 (for the general population) was considered sufficient, resulting in a DNEL of 800 ng/mL (ECHA, 2015a). No 'external' DNEL was calculated.

Bernauer (2010) from the German Federal Institute for Risk Assessment (BfR) has identified five different NOAEL values (serum PFOA concentrations in µg/mL) and used the lowest value

[13] The BMD method in risk assessment makes use of the entire dose response curve for an effect, in contrast to NOAEL, which uses the lowest exposure without effect. $BMDL_{10}$ is the dose where the change in Response is likely to be smaller than 10 %, where the term 'likely' is defined by the statistical confidence level, usually 95% confidence.

from a human epidemiological study to calculate an internal DNEL of 0.8 µg PFOA/mL serum and an external DNEL of 0.08-0.17 µg PFOA/kg bw/day. This DNEL is estimated to be 2-10 times lower than the DNEL calculated from animal experiments. It should be mentioned that the RAC concluded that the available epidemiological studies are not suitable for quantitative risk assessment.

4.2.2 Perfluorobutanoic acid (PFBA)

4.2.2.1 Database

Many data are obtained from the Danish Environmental Protection Agency's previous literature study of environmental and health effects of short-chain PFAS (Kjølholt *et al.*2015). These are supplemented with data in later articles/reports from the authors' archive or found in searches on Google Scholar. Data for physicochemical properties are also sought in PubChem, Comptox, Guidechem, Molbase, and other internet-based databases.

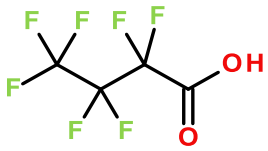
4.2.2.2 Identification

CAS no. 375-22-4
EC no. 206-786-3
UN no. 3265

Molecular formula

$C_4HF_7O_2$

Structural formula



Synonyms

2,2,3,3,4,4,4-heptafluorobutanoic acid, heptafluorobutyric acid.

Salts

	Sodium heptafluorobutyrate (NaPFB)	Potassium heptafluorobutyrate (KPFB)	Silver heptafluorobutyrate (AgPFB)	Ammonium heptafluorobutyrate (APFB)
CAS no.	2218-54-4	2966-54-3	3794-64-7	10495-86-0
EC no.	218-721-6		223-266-1	
Molecular formula	$C_4F_7NaO_2$	$C_4F_7KO_2$	$C_4AgF_7O_2$	$C_4H_4F_7NO_2$

4.2.2.3 Physical-chemical properties

Property	PFBA	NaPFB	KPFB	AgPFB	APFB
Molecular weight	214.038	236.021	252.129	320.90	231.07
Boiling point °C	[a]121; [cd]120	[b]120.2			
Melting point °C	[ad]-17.5; 18	[d]248-250;			
Solubility in water	[d]Soluble [a]0.345 mol/L = 74 g/L	[a]1.01 mol/L = 238 g/L		[a]1.01 mol/L = 238 g/L	
Density (at 25°C), g/cm^3	[cd]1.645; [a]1.68				
Vapour pressure (at 25 °C)	[d]≈10 mm Hg = 1333 Pa; [c]1300 Pa;				
Partition coefficient Log P_{ow}	[a]2.66; 2.82	[a]2.22		[a]2.22	[c]2.08

[a]Comptox; [b]Chemnet; [c]Sigma-Aldrich; [d]Chemicalbook;

PFBA is a colourless liquid.

4.2.2.4 CLP classification

There are no harmonised classifications for PFBA. Ninety-one companies have made notified classifications according to CLP criteria (ECHA C&L Inventory, 2017).

Hazard class and category for PFBA	Hazard Statement Code(s)	Hazard Statements
Skin Corr. 1A Eye dam. 1 (59 notifiers)	H314	Causes severe skin burns and eye damage
	H318	Causes serious eye damage
Skin Corr. 1A (24 notifiers)	H314	Causes severe skin burns and eye damage
Skin Corr. 1B (5 notifiers)	H314	Causes severe skin burns and eye damage
No info on hazard class and category (1 notifier)	H314	Causes severe skin burns and eye damage
	H318	Causes serious eye damage
	H370	Causes damage to organs
Skin Corr. 1B Eye dam. 1 Met. Corr. 1 (1 notifier)	H314	Causes severe skin burns and eye damage
	H318	Causes serious eye damage
	H290	May be corrosive to metals
Skin Corr. 1B STOT SE 3 (1 notifier)	H314	Causes severe skin burns and eye damage
	H335	May cause respiratory irritation

A single company has submitted a notified classification of the sodium salt according to the CLP criteria:

Hazard class and category for NaPFB	Hazard State-ment Code(s)	Hazard Statements
Skin irrit. 2	H315	Causes skin irritation
Eye irrit. 2	H319	Causes serious eye irritation
STOT SE 3	H335	May cause respiratory irritation

Twenty-three companies have submitted a notified classification of the silver salt according to the CLP criteria:

Hazard class and category for AgPFB	Hazard Statement Code(s)	Hazard Statements
Eye dam. 1	H318	Causes serious eye damage

4.2.2.5 Toxicokinetics and metabolism

Chang *et al*. (2008) compared toxicokinetics of a single dose of PFBA in rats, mice and monkeys. In the experiments with rats and mice, the ammonium salt was used and in monkeys the potassium salt was used. After oral exposure, stomach acid makes this difference irrelevant, as the equilibrium is shifted so that most PFBA in both cases occurs as perfluorobutanoic acid. The results are reviewed below.

Data for humans are derived from occupational exposure (inhalation and dermal absorption) or from oral exposure to contaminated drinking water; therefore, not to single doses of single substances, but rather prolonged exposure to an unspecified mixture of compounds measured as PFBA in blood serum (Chang *et al*., 2008).

Absorption

In female rats exposed to a single dose of 10, 30, 100 or 300 mg of ammonium perfluorobutyrate/kg of bw dissolved in water via stomach tube, the absorption in the gastrointestinal tract was estimated to be complete (100%) because all of the PFBA was recovered in urine within a

day (Chang *et al*., 2008). For male rats, the elimination in urine was only 50-90%. In mice and monkeys, an even smaller fraction of PFBA (35-68%) was excreted in urine after 24 hours. These lower eliminations imply a smaller uptake or a longer elimination time. Direct absorption was not determined in the experiments.

The dermal uptake of PFBA as acid or salt was not investigated by Chang *et al*. (2008), but it is likely that absorption through the skin of a water-soluble PFBA salt would be minimal and much less than the absorption through the gastrointestinal tract.

Distribution

The absorbed PFBA is bound to albumin in the blood and is transported around the body until it is either eliminated or deposited in tissues and organs. The binding constant for PFBA to albumin in humans measured by fluorescence was 1.1×10^6 per mole, five times more than for PFOA (Chen and Guo, 2009).

In the blood, the elimination half-life of PFBA in rats was nine and two hours respectively in males and females. For comparison the mean half-life was to 5-16 hours in male mice and three hours in female mice; in monkeys 41-46 hours and in humans 72 and 87 hours (Chang *et al*., 2008).

Out of 177 subjects with current or previous occupational exposure to material which can be metabolised to PFBA, 72% of subjects demonstrated less than the quantification limit of 0.5 ng PFBA/mL in the blood and 96% had less than 2.0 ng PFBA/mL in blood. There were more current workers that had quantifiable concentrations of PFBA than previous workers. The half-life in the blood serum of PFBA was in a sample of this working population for <7 days. This is much shorter than for PFOA, for which half-life is 2-8.5 years (Wang *et al*., 2015).

In a recent study, distribution in tissues and organs of PFOA, PFHxA and PFBA in mice after low exposures for ^{18}F-labeled radioactive compounds was investigated (Burkemper *et al*., 2017). Four hours post-injection, radioactivity was measured in tissues/organs as a percent of dose per gram of tissue. PFBA concentrations were highest in the stomach, where 7.5% PFBA was being distributed much more than the two other substances together. There was very little PFBA in the fat, muscles and brain in this study. More details are discussed in the summary in section 4.2.6.2.

In a Spanish study of organs from 20 deceased people, PFBA was the most common PFAS in lungs and kidneys with median values of 807 and 263 ng/g wet weight, respectively, whereas the content of PFOA in lungs was only one-tenth of PFBA (Perez *et al*. 2013). The content of PFBA in brain and liver was also significant. The mean concentration of PFBA in the liver was approximately the same as PFOA: 13.6 and 12.9 ng/g wet weight, respectively. There was an average of 13.5 ng PFBA/g wet weight in the brain, but no PFOA in the brain tissue.

Metabolism

Derivatives of perfluoroalkanoic acids, e.g. telomer alcohols, can be metabolised to perfluoro-alkanoic acids, but the acids cannot be further metabolised.

Elimination

The primary elimination route for PFAS is via the kidneys in the urine. Female rats and female mice have a greater and faster elimination process due to minor resorption in the kidneys. In experiments with rats, 51-90% and 101-112% of the administered dose of PFBA as ammonium salt were excreted in the urine in males and females, respectively, over a 24-hour period. In similar experiment with mice, 35% and 65-68% of the administered dose of PFBA as ammonium salt were excreted in the urine in males and females, respectively. Likewise, in mon-

keys, 41 and 46% of the administered dose of PFBA as potassium salt was excreted in urine of males and females, respectively, within a 24-hour period (Chang *et al*., 2008).

In rodents, elimination of PFAS with urine generally increases with shorter chain length (Kudo *et al*. 2001). However, PFBA behaves slightly differently and is e.g. eliminated more slowly in rats than PFHxA (Yang *et al*., 2009).

In South Korea, PFBA was determined in urine samples from 20-29-year olds in concentrations of ND-1,720 ng/L (Kim *et al*., 2014).

PFAS is less excreted with breast milk than lipophilic environmental toxins. The short-chain PFCA has not been studied as often in breast milk as PFOA. In a French study of PFAS in 48 samples of breast milk, PFBA was determined in 17% of the samples with an average concentration of 81 ng/L and a maximum concentration of 134 ng/L, while PFOA was determined in 98% of the samples with the same mean concentration as PFBA but with a higher maximum concentration (224 ng/L) (Antignac *et al*., 2013). In the neighbouring country of Spain, PFBA was detected in all 10 samples of breast milk at an average concentration of 50 ng/L and with a maximum concentration of 155 ng/L. In comparison, the concentrations of PFOA were 177 and 980 ng/L, respectively (Lorenzo *et al*., 2016).

In 264 samples of breast milk from South Korea, PFBA was not determined, while PFOA was determined in > 98% of the samples with an average concentration of 72 ng/L (Kang *et al*., 2016). In a later study of 293 samples, PFBA was not determined and the determined PFOA concentration was slightly lower at 55 ng/L on average as compared to the 2016 study (Lee *et al*., 2018).

4.2.2.6 Irritation and allergy

As stated by the notified classifications, PFBA as acid and salts may cause skin, eye and respiratory irritation (see section 4.2.2.4). There is no information about potential allergenic effects.

4.2.2.7 Acute and chronic effects

Short-term animal studies

Continuous 28-day and 90-day oral toxicity studies of ammonium perfluorobutyrate (PFBA) were performed with male and female rats exposed to daily PFBA doses of 0, 6, 30 and 150 mg/kg in the 28-day study and 0, 1, 2, 6 and 30 mg/kg in the 90-day study via stomach tube. In a comparison study, 30 mg/kg ammonium perfluorooctanoate (PFOA) was administered to rats daily for 28 days (Butenhoff *et al*., 2012). The effects in male rats were *inter alia* increased liver weight, enlarged liver cells, and reduced blood cholesterol and thyroxine levels. NOAEL was 6 mg/kg bw/day and LOAEL was 30 mg/kg bw/day, both in the 28- and 90-day study. There were no observed effects in the female rats. The difference in sensitivity was explained by the fact that female rats had lower PFBA concentration in blood and liver because they eliminate PFBA more easily. In the comparative study with PFOA, clinical signs of poisoning were observed in both female and male rats, illustrating the greater toxicity of PFOA.

No long-term animal studies have been identified for this substance.

Toxicological mechanisms

As with other perfluoroalkyl acids and salts, PFBA can activate "peroxisome proliferator-activated receptor-α" (PPAR-α) in rat liver cells *in vivo* and therefore cause peroxisome proliferation, enlarged liver and increased fatty acid oxidation, but PFBA is less effective than PFOA in this matter (Ikeda *et al*., 1985).

In special *in vitro* model systems with animal cells, this effect on PPAR α has been shown to be about 20 times less for PFBA than for PFOA. However, PFBA was twice as active as PFOS in these tests (Wolf *et al*., 2008).

In addition, PPAR-α was more readily induced by PFBA in mouse cells than in humans in this *in vitro* test (Wolf *et al*. 2008) and in an *in vivo* test (Foreman *et al*., 2009). Unlike other PFCA, PFBA induces only PPAR-α, not PPAR-γ (Rosenmai *et al*., 2016).

In other *in vitro* test systems with rat cells, there was a clear tendency for activity to grow with the chain length from PFPrA, PFBA, PFHxA and PFOA, with PFOA being approximately 7 times more active than PFBA (Bjork and Wallace 2009). However, there was no significant activity in *in vitro* experiments with cultures of human cells, except in an *in vitro* test system with human hepatocarcinoma cell line HepG2, where the cytotoxicity of PFCA increased with the chain length. Therefore, PFBA had 20-fold less cytotoxicity than PFOA (Buhrke *et al*., 2013).

Mutagenicity/genotoxicity
In this study, relevant studies have not been identified.

Carcinogenicity
In this study, relevant studies have not been identified.

Reproductive toxicity
In an earlier study, pregnant mice were exposed daily to PFBA as ammonium salt from days 1-17 at doses of 35, 175 and 350 mg/kg bw. There were liver effects on the mother animal at the two high doses as well as more full litter resorptions and delayed vaginal opening, but no significant effects on the progeny at the lowest dose, except that the foetus' eye opening was 1-1½ days delayed (Das *et al*. 2008). Similar effects were seen for PFOA at much lower doses. This indicates that PFBA is less reprotoxic than PFOA.

Hormone-disruptive effects
It is apparent from the rat studies reviewed above (Butenhoff *et al*. 2012) that exposure to PFBA may decrease the concentration of thyroxine in the blood. PFBA has a disruptive effect on thyroid hormone in zebrafish, but this effect is 28 times less than for PFOA (Godfrey *et al*., 2017).

Some PFAS may affect the function of thyroxin's transport proteins, including transthyretin (TTR) in competition for the receptors (Ren *et al*., 2016). The different PFAS have different binding potentials. Among PFCA, PFOA has the highest potential for binding to TTR. The potency of PFBA is about 300 times less.

In contrast to PFOA, PFBA had no estrogenic effect in *in vitro* test systems (Rosenmai *et al*., 2016).

4.2.2.8 Critical effect
The critical effect is on the liver. For PFBA, NOAEL was 6 mg/kg/day for liver effects in both the 28- and 90-day studies with male rats. In similar studies, NOAEL for PFOA was 0.06 mg/kg bw/day or 100 times less, so PFBA is much less hepatotoxic than PFOA. There is no NOAEL for long-term exposure or for dermal exposure to PFBA.

4.2.3 Perfluoropentanoic acid (PFPeA)

4.2.3.1 Database

Most data are obtained from the Danish Environmental Protection Agency's previous literature study of environmental and health effects of short-chain PFAS (Kjølholt *et al.*2015). These are supplemented with data in later articles/reports from the authors' archive or found in searches on Google Scholar. There are very few publicly available data for PFPeA. Data for physico-chemical properties were also sought in PubChem, Comptox, Guidechem, Molbase, and other internet-based databases.

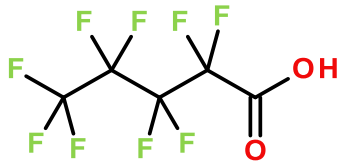
4.2.3.2 Identification

CAS no. 2706-90-3
EC no. 220-300-7
UN no. 3265

Molecular formula

$C_5HF_9O_2$

Structural formula



Synonyms

2,2,3,3,4,4,5,5,5-nonafluoropentanoic acid, perfluorovaleric acid (PFPA).

Salts

	Sodium perfluoropentanoate (NaPFPe)	Ammonium perfluoropentanoate (APFPe), ammonium perfluorovalerate
CAS no.	2706-89-0	68259-11-0
EC no.	220-299-3	269-514-2
Molecular formula	$C_5F_9NaO_2$	$C_5H_4F_9NO_2$

4.2.3.3 Physical-chemical properties

Property	PFPeA	NaPFPe	APFPe
Molecular weight	264.047	286.028	281.078
Boiling point °C, (at 1 atm.)	[a]138; [cdf]140;	[a]143; [e]124.4	[a]143; [b]124.4
Melting point °C	[a]14.3	[a]7.1	
Solubility in water	[a]0.235 mol/L = 62 g/L	[a]0.935 mol/L = 267 g/L	[a]0.935 mol/L = 263 g/L
Relative density (at 25°C)	[a]1.67;; [de]1.713;		
Vapour pressure (at 25 °C)	[e]7.93 mm Hg = 1057 Pa; [a]3.54 mm Hg = 472 Pa	[a]4.84 mm Hg = 645 Pa; [e]7.94 mm Hg = 1059 Pa	[a]4.84 mm Hg = 645 Pa; [b]7.93 mm Hg = 1057 Pa
Partition coefficient Log P_{ow}	[a]3.64; [e]2.54	[a]3.33; [e]1.20	[a]3.33

[a]Comptox; [b]Chemnet;[c]Sigma-Aldrich; [d]Chemicalbook; [e]Molbase; [f]Chemspider

PFPeA is a colourless liquid.

4.2.3.4 CLP classification

There is no harmonized classification of PEPeA.
For PFPeA, 31 companies have submitted a notified classification according to the CLP criteria (ECHA C&L Inventory, 2017).

Hazard class and category	Hazard Statement Code(s)	Hazard Statements
Skin Corr. 1B (30 notifiers)	H314	Causes severe skin burns and eye damage
Met. Corr. 1 Skin Corr. 1C Eye Dam. 1 (1 notifier)	H290	May be corrosive to metals
	H314	Causes severe skin burns and eye damage
	H318	Causes serious eye damage

4.2.3.5 Toxicokinetics and metabolism

There are no studies of toxicokinetics for PFPeA, but as other PFCA, the substance would be metabolically inert.

In a recent study, the urine from Employees of the Austrian Environmental Protection Agency was examined for the presence of 12 PFAS (Hartmann *et al*., 2017). All urine samples contained PFOS, PFOA PFNA and PFHxA, but PFAS with chain length ≥ 10 carbon was not detected. PFPeA was found in 73% of the samples at concentrations of ND-8.5 ng/L, so there is probably some exposure to the substance among the general population, as well as some uptake and excretion in urine.

PFAS is excreted in breast milk less than lipophilic environmental toxins. The short-chain PFCA has not been studied as often in breast milk as PFOA. In a French study of PFAS in 48 samples of breast milk, PFPeA was not found in concentrations above the detection limit (between 0.05 and 0.07 µg/L), while PFOA was determined in 98% of the samples with an average concentration of 82 ng/L with a maximum of 224 ng/L(Antignac *et al*., 2013). In the neighbouring country of Spain, PFPeA was not detected in 10 tested samples (Lorenzo *et al*., 2016).

In 264 samples of breast milk from South Korea, PFPeA was determined in 82% of the samples with a median concentration of 58 ng/L, while PFOA was determined in > 98% of the samples with an average concentration of 72 ng/L (Kang *et al*., 2016). In a later study of 293 samples, PFPeA was determined only in one of the samples at a concentration of 4 ng/L. The content of PFOA was > 10 times higher at 55 ng/L on average and 657 ng/L at maximum (Lee *et al*., 2018).

In pregnant women, PFAS can be transferred from the mother's blood to the placenta (Zhang *et al*., 2013). Unlike PFHxA, PFHpA and PFOA which have been detected in the mother's blood, umbilical cord blood, placenta and foetal water, PFPeA was detected only in foetal water.

In a Spanish study of organs from 20 deceased people, PFPeA was detected only in lung tissue with a median value of 44.5 ng/g wet weight, almost twice as high as the concentration of PFOA in lungs (Perez *et al*., 2013).

4.2.3.6 Irritation and allergy

As stated by the notified classifications, PFPeA as acid and salts may cause skin, eye and respiratory irritation (see section 4.2.3.4). There is no information about potential allergenic effects.

4.2.3.7 Acute and chronic effects

In this study, no toxicological studies with animals exposed to PFPeA have been identified.

Toxicological mechanisms

Many perfluoroalkyl acids and salts, including PFPeA, can induce peroxisome proliferation, induction of peroxisomal fatty acid oxidation and enlarged liver, by activating "peroxisome proliferator-activated receptor α" (PPAR-α) in the nucleus.

In a recent study, PFPeA was shown to be a weak peroxisome proliferator in cells from mice and humans with a potency between those of PFBA and PFHxA (Wolf *et al*., 2013).

PFPeA and PFOA were active in both PPAR-α and PPAR-γ "reporter gene assays" (Rosenmai *et al*., 2016).

Mutagenicity/genotoxicity

In the present study, no relevant studies have been identified, but as with other PFCAs, PFPeA is probably not genotoxic.

Carcinogenicity

In this study, relevant studies have not been identified.

Reproductive toxicity

In this study, relevant studies have not been identified.

Hormone-disruptive effects

In contrast to PFOA, PFPeA had no estrogenic effect in *in vitro* test systems (Rosenmai *et al*., 2016).

4.2.3.8 Critical effect

No toxicological studies with animals exposed to PFPeA have been identified in this study; therefore, the critical effect cannot be determined, but presumably, effects on the liver via PPAR-α would be critical, considering that PFPeA is a potent peroxisomal proliferator. However, PFOA is about 10 times more active than PFPeA.

Therefore, there is no data available for determining NOAEL values.

4.2.4 Perfluorohexanoic acid (PFHxA)

4.2.4.1 Database

Most data are obtained from the Danish Environmental Protection Agency's previous literature study of environmental and health effects of short-chain PFAS (Kjølholt *et al.*2015). These are supplemented with data in later articles/reports from the authors' archive or found in searches on Google Scholar. Data for physicochemical properties were also sought in PubChem, Comptox, Guidechem, Molbase, and other internet-based databases.

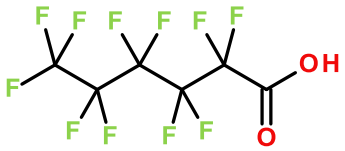
4.2.4.2 Identification

CAS no. 307-24-4
EC no. 206-196-6
UN no. 3265

Molecular formula

$C_6HF_{11}O_2$

Structural formula



Synonyms

2,2,3,3,4,4,5,5,6,6,6-undecafluorohexanoic acid, undecafluorohexanoic acid, perfluorocaproic acid.

Isomers and salts

	Ammonium per-fluorohexanoate (APFHx)	Sodium perfluo-rohexanoate (NaPFHx)	Ethylammonium per-fluoroisohexanoate (ethylammonium salt of branched isomer)
CAS no.	21615-47-4	2923-26-4	68015-84-9
EC no.	244-479-6	220-881-7	268-149-6
Molecular formula	$C_6H_4F_{11}NO_2$	$C_6F_{11}NaO_2$	$C_9H_8F_{13}NO_2$

4.2.4.3 Physical-chemical properties

Property	PFHxA	NaPFHx	APFHx	Ethylammo nium salt
Molecular weight	314.053	336.036	331.085	409.147
Melting point °C	[ace]14;	[a]61.5		[a]50.5
Boiling point °C (at 1 atm.)	[acde]157;	[a]202.	[a]168	[a]163
Solubility in water (at 25 °C)	[d]15.7 g/L; [a]0.298 mol/L= 94 g/L;;	[a]0.225 mol/L = 76 g/L	[a]0.892 mol/L = 295 g/L	[a]0.433 mol/L = 177 g/L
Density g/cm^3	[a]1.72; [c]1.759 (20°C); [e]1.762; [e]1.722;	[a]1.69		[a]1.74;

Property	PFHxA	NaPFHx	APFHx	Ethylammonium salt
Vapour pressure (at 25 °C)	[d]1.98 mm Hg = 264 Pa; [a]1.63 mm Hg = 217 Pa;	[a]1.45 mm Hg = 193 Pa: [fg]3.09 mm Hg = 4.11 Pa;	[a]1.65 mm Hg = 220 Pa [fb]3.09 mm Hg = 4.11 Pa;	[a]0.756 mm Hg = 100 Pa
Partition coefficient Log P_{ow}	[a]4.10; [d]3.45;	[a]3.33; [g]1.83	[a]2.78; [g]3.50	[a]4.93

[a]Comptox; [b]ChemSrc; [c]Chemicalbook; [d]PubChem; [e]Chemspider; [f]Chemnet

PFHxA is a colourless liquid and a strong acid, while the salts are solids.

4.2.4.4 CLP classification

PFHxA is pre-registered under the REACH Regulation. PFHxA, its salts and precursors are under review for Germany's "risk management options" with recent conclusions (RMOA 2017). There are no harmonised classifications for PFHxA.

For PFHxA, 29 companies have submitted notified classifications according to the CLP criteria (ECHA C&L Inventory, 2017).

Hazard class and category for PFHxA	Hazard Statement Code(s)	Hazard Statements
Skin Corr. 1B (24) notifiers)	H314	Causes severe skin burns and eye damage
Skin Corr. 1B (3 notifiers)	H314	Causes severe skin burns and eye damage
	H335	May cause respiratory irritation
Met. Corr. 1 Skin Corr. 1B Eye Dam. 1 (1 notifier)	H290	May be corrosive to metals
	H314	Causes severe skin burns and eye damage
	H318	Causes serious eye damage
Acute Tox 3 Acute Tox 3 Skin Corr. 1B Acute Tox. 2 (1 notifier)	H301	Toxic if swallowed
	H311	Toxic in contact with skin
	H314	Causes severe skin burns and eye damage
	H330	Fatal if inhaled

4.2.4.5 Toxicokinetics and metabolism

Absorption

In rats and mice administered 2 or 100 mg PFHxA/kg bw (^{14}C-labeled and as sodium salt) orally, the blood serum concentrations were maximal after 15-30 minutes and almost 100% of an oral dose of PFHxA was excreted with urine within a day (Gannon *et al.*, 2011).

In another study with a single intravenous administration of 10 mg PFHxA/kg bw (as acid), 80% was excreted in urine within 24 hours. Following repeated oral administrations, 90% in male rats and 70-100% in female rats was excreted (Chengelis *et al.*, 2009a)

Based on these studies, the uptake of PFHxA in the gastrointestinal tract in the rat and mouse is assumed to be rapid and complete. How the salts are absorbed is not known. No studies have been identified where the dermal uptake of PFHxA or its salts have been investigated.

Distribution

In the blood, PFHxA is bound to another serum albumin than PFOA, but PFOA is more strongly bound, since 5-6 PFOA molecules can bind to each albumin molecule (D'eon and Mabury, 2010).

In a recent study, distribution in tissues and organs of PFOA, PFHxA and PFBA in mice after low exposures to ^{18}F-labeled radioactive compounds was investigated (Burkemper *et al*., 2017). Four hours post-injection, radioactivity was measured in tissues/organs as a percent of dose per gram of tissue. Except in the stomach, the concentration of PFHxA was far higher than for PFBA. There was very little of all three in the fat, muscles and brain in this study. Details are discussed in the summary in Section 4.2.6.2.

In a Spanish study of organs from 20 deceased people, PFBA was the most common PFAS in lungs and kidneys with median values of 807 and 263 ng/g wet weight, respectively, whereas the content of PFOA in lungs was only one-tenth of PFBA (Perez *et al*. 2013). The content of PFBA in brain and liver was also significant. The mean concentration of PFBA in the liver was approximately the same as PFOA, 13.6 and 12.9 ng/g wet weight, respectively. There was an average of 13.5 ng PFBA/g wet weight in the brain, but no PFOA in the brain tissue.

In a Spanish study of organs of 20 deceased people, the liver and brain contained the highest concentrations of perfluorohexanoic acid (PFHxA) with median values of 68.3 and 141 ng/g wet weight respectively (Perez *et al*., 2013).

Toxicokinetics in humans of 11 PFAS substances - including PFOA, PFHxA and PFHpA - were studied by Fàbrega *et al*. (2015) using a validated PBPK model. The distribution in the body was described by a distribution coefficient between the concentration in a particular tissue and the concentration in the blood. There was no significant correlation between this distribution and the chain length. PFHxA had a relatively high distribution to the brain and liver, but also occurred to a large extent in the lungs and bone marrow. The absolute concentration of PFHxA in the brain was 10 times higher than that of PFOA. Apart from PFOS, PFOA had a relatively larger proportion of blood distributed among the 11 PFASs studied, and PFOA also had the highest PFAS concentration found in blood, bone marrow and lungs.

Half-life for serum elimination

The half-life of PFHxA (acid) in blood serum following a single intravenous dose of 10 mg PFHxA/kg bw was 0.4 and 1.5 hours in female and male rats respectively (Chengelis *et al*. 2009a). In rats given repeated oral daily doses of 50, 150 and 300 mg PFHxA/kg bw for 26 days, the half-life in serum was 2-3 hours, regardless of dose size, number and sex.

In another study, half-lives for serum elimination of a single orally administered dose of PFHxA (as sodium salt) were 1.6 hours in male rats and 0.6 hours in female rats (Gannon *et al*., 2011). This corresponds to findings after intravenous administration of the acid in the previous study by Chengelis *et al*. (2009a).

In monkeys administered a single intravenous dose of 10 mg PFHxA/kg bw, serum half-life was 2-5 hours without clear gender differences (Chengelis *et al*., 2009a).

In pigs, plasma elimination half-life of PFHxA was 4.1 days, while it was 236 days for PFOA - i.e. more than 50 times faster (Numata *et al*., 2014).

Calculations have shown that the mean ("geomean") serum elimination half-life of PFHxA in humans was 32 days with an interval of 14-49 days (Russell *et al*., 2013). The study showed that the half-life of PFHxA is much longer in humans than in experimental animals, but still 40-80 times faster than for PFOA.

In the general population, concentrations of PFHxA in blood serum/plasma are usually low and below the detection limit (LOD). For residents near companies that produce fluorine substances, a study from the United States showed that PFHxA could only be measured in blood serum in about half of the population and with an average/median concentration of PFHxA at 1.4/1.0 ng/mL (Frisbee *et al*., 2009).

Metabolism
Gannon *et al*. (2011) examined and confirmed that PFHxA cannot be metabolized *in vitro* or *in vivo*.

Elimination
The main elimination pathway for PFHxA occurs in urine. In a Japanese study of rats and mice exposed to PFHxA (as ^{14}C-labeled ammonium salt) with stomach tube in a single dose of 50 mg/kg bw or as repeated doses for 14 days, up to 90% was recovered in urine and the rest was found in faeces (Iwai, 2011).

The fraction that was eliminated in faeces is probably that portion of the intake that was not absorbed in the gastrointestinal tract. In sheep, 4.35% of PFHxA intake is eliminated in the faeces. By comparison, the elimination of PFOA in faeces from sheep is only 3.95% (Numata *et al*., 2014).

Daily elimination of toxic substances and reabsorption of useful anionic metabolites in the kidneys are carried out by transport proteins (e.g. Oat1) located in cell membranes. Both PFHxA and PFOA inhibit Oat1 mediated β-aminohippurate transport in the kidneys; however, PFHxA does this to a greater extent (Weaver *et al*., 2010).

In a recent study, the urine from Employees of the Austrian Environmental Protection Agency, was examined for the presence of 12 PFAS (Hartmann *et al*., 2017). In addition to PFOS and PFNA, all urine samples contained PFHxA in concentrations from <0.5 to 3.0 ng/L (median 1.5 ng/L) and PFOA at concentrations of 0.79-5.1 ng/L (median 1.9 ng/L). PFAS with chain lengths ≥ 10 carbon were not detected in the urine.

PFAS is excreted less with breast milk than lipophilic environmental toxins are. The short-chain PFCA has not been studied as often in breast milk as PFOA. In a French study of PFAS in 48 samples of breast milk, PFHxA was determined in 2% of the samples with a maximum concentration of 53 ng/L, while PFOA was determined in 98% of the samples with an average concentration of 82 ng/L and a maximum concentration of 220 ng/L (Antignac *et al*., 2013). PFHxA was detected in one out of 10 tested breast milk samples at a concentration of 6 ng/L. In comparison, the mean concentration of PFOA was 177 ng/L and the maximum concentration 980 ng/L (Lorenzo *et al*., 2016).

In 264 samples of breast milk from South Korea, PFPeA was determined in 71% of the samples with a median concentration of 47 ng/L, while PFOA was determined in > 98% of the samples with an average concentration of 72 ng/L (Kang *et al*., 2016). In a later study of 293 samples, PFHxA was determined in 40% of the samples with an average concentration of 13 ng/L and maximum concentration of 129 ng/L. The content of PFOA was four times higher at 55 ng/L on average and 657 ng/L as a maximum (Lee *et al*., 2018).

In pregnant women, PFAS can be transferred from the mother's blood to the placenta (Zhang *et al*., 2013). PFHxA and PFOA were, for example, detected in the mother's blood, umbilical cord blood, placenta and foetal water.

4.2.4.6 Irritation and allergy

In the present study, no relevant data on irritation and allergenic effects have been identified, but PFHxA would, as a relatively strong acid, be irritating to skin, eyes and mucous membranes.

A possible association between PFHxA exposure and childhood asthma has been investigated, but there were no differences in the measured serum concentrations (median = 0.2 ng/mL) in 10-15-year-old children with and without asthma and no dose response relationship (Dong *et al*. 2013).

4.2.4.7 Acute and chronic effects

Most studies were carried out with oral administration of PFHxA or its salts. In the present study, no toxicity studies were identified with dermal or inhalation exposures.

Acute toxicity

Sodium perfluorohexanoate (NaPFHx), which is the sodium salt of PFHxA, has a low acute oral LD50 of > 1,750 mg/kg bw (Loveless *et al*., 2009).

Toxicological mechanisms

Many perfluoroalkyl acids and salts, including PFHxA, can induce peroxisome proliferation, induction of peroxisomal fatty acid oxidation and enlarged liver, by activating "peroxisome proliferator-activated receptor α" (PPAR α) in the nucleus (Wolf *et al*., 2008). In addition, PPAR-α is more readily induced in mice than in human cells.

In other test systems with rat cells, there was also a clear tendency for activity to grow with the chain length, with PFOA being two times more active than PFHxA (Bjork and Wallace 2009). There was no significant activity in human cells.

Both PFHxA and PFOA were active in PPAR-α and PPAR-γ "reporter gene assays" (Rosenmai *et al*., 2016).

Cell Toxicity

In an *in vitro* test system with human hepatocarcinoma cell line HepG2, PFHxA had cytotoxicity eight times lower than that of PFOA (Buhrke *et al*., 2013).

Mulkiewicz *et al*. (2007) examined the cytotoxicity of several PFCAs, including PFHxA, in several *in vitro* test systems. The toxicity was relatively insignificant, but increased with chain length. PFHxA was about 10 times less toxic in this test as compared to PFOA.

In another *in vitro* model with human colon cancer cells (HCT116), the estimated effect concentrations (EC_{50}) decreased the longer the perfluoroalkyl chain was: PFHxA> PFHpA> PFOA> PFNA etc. Therefore, PFHxA had less effect than PFOA (Kleszczynski *et al*. 2007).

Short-term animal studies

In a 90-day study rats were given different concentrations of the sodium salt of PFHxA via stomach tube (Loveless *et al*., 2009). Based on liver effects and blood parameters, NOAEL in rats was determined at 20 mg/kg bw/day. This value was three times higher than for PFOA, where NOAEL was 6 mg/kg/day in similar experiments.

In another 90-day test, 10, 50 and 200 mg/kg of PFHxA as acid dissolved in water was administered to rats via stomach tube (Chengelis *et al*., 2009b). In all dose groups, the weight gain of male rats was reduced, whereas this only occurred for the female rats at the two highest exposures. Mild liver enlargement (hepatocellular hypertrophy) and increased liver weight could be observed in the male rats, while there was no effect on the behaviour of the animals. Based on liver effects, NOAEL was determined at 50 mg/kg bw/day in male rats and 200 mg/kg bw/day in female rats. These NOAEL values were 30 times higher than for PFOA.

Mutagenicity/genotoxicity
The sodium salt of perfluorohexanoic acid (NaPFHx) was neither mutagenic in the Ames test nor induced chromosomal aberrations in human lymphocytes (Loveless *et al*., 2009).

In contrast to PFOA, PFHxA did not generate reactive oxygen compounds nor did it induce DNA damage in human HEPG2 cells (Eriksen *et al*., 2010).

Carcinogenicity
There is a recent long-term study (104 weeks/24 months) in which male rats received 2.5, 15 and 100 mg PFHxA/kg bw as acid dissolved in water with stomach tube daily, while female rats were administered double doses (Klaunig *et al*. 2015). The highest dose used corresponded to the maximum tolerated dose that does not endanger the survival of the rat (MTD). No significant effects of PFHxA on body weight, feed intake, behaviour, blood composition or hormone disturbances were observed. However, in the highest exposed group of female rats there were effects on the kidneys, liver and stomach while urine was more acidic in the highest exposed male rats. Therefore, NOAEL was determined at 15 mg/kg bw/day for male rats and 30 mg/kg bw/day in female rats. It is reported that no signs of tumours were found in the investigated bodies, but this was not documented in the article.

Reproductive toxicity
Perfluorohexanoic acid (PFHxA) was identified as a potentially foetal and developmental toxic substance in a screening test for embryos from frogs ("Xenopus (FETAX) assay") (Kim *et al*., 2015).

In a 90-day one-generation reprotoxicity study, rats were given different concentrations of the sodium salt of PFHxA via stomach tube (Loveless *et al*., 2009). A NOAEL value of 100 mg/kg bw/day was calculated based on effects on rat offspring development. PFHxA, on the other hand, had no undesirable effects on rats' reproduction and behaviour at the highest exposure of 500 mg/kg bw/day.

Reproductive toxicity of the ammonium salt of PFHxA was investigated in pregnant female mice exposed to a daily oral dose of up to 500 mg/kg bw on day 6 to 18 during the gestation period. At exposures of 175 mg/kg bw/day there was an increased number of stillbirths and young mice who died the first day. In addition, the young mice had weight reduction. NOAEL for reprotoxicity was determined at 100 mg/kg bw/day in this study (Iwai and Hoberman, 2014).

Hormone-disruptive effects
Some PFAS may affect the function of thyroxin transport proteins transthyretin (TTR) and thyroxine-binding globulin (TBG) in competition for the receptors (Ren *et al*., 2016). The different PFAS had different binding potential. Among the investigated PFCA, PFOA had the highest potential for binding to TTR. The potency of PFHxA was about 10 times lower.

There are studies indicating that PFHxA may interfere with the function of thyroid hormone and affect the development of the nervous system in birds (Vongphachan *et al*., 2011; Cassone *et al*., 2012).

In contrast to PFOA, PFHxA had no estrogenic effect in *in vitro* test systems (Rosenmai *et al*., 2016).

In a group of 13-15-year-olds in Taiwan, hormone levels in blood were compared with serum PFAS concentrations, including PFOA (mean: 0.5 ng/mL) and PFHxA (mean: 0.2 ng/mL). Most PFAS were determined in > 94% of the samples. The results showed that higher serum PFAS levels were associated with lower testosterone levels and higher estradiol levels, but there was no statistically significant relationship specific to PFHxA.

4.2.4.8 Critical effect

The critical effect of PFHxA is on the liver, where the NOAEL value for PFHxA in a long-term study was 20 mg/kg bw/day. The effect of PFHxA on the liver is 3-400 times less than for PFOA, depending on the data with which it is being compared.

Russell *et al*. (2013) calculated a benchmark dose ($BMDL_{10}$) to 13 mg PFHxA/kg bw.

4.2.5 Perfluoroheptanoic acid (PFHpA)

4.2.5.1 Database

Most data were obtained from the Danish Environmental Protection Agency's previous literature study of environmental and health effects of short-chain PFAS (Kjølholt *et al*., 2015). These are supplemented with data in later articles/reports from the authors' archive or found in searches on Google Scholar. Data for physicochemical properties were also sought in PubChem, Comptox, Guidechem, Molbase, and other internet-based databases.

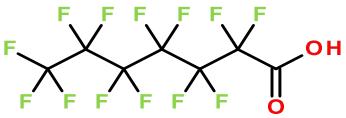
4.2.5.2 Identification

CAS no. 375-85-9
EC no. 206-798-9
UN no. 3261

Molecular formula

$C_7HF_{13}O_2$

Structural formula



Synonyms

2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptanoic acid.

Isomers and salts

	Sodium perfluoroheptanoate (NaPFHp)	Ammonium perfluoroheptanoate(APFHp)
CAS no.	20109-59-5	6130-43-4
EC no.	243-518-4	228-098-2
Molecular formula	$C_7F_{13}NaO_2$	$C_7H_4F_{13}NO_2$

4.2.5.3 Physical-chemical properties

Property	PFHpA	NaPFHp	APFHp
Molecular weight	364.061	386.044	381.093
Boiling point °C (at 1 atm)	[a]179. [c]175; b176	[ab]176; [d]175.8	[a]176
Melting point °C	[ac]30; [ab]31-36	[a]35.7;	[a]164
Solubility in water (at 25 °C)	[a]0.217 mol/L = 79 g/L; 4.2 g/L	[a]0.867 mol/L = 335 g/L	[a]0.867 mol/L = 330 g/L
Density (at 25°C) g/cm^3	[ab]1.792	[d]1.735	
Vapour pressure (at 25 °C)	[b]10 mm Hg = 1333 Pa	[a]0.128 mm Hg = 17 Pa; 0.539 mm Hg	[a]0.128 mm Hg =
Partition coefficient, Log P_{ow}	4.15; [a]4.91; 4.67	[a]3.45	[a]3.45

[a]Comptox; [b]Chemspider; [c]Sigma-aldrich; [d]Guidechem

PFHpA is a beige coloured crystalline substance.

4.2.5.4 CLP classification

There is no harmonized classification of PFHpA.
For PFHpA, 32 companies have submitted notified classifications according to the CLP criteria (ECHA C&L Inventory, 2017).

Hazard class and category	Hazard Statement Code(s)	Hazard Statements
Acute Tox. 4 Skin Corr. 1B (24 notifiers)	H302	Harmful if swallowed
	H314	Causes severe skin burns and eye damage
Not classified (3 notifiers)		
Skin Corr. 1C Met. Corr. Eye Dam. (1 notifier)	H314	Causes severe skin burns and eye damage
	H290	May be corrosive to metals
	H318	Causes serious eye damage
Skin Corr. 1B (4 notifiers)	H314	Causes severe skin burns and eye damage

4.2.5.5 Toxicokinetics and metabolism

Absorption and distribution

In the present study, no studies of the absorption of PFHpA or its salts following oral, inhalation or dermal exposure have been identified.

As with other PFAS, almost all of the absorbed PFHpA is bound to albumin in the blood and transported around the body until it is either eliminated or deposited in tissues and organs. The binding constant of PFHpA in humans measured by fluorescence was 9.4 x 10^3 per mole. This was two times more than for PFOA (Chen and Guo, 2009).

In a study with male and female rats, the serum elimination half-life of PFHpA (administered intravenously as the acid) was 2.4 hours and 1.2 hours, respectively. In male rats this was 50 times less time than for PFOA. For female rats the half-life was about the same as for PFOA. Elimination via the kidneys in male rats was more effective for PFHpA than for PFOA, PFNA and PFDA, whereas the elimination of PFHpA for female rats was the same as for PFOA, but more effective than for the longer chain PFCA (Ohmori *et al*., 2003).

In pigs, plasma elimination half-life of PFHpA was 74 days, while it was 236 days for PFOA (Numata *et al*., 2014).

In the general population, concentrations of PFHpA in blood serum/plasma are usually low and below the detection limit (LOD). For residents near companies that produce fluorinated substances, a study from the United States showed that PFHpA could only be measured in blood serum in about half of the population, with an average/median concentration of PFHpA of 1.2/0.9 ng/mL (Frisbee *et al*., 2009).

In pregnant women, PFAS can be transferred from the mother's blood to the placenta (Zhang *et al*., 2013). PFHxA, PFHpA and PFOA were, for example, detected in the mother's blood, umbilical cord blood, placenta and foetus, while PFPeA was only detected in foetal water. PFHpA was transferred to the placenta more than twice as much as PFOA.

Toxicokinetics of 11 PFAS substances - including PFOA, PFHxA and PFHpA - in humans were studied by Fàbrega *et al*. (2015) using a validated PBPK model. The distribution in the body was described by a distribution coefficient between the concentration in a particular tissue and the concentration in the blood. There was no significant correlation between this partition coefficient and the chain length. PFHpA had an extremely high relative distribution to bone marrow and liver, but also to the lungs and kidneys.

Elimination

In an older comparative study of PFHpA, PFOA, PFNA and PFDA as acids administered by a single intravenous injection of 25 mg/kg bw in rats, urinary elimination decreased with chain length while elimination in faeces increased (Kudo *et al*. 2001). After 120 hours, 92% and 55% of PFHpA and PFOA dose, respectively, were excreted with urine in male rats, while PFCA with longer chains showed little excretion with urine. Female rats, which eliminate PFOA faster than male rats, also eliminated PFHpA faster than PFOA. The order of elimination of these PFCAs with faeces was 2-5%.

In sheep, 3.20% of the absorbed PFHpA was eliminated in the faeces. In comparison, the elimination of PFOA in faeces from sheep was 3.95% (Numata *et al*., 2014).

Daily elimination of toxic substances and reabsorption of useful anionic metabolites in the kidneys are carried out by transport proteins (e.g. Oat1) located in cell membranes. PFHpA inhibits Oat1-mediated p-aminohippurate transport in the kidneys more than PFOA does (Weaver *et al*., 2010).

In male rats, PFHpA was rapidly eliminated in urine as 92% of an intravenously administered dose was eliminated within 120 hours (Kudo *et al*. 2001). For PFOA, only 55% of the dose was eliminated after 120 hours.

In a recent study, the urine from Employees of the Austrian Environmental Protection Agency was examined for the presence 12 PFAS (Hartmann *et al*., 2017). All urine samples contained PFOS, PFOA, PFNA and PFHxA, while PFHpA was found in 91% of the samples in concentrations ranging from <0.20 to 0.99 ng/l. PFAS with chain lengths ≥ 10 carbon were not detected in the urine.

PFAS excreted less with breast milk than lipophilic environmental toxins are. The short-chain PFCA has not been studied as often in breast milk as PFOA, but in South Korea, PFHpA was found in 87% of the samples with a median concentration of 28 ng/L milk, equivalent to half the concentrations of PFPeA and one-third of levels of PFOA (Kang *et al*. 2016). Based on a questionnaire survey on habits and consumption among the 215 women in the study, a strong significant correlation ($p < 0.001$) between the use of non-stick frying pans and levels of PFHpA in the milk was found, and statistically significant correlation ($p = 0.027$) between the use of cosmetic products and levels of PFHpA in the milk.

In a recent study from the same research group as in the above study, breast milk from 128 women from Korea was investigated. PFHpA was detected only in 26% of the samples and at a much lower average concentration of 6.25 ± 12.9 ng/L (Lee *et al*., 2018). The difference between the results of the two studies is not commented on in the article.

4.2.5.6 Irritation and allergy

As a relatively strong acid, PFHpA may, like the other short-chained PFAS, cause irritation to skin, eyes and mucous membranes. In addition, the notified CLP classifications indicates irritation effects.

Dong *et al*. (2013) studied asthma incidence among Taiwanese children and found a correlation between the concentration of PFAS in serum and asthma disease. For PFHpA, there were significantly higher mean serum concentrations among asthmatics and a greater proportion (70% vs. 53%) of the samples contained measurable concentrations.

4.2.5.7 Acute and chronic effects

In this study, relevant studies on acute and chronic effects of PFHpA have not been identified.

Toxicological mechanisms

Many perfluoroalkyl acids and salts, including PFHpA, can induce peroxisome proliferation, induction of peroxisomal fatty acid oxidation and enlarged liver, by activating "peroxisome proliferator-activated receptor α" (PPAR-α) in the nucleus (Wolf *et al*., 2008). However, PPAR-α is more readily induced in mice than in human cells, where no significant activity was observed.

In other rat cell test systems, PFHpA and PFOA were the most active in PPAR-α activation, while PFCA with shorter and longer perfluoroalkyl chains had less activity (Bjork and Wallace 2009). PFHpA and PFOA were also active in both PPAR-α and PPAR-γ "reporter gene assays" (Rosenmai *et al*., 2016).

In another *in vitro* model with human colon cancer cells (HCT116), the estimated effect concentrations (EC_{50}) decreased the longer the perfluoroalkyl chain was: PFHxA> PFHpA> PFOA> PFNA etc. Therefore, PFHpA had less effect in this test than PFOA but more than PFHxA (Kleszczynski *et al*., 2007).

Mutagenicity/genotoxicity

In the present study, no relevant studies have been identified, but as with other PFCA, PFHpA is not likely to be genotoxic.

Carcinogenicity

In this study, relevant studies have not been identified.

Reproductive toxicity

Perfluorohexanoic acid (PFHxA) and perfluoroheptanoic acid (PFHpA) were examined in a screening test for teratogenicity with embryos from frogs ("Xenopus (FETAX) assay"), where they were identified as potential foetal- and developmentally toxic substances (Kim *et al*., 2015). PFHpA was most potent and induced the most serious effects on liver and heart development by significantly increasing phosphorylation of the enzymes extracellular signal-regulated kinase (ERK) and "c-Jun N-terminal" kinase (JNK).

Hormone-disruptive effects

Some PFAS may affect the function of thyroxin transport proteins transthyretin (TTR) and thyroxine-binding globulin (TBG) in competition for the receptors (Ren *et al*., 2016). The differ-

ent PFAS have different binding potential. Among PFCA, PFOA has the highest potential for binding to TTR. The potency of PFHpA is about three times less than for PFOA.

Unlike PFOA, PFHpA had no estrogenic effect in *in vitro* test systems (Rosenmai *et al*., 2016).

In a group of 13-15-year-olds in Taiwan, hormone levels in blood were compared to serum concentrations of PFAS, including PFOA (gene 0.5 ng/mL), PFHxA (gene 0.2 ng/mL) and PFHpA (Zhou *et al*., 2016). Most PFAS were determined in > 94% of the samples, but for PFHpA, levels were only above LOQ (= 0.05 ng/mL) in 53% of the samples. The results showed that higher serum PFAS levels were associated with lower testosterone levels and higher estradiol levels, but there was no significant association specific for PFHxA or PFHpA.

4.2.5.8 Critical effect

There are insufficient data to determine the critical effect, but liver effects would likely be critical, considering that PFHpA is a potent peroxisomal proliferator and almost as active as PFOA. There is no data available for determining NOAEL values.

4.2.6 Summary and conclusion of the hazard assessment

4.2.6.1 Summary of half-lives for serum elimination of PFAS.

As shown in the previous sections, there are large differences in serum/plasma half-lives of the perfluoroalkyl acids in different animals and humans, as well as between the different sexes. Table 12 lists some typical values where the half-life of PFHpA in humans is estimated by read-across from the difference between PFOA and PFHpA in pigs. There are no data for PFPeA.

Table 12 Summary of serum elimination half-life in various animal species. There are no data for PFPeA.

Species	PFBA		PFHxA		PFHpA		PFOA	
	Male	Female	Male	Female	Male	Female	Male	Female
Rat	9 hours	2 hours	1.6 hours	0.6 hours	2.4 hours	1.2 hours	4-6 days	2-4 hours
Mouse	5-16 hours	3 hours	1 hour				19 days	17 days
Monkey	40 hours	41 hours	5.3 days	2.4 days			21 days	33 days
Pig					74 days		236 days	
Human	72 hours	87 hours	32 days		1 year (read across)		2-8.5 years	

4.2.6.2 Summary of distribution of PFAS in the organism

There are, for obvious reasons, very few studies of PFCA in human tissues and organs besides blood, milk and urine, as it is difficult and unethical to experiment with humans. Therefore, investigating distribution in deceased people may be an option. This has been done in a study from Catalonia, from which relevant data are listed in Table 13 below (Perez *et al*., 2013).

Table 13 Content of PFAS in various organs from 20 deceased people from Catalonia (Perez *et al*., 2013)

PFCA	Liver	Bones	Brain	Lungs	Kidneys
	Average concentration ng/g wet weight				
PFBA	12.9	< LOD	13.5	204	464
PFPeA	1.4	0.8	< LOD	44.5	<LOD
PFHxA	11.5	35.6	18.0	2.4	23.7
PFOA	13.6	60.2	<LOD	29.2	2.0

According to the data, the highest concentrations of PFBA have been found in kidneys and lungs: PFPeA was found most often in lungs, PFHxA in the bones, kidneys and brain, and PFOA in the bones and lungs. The relatively high content found in the lungs may be due to inhalation of the more volatile precursors that are converted in the lungs.

In addition, data from animal studies are available. The highest concentration of PFOA in rats can be measured in blood, liver, kidneys and lungs. In a recent study, the distribution of low exposures of PFOA, PFHxA and PFBA in mice was investigated after intravenous injection of 7.22 MBq ^{18}F-labeled radioactive compounds (Burkemper *et al*., 2017). Four hours post-injection, radioactivity was measured in tissues/organs as a percent of dose per gram of tissue. The highest content of PFOA was in the liver (7 ± 2%) and thigh bones (4 ± 1%). The concentration of PFHxA was generally higher than for PFOA, as well as highest in the liver (10 ± 2%) and in thigh bones (5 ± 1%). PFOA was only higher than PFHxA in the lungs (4 ± 3%

and 3.5 ± 0.5%, respectively). PFBA was lowest in all cases except in the stomach where PFBA was several times higher than the two other substances combined. The distribution in the stomach was as follows: PFBA: 7.5 ± 1.5%, PFHxA: 2 ± 0.5% and PFOA: <1%. There was very little of all three substances in fat, muscles and brain. Selected rounded data is shown in Figure 1.

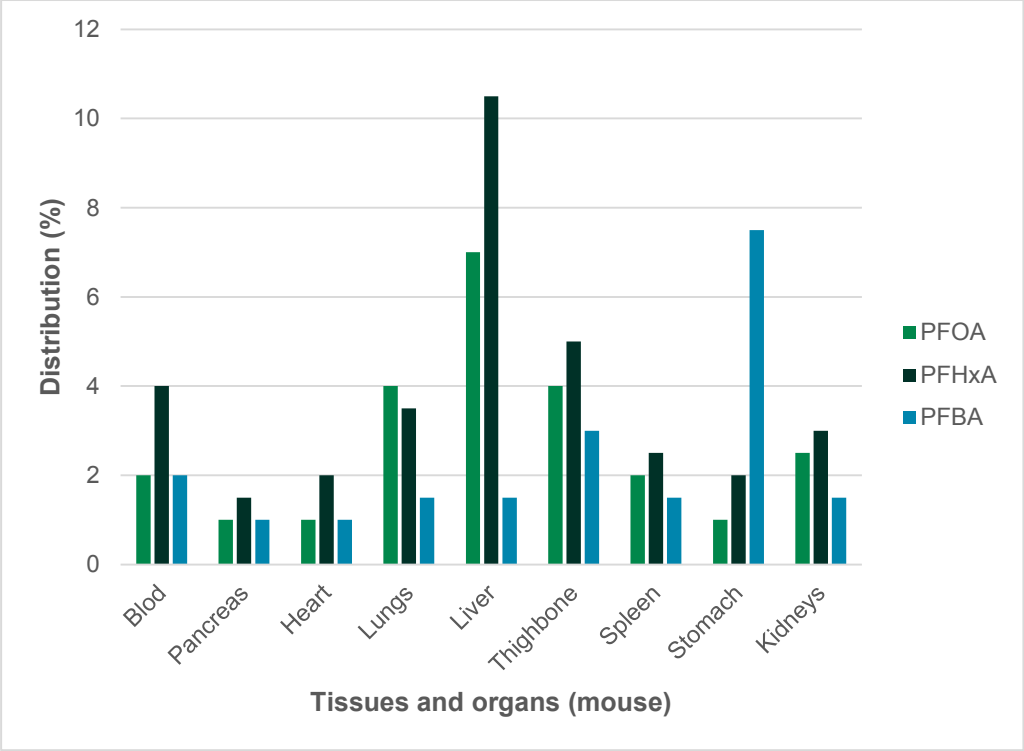


Figure 1 Distribution (%) of PFOA, PFHxA and PFBA in selected tissues and organs in mice 4 hours after intravenous injection of 7.22 MBq ^{18}F-labeled radioactive compounds (Burkemper *et al*., 2017).

It has previously been described that humans resemble mice more than rats with regard to toxicokinetics for PFCA, and there is also relatively good consistency with the findings in Perez *et al*. (2013).

4.2.6.3 Summary of the individual substances' properties compared to PFOA

PFBA

- Was most common in stomach in mice and in the lungs and kidneys in humans compared to the other PFAS.
- PFBA has almost 10 times higher concentrations in human lungs than in the case of PFOA, while liver concentrations were comparable.
- A relatively large incidence of PFBA in the brain has been found in a study of organs from 20 deceased people.
- PFBA is 20 times less active as a peroxisomal proliferator than PFOA and induces PPAR-α only.
- The cell toxicity of PFBA was 7 times lower than for PFOA.
- PFBA was less reprotoxic than PFOA.
- PFBA binds approx. 300 times less effectively for the protein TTR than PFOA, and PFBA is a minor hormone-disruptor of the thyroid gland.
- PFBA is eliminated faster than PFOA in experimental animals.
- Serum elimination time in humans is faster for PFBA than for PFOA.

PFPeA

- PFPeA is 10 times less active as a peroxisomal proliferator than PFOA
- PFPeA had relatively high concentrations in lungs, while concentrations of the substance were very low in other human organs. There are no data for the distribution of PFPeA in mice, as is otherwise the case for PFBA, PFHxA and PFOA in Burkemper *et al*. (2017).

PFHxA

- PFHxA has a 30-fold lower effect on the liver than PFOA
- PFHxA is toxic to the kidney in long-term studies with male rats. At the same time, PFHxA has a distribution in kidneys in mice comparable to PFOA and PFBA.
- PFHxA is two times less active as a peroxisomal proliferator than PFOA.
- PFHxA has about 10 times lower toxicity than PFOA in a cell test.
- The NOAEL value for PFHxA in short-term studies is 30 times higher than for PFOA.
- PFHxA was identified as a potentially foetal- and developmentally toxic substance in a screening test for teratogenicity with embryos from frogs.
- PFHxA binds approx. 10 times less effectively for the protein TTR than PFOA, but is 30 times more active than PFBA.
- PFHxA is eliminated faster than PFOA in experimental animals.
- Serum elimination half-life of PFHxA in humans is 40-80 times shorter than for PFOA.
- PFHxA has the largest distribution in the human brain of all PFCA examined: 10 times more than PFOA.
- The concentration of PFHxA in the human liver was also relatively high, like PFBA and PFOA.
- The concentration of PFHxA in livers from mice was far higher than for PFBA and PFOA.

PFHpA

- PFHpA bind twice as strongly to albumin in the blood as PFOA
- PFHpA inhibits Oat1-mediated p-aminohippurate transport in the kidneys to a greater extent than PFHxA and PFOA.
- PFHpA is eliminated faster than PFOA in experimental animals.
- The serum elimination half-life of PFHpA is approximately three times shorter in humans than for PFOA.
- PFHpA has an extremely high relative distribution to bone marrow and liver, but also to the lungs and kidneys.
- PFHpA and PFOA are the most active PFAS for PPARα activation. PFAS with shorter and longer chains are less active.
- Regarding cell toxicity, PFHpA lies between PFHxA and PFOA, where PFOA is highest.
- PFHpA was more potent than PFHxA and provoked the most serious effects in a screening test for teratogenicity with embryos from frogs.
- PFHpA is bound three times less efficiently to the protein TTR than PFOA.
- PFHpA was transferred to placenta more than twice as easily as PFOA.

Generally

- There are far more test results for PFOA and its salts than for the other substances studied. Where NOAELs are available in comparable studies, PFOA has the lowest NOAEL (0.06 mg/kg bw/day) in all cases.
- Based on existing data, PFOA is apparently the only PFCA selected which: i) has an estrogenic effect in animal experiments and *in vitro* test systems; ii) is potentially carcinogenic; and iii) has an effect on the mammary gland.
- For the selected PFAS, there were major differences in the serum/plasma half-life of the perfluoroalkyl acids in different animals and humans, as well as between the sexes. PFOA has the longest half-life of the selected PFCA (2-8.5 years in humans).
- PFOA is detected in the highest concentrations in bone and bone marrow in humans. The substance is also detected in high concentrations in human blood, lungs and liver as well as

in the liver, bones and kidneys of mice. For humans, occurrence of PFOA in the brain has not been detected; however, brain levels of PFBS and PFHxA have been detected. However, there are no data on potential toxicity associated with this occurrence.

- PFOA has the most effective binding to the protein TTR and thus the greatest effect on the thyroid gland out of the selected PFCA.

PFOA has the strongest binding to albumin in the blood relative to the other PFCA under consideration in this report.

Table 14 Summary of the results from the hazard assessment

Substance	Classification H: Harmonized N: Notified	NOAEL [mg/kg bw/day]	Systemic NOAEL [mg/kg bw/day]	Serum elimination half-life (human)	Oral absorption [%]	Dermal absorption [%]	Dissociation constant pKa*
PFBA	N: Skin Corr. 1A, Skin Corr. 1B, Eye dam. 1, Met. Corr. 1, STOT SE 3	No data	No data	72-87 timer	No data	No data	-0.6-1.78
NaPFB	N: Skin irrit. 2, Eye irrit. 2, STOT SE 3		No data	No data	No data	No data	
AgPFB	N: Eye dam. 1		No data	No data	No data	No data	
APFB	Not pre-registered or classified		6 (28 d, 90 d)	No data	50-90 (male rats) 35-68 (mice, monkeys)	No data	
PFPeA	Not classified	No data	No data	No data	No data	No data	-0.5 -2.27
PFHxA	N: Skin Corr 1B, Met Corr. 1, Acute Tox 2, Acute Tox 2, Eye dam. 1	100 (reproduction toxicity)	15-30 (2 years) 50-200 (90 d)	32 days	100 (rats and mice), 90 (male rats), 70-100 (female rats)	No data	-0.6 – 2.17
APFHx	N: Eye Dam. 1		20	No data	No data	No data	
NaPFHx		100 (reproduction toxicity)	20	No data	No data	No data	
PFHpA (acid)	N: Acute Tox. 4, Skin Corr. 1B, Skin Corr. 1C, Met. Corr., Eye Dam. 1	No data	No data	1 year (read-across)	No data	No data	-0.4-2.26
PFOA (acid)	H: Carc.2, Repr. 1B, Lact, STOT RE 1 (Liver),	No data	No data	2 - 8.5 years	No data	50-70	-0.5 – 3.8
APFO		LOAEL < 20 (skin)	0.3 (14 d), 0.06 (90 d)	No data	93	1.5	

Sub-stance	Classifica-tion H: Harmo-nized N: Notified	NOAEL [mg/kg bw/day]	Systemic NOAEL [mg/kg bw/day]	Serum elim-ination half-life (human)	Oral ab-sorption [%]	Dermal absorp-tion [%]	Dissocia-tion con-stant pKa*
	Acute tox. 4,	1 (reproduc-tion toxicity)	1.3-1.6 (2 year)				

*Fluorine-substituted carboxylic acids usually have increased acidity relative to the analogous carboxylic acids without fluorine, but due to the surface activity and low water solubility of ≥C6 (PFHxA) and because the substances are brought into aqueous solution using e.g. alcohols and glycols, the determination of pKa is uncertain. In some cases, pKa for the acids are mixed together with pKa for the salts. In addition, different experimental methods and calculation models are used. Therefore, the results are highly varied and it may be difficult to determine a final value (Kutsuna & Hori 2008; Burns *et al*. 2008; Goss 2008; Vierke *et al*., 2013; Cabala *et al*., 2017). Therefore, intervals are given for the pKa values.

4.2.6.4 Conclusion of the hazard assessment

PFOA and its salts are important and relatively well-researched substances compared to the four other PFCAs with shorter perfluoroalkyl chains. With respect to these substances, PFBA and PFHxA are reasonably well-studied, while there are hardly any relevant data for PFPeA and PFHpA, either in experimental animals or in humans. The missing or limited data means that it is difficult to compile a balanced assessment of the short-chain PFCA compared to PFOA. PFOA is also the only substance that has been shown to be carcinogenic, while long-term animal studies are lacking for the other substances.

The physicochemical difference between the acids and the salts also result in different biological properties, and it is not as straightforward to extrapolate from studies with the almost neutral salts to the same effect of the highly acidic acids, even though this is often done.

The investigated substances are all more or less hepatotoxic in experimental animals with PFOA as the most potent substance with the lowest NOAEL value. This is the critical effect of PFOA and probably also of the four other substances, as this effect is seen at the lowest exposures. It also appears that PFOA is the most potent with regard to reproductive effects.

However, we know too little about PFCA with shorter chains to rule out that these substances may in some cases be as or more dangerous to health as PFOA. It is *inter alia* worrying that PFBA and PFHxA accumulate in human brain tissue to a greater extent than PFOA. There are no data to elucidate possible effects of this, but the overall surfactant properties of the substances, which may result in undesirable changes in the functioning of the cell membranes in the brain, are of concern.

The relatively high concentration of PFBA in lungs in both mice and humans may reflect the fact that PFBA is the most volatile of the acids, but the relatively high concentration in the kidneys is surprising as available data suggests rapid excretion of PFBA through the kidneys. On the other hand, PFBA is more slowly excreted with urine than PFHxA in rats. However, PFHxA is the only one of the four substances that has shown toxic effects on the kidneys.

Of the four PFCAs, PFHpA is the one which resembles PFOA the most with regard to its properties (including hepatotoxicity). PFHpA and PFOA are the most active PFAS in PPAR-α activation. PFAS with shorter and longer chains are less active. This is important, as PFHpA has an extremely high relative distribution to the liver and bone marrow, but also to the lungs and kidneys. PFHpA binds twice as strongly to albumin in the blood as PFOA, and it is transferred to the placenta more than twice as much than PFOA. It is also interesting that PFHpA was the most potent and provoked the most serious effects in a screening test for teratogenicity with embryos from frogs.

Table 12 shows that serum elimination in humans is very slow for PFOA - both in comparison to experimental animals and with the other investigated substances. This supports the idea that PFOA would provide a larger internal dose and thereby be more potent than the other substances for the same type of exposure.

4.2.6.5 Selection of NOAEL for the MoS calculations

Based on the data reviewed above, it is seen that, although data for PFPeA and PFHpA are lacking, the available data suggests that PFOA is the most potent of the selected PFCA and the substance that has the lowest NOAEL value. PFNA (C_9) and PFDA (C_{10}) both have harmonised classifications as Repr 1B (may damage fertility or the unborn child), and these classifications are (partially) based on read-across to APFO/PFOA. In the context of the classifications of PFNA and PFDA, RAC has given NOAELs in line with or above the NOAELs of PFOA (ECHA, 2014; ECHA, 2015c).

The exposure and risk assessment will therefore initially based on PFOA, assuming that all measured PFAS content in the product is PFOA.

Section 4.2.1.8 discusses different data sets and NOAELs for PFOA and it is clear that there is no immediate consensus on a NOAEL for PFOA. The MoS calculations will therefore be made for three scenarios with the following starting points:

- **Scenario 1 (dose approach)**: External oral NOAEL = 0.06 mg/kg bw/day (Perkins *et al*. 2004), which is the lowest NOAEL value from animal studies. This study is also used by EFSA, who, however, converts the value to a $BMDL_{10}$ of 0.3 mg/kg BW/day, before an assessment factor of 200 is applied. Assuming that the oral absorption is 93% (reported in IARC, 2017), an internal NOAEL is calculated at: 0.056 mg/kg bw/day.
- **Scenario 2 (dose approach)**: External oral NOAEL = 1 mg/kg bw/day (Lau *et al*. 2006), as proposed as NOAEL by RAC in their assessment of PFOA (ECHA, 2015a). As above, an internal NOAEL of 0.93 mg/kg bw/day is calculated.
- **Scenario 3 (serum concentration approach):** As discussed above, the elimination of PFOA in humans is different from that in experimental animals. In order to take into account the difference in elimination of PFOA between humans and animals, a risk assessment is also performed which compares internal serum concentration values. As NOAEL, 20,000 ng/mL (equivalent to the external NOAEL of 1 mg/kg bw/day reproduced above) is used, as determined in Lau *et al*. (2006), which is also used in RAC's risk assessment (EHCA, 2015a).

5. Exposure assessment

5.1 Introduction

As concluded in Chapter 3, the exposure scenarios will be prepared for the following product types:

- Body lotion
- CC cream/foundation
- Concealer.

5.2 Method

Assessment of exposure and systemic risk from using cosmetic products containing PFAS will be carried out in accordance with the principles from the guidance for safety assessment of chemical substances in cosmetic products from the Scientific Committee for Consumer Safety (SCCS): "Notes of Guidance for the Testing of Cosmetic Products and Their Safety Evaluation" (SCCS, 2016) (hereinafter referred to as "Notes of Guidance").

Perfluorooctanoic acid (PFOA) is selected as a reference substance as described in section 4.2.6.5. Table 15 shows an overview of the product types in which the selected substances are found.

Table 15 Overview of product types that the selected PFAS appears in according to the results from the chemical analyses.

Substance name	Facial cream	Body lotion	Facial scrub	Foundation/ BB cream/ CC cream	Eyeliner	Powder	Eye shadow	Highlighter	Concealer
Perfluorooctanoic acid (PFOA)	x	x		x			x	x	x
Perfluorobutanoic acid (PFBA)	x	x	x	x	x	x	x	x	x
Perfluoropentanoic acid (PFPeA)	x	x	x	x		x	x	x	x
Perfluorohexanoic acid (PFHxA)	x	x	x	x		x	x	x	x
Perfluoroheptanoic acid (PFHpA)	x	x	x	x		x	x	x	x

Exposure scenarios are prepared for the following usage situations which the selected substances *inter alia* are used in:

- Body lotion
- CC cream/foundation
- Concealer.

As also described in section 3.3.1, the latter two product types are selected because the highest concentrations of fluoroalkyl substances are found in these. Body lotion is added as this product type is used in the larger amounts over the entire body.

The exposure scenarios for the selected substances are described below, following the principles of Notes of Guidance (SCCS, 2016).

The Systemic Exposure Dosage (SED) is determined in scenarios using the default parameters specified in Notes of Guidance for adult consumers (standard weight 60 kg) (SCCS, 2016). None of the analysed products are marketed specifically for children.

Daily exposure is calculated using the formula below, where SED is calculated as a function of the amount of cosmetic product applied daily, the concentration of the substance in the finished cosmetic product, the dermal absorption of the substance and an average human body weight value:

$$SED = A\left[\frac{mg}{kg\ bw\ \times\ day}\right] \times C[\%]/100 \times DA_p[\%]/100$$

A (mg/kg bw/day) = Estimated daily exposure to a cosmetic product per kg body weight
C (%) = Concentration of the substance in the finished cosmetic product expressed in percentage
DA_P (%) = Dermal Absorption expressed as a percentage
bw (kg) = Body weight

5.2.1 Exposure scenarios

As mentioned above, three product types were selected for the exposure assessment. As none of the selected products occur in spray form and because there are no volatile substances, exposure through inhalation is not considered relevant in this project. Oral exposure is also not considered relevant as no products for lips have been identified and unintentional ingestion of the products is thought to be extremely rare as the identified products are intended exclusively for adult consumers. Therefore, dermal exposure scenarios were the only ones taken into account.

5.2.2 Data used in the exposure scenarios

Data for the estimated daily exposure (A) is specified in "Notes of guidance" for different product types (SCCS, 2016). In the event that there were no values for the daily exposure for a given product type, these were estimated based on data for other similar product types.

The retention factor is an expression of how the product is used, i.e. whether the product is intended to stay on the skin (leave-on products) or if it is washed off (rinse-off products) or diluted (for products to be applied to wet skin or hair). In this study, all three products (body lotion, CC cream/foundation and concealer) are non-diluted leave-on products, and the retention factor is therefore 1.

Table 16 Data for the estimated daily exposure for relevant product types according to Notes of Guidance. SCCS assumes a standard body weight of 60 kg (SCCS, 2016).

Product type	Relative amount applied (mg/kg bw/day)	Retention factor	Calculated relative daily exposure (A) (mg/kg bw/day)	Comment
Body lotion	123.2	1	123.2	
Liquid foundation/BB-/CC cream	7.90	1	7.90	
Concealer	3.95	1	3.95	No value for concealer is provided by

Product type	Relative amount applied (mg/kg bw/day)	Retention factor	Calculated relative daily exposure (A) (mg/kg bw/day)	Comment
				SCCS. It is assumed that the daily exposure is ½ the value used for floating foundation *

* This assumption is based on how a concealer is typically used. The concealer is often thicker in the texture than the foundation and is used spot-wise on the face to cover dark circles under the eyes, impurities and the like, whereas the foundation is typically used all over the face. However, it cannot be ruled out that some consumers use concealer to cover a larger area of the face; therefore, exposure is set to half the value used for liquid foundation.

In the assessment of exposure, data for total PFAS content (calculated as the sum of each measured PFAS) are used for relevant product types. The highest measured total PFAS concentration within each product type will be used in the calculation - see Table 17.

PFOA and the other PFCAs that were analysed in the cosmetic products are believed to occur both as acids and salts, depending on pH. Since dermal absorption is thought to be significantly greater for the acid than for salts (see section 4.2.1.5), two situations are considered; one for worst-case absorption for salts and one for worst-case absorption for the acid.

1. A 2% dermal absorption situation is considered as a conservative estimate for how much of the salts are absorbed (this value is e.g. used in Lassen *et al*. (2015)).
2. A 70% dermal absorption situation is considered where it is assumed that all PFAS occurs in the form of the acid. This value is based on data from Franko *et al*. (2012) for PFOA (as acid). The study indicated an uptake through the skin of 23-25% in humans, while approximately 45% of the substance was detected in the epidermis. Therefore, when using 70% as the dermal absorption situation, it is very conservatively assumed that the 45% in the epidermis would also be systemically available. Using 70% as the dermal absorption situation is also conservative because, as mentioned above, certainly not all PFOA would be present in the acid form in the products.

Table 17 Highest values for total PFAS content in the selected product types, cf. the chemical analyses. Values are given in ng/g and additionally converted to % content in the products.

Product type	Total PFAS-content [ng/g]	Total PFAS content [%]
Body lotion no. 21a	83	8.3×10^{-6}
Concealer no. 4a	10,700	1.07×10^{-3}
Foundation no. 14a	4,970	4.97×10^{-4}

5.2.3 Calculation of the systemic exposure dosage

The resulting SED calculated using 2% and 70% as dermal absorption is shown in Table 18 and Table 19 below.

Table 18 Calculation of SED for total PFAS content for the selected product types (2% dermal absorption (PFOA as salt (APFO))

Product type	Calculation of SED
Body lotion	$SED = 123.2\ mg/kg\ bw/day \times \frac{8.3 \times 10^{-6}\ \%}{100} \times \frac{2\ \%}{100} = 2.05 \times 10^{-7}\ mg/kg\ bw/day$

Product type	Calculation of SED
Concealer	$SED = 3.95\ mg/kg\ bw/day \times \frac{1.07\ \times\ 10^{-3}\ \%}{100} \times \frac{2\ \%}{100} = 8.45\ \times\ 10^{-7}\ mg/kg\ bw/day$
Liquid foundation	$SED = 7.9\ mg/kg\ bw/day \times \frac{4.97\ \times\ 10^{-4}\ \%}{100} \times \frac{2\ \%}{100} = 7.85\ \times\ 10^{-7}\ mg/kg\ bw/day$

Table 19 Calculation of SED for total PFAS content for the selected product types (70% dermal absorption (PFOA))

Product type	Calculation of SED
Body lotion	$SED = 123.2\ mg/kg\ bw/day\ \times \frac{8.3\ \times\ 10^{-6}\ \%}{100} \times \frac{70\ \%}{100} = 7.16 \times\ 10^{-6}\ mg/kg\ bw/day$
Concealer	$SED = 3.95\ mg/kg\ bw/day \times \frac{1.07\ \times\ 10^{-3}\ \%}{100} \times \frac{70\ \%}{100} = 2.96 \times\ 10^{-5}\ mg/kg\ bw/day$
Liquid foundation	$SED = 7.9\ mg/kg\ bw/day \times \frac{4.97\ \times\ 10^{-4}\ \%}{100} \times \frac{70\ \%}{100} = 2.75 \times\ 10^{-5}\ mg/kg\ bw/day$

It was found that the highest estimated daily exposure (SED) for total PFAS was found using the concealer, primarily due to the relatively high content of PFAS in the specific product found in the chemical analyses.

For the third scenario (serum concentration approach) described in section 4.2.6.5, the estimated external exposure dose should be converted to an internal concentration. This is done in line with the conversion between external dose and internal concentration in humans made in Bernauer (2010) using the following formula:

$$Internal\ concentation\ [mg/mL] = \frac{External\ dose\ [mg/kg\ bw/day] \times absorbed\ fraction}{Clearance\ [ml/day/kg\ bw]}$$

$$= \frac{SED\ [mg/kg\ bw/day]}{Clearance\ [ml/day/kg\ bw]}$$

SED is calculated above for PFOA as salt and as acid, respectively (Table 18 and Table 19), which means that SED is 8.45 x 10^{-7} and 2.96 x 10^{-5} mg/kg bw/day, respectively, for the concealer.

A total clearance[14] value of 0.051 mL/day/kg is used in Bernauer (2010)[15].
This gives an internal concentration for the two dermal absorption situations of:

2% dermal absorption (PFOA as a salt (APFO) calculated as total PFAS):

$$\frac{8.45\ \times\ 10^{-7}\ mg/kg\ bw/day}{0.051\ ml/day/kg} = 1.66\ \times\ 10^{-5}\ mg/ml\ (corresponding\ to\ 16.6\ ng/ml)$$

70% dermal absorption (PFOA as acid) calculated as total PFAS:

$$\frac{2.96\ \times\ 10^{-5}\ mg/kg\ bw/day}{0.051\ ml/day/kg} = 5.80\ \times\ 10^{-4}\ mg/ml\ (corresponding\ to\ 580\ ng/ml)$$

[14] Clearance is a measure of the rate at which the body eliminates a given substance expressed at the rate of elimination relative to the concentration of the substance in the blood

[15] Bernauer (2010) indicates a clearance between 0.051-0.108 ml/day/kg. As the worst case, the lowest value in this range is used

Since, as described in sections 4.2.1.5 and 5.2.2, there is some uncertainty as to what the actual dermal absorption is, it is relevant to compare the above calculated internal concentrations of PFOA with measured values. The calculated internal concentrations of PFOA are calculated from the total PFAS content in the concealer (Product No. 4), where PFOA represents approximately 22 % of the total PFAS content (2,300 ng/g of 10,600 ng/g). Taking this into account in the above calculations, the internal concentrations of PFOA are 3.7 ng/ml and 127.6 ng/ml for 2 and 70 % dermal absorption, respectively.

In the background document for the REACH Annex XV PFOA restriction proposal (ECHA, 2015b) a list of PFOA serum/plasma concentrations based on studies from several EU countries is presented. Based on these data, the RAC concludes in the final assessment (ECHA, 2015a) that a serum value of 3.5 ng/ml for the typical adult consumer and a value of 21 ng/ml as a reasonable worst case for the adult consumer should be used for risk characterization. It should be emphasized that many other sources than cosmetic products are expected for these serum levels, such as, for example, food, drinking water and intake of dust in the household containing PFOA and/or PFOA related substances.

The calculated internal concentration of 127.6 ng/ml from using one cosmetic product (concealer) when assuming 70 % dermal absorption is much higher than the values used by RAC for the risk characterization. If instead a 25 % derma absorption is assumed (as found in Franko *et al*., 2012 cf. Section 5.2.2), a calculated internal concentration of 45.7 ng/ml is obtained for the concealer (Product 4), which is also high compared to the values by RAC.

6. Risk assessment

6.1 Introduction

The risk assessment is done stepwise/iteratively, meaning that initially the total content of PFAS from Table 10 is used and the potency of the individual PFAS substances is not taken into account, thus assuming that all identified PFAS substances are as potent as the most potent PFAS (worst case consideration in relation to the hazard assessment). Thus, the highest calculated exposure values for total PFAS content will be held against the NOAEL value for PFOA, as the most potent of the selected PFAS. If no risk is identified in the first step, it is not necessary to proceed. If a risk is identified in this first step, the risk assessment will be expanded, taking into account the content and potency of the individual PFAS substances, in order to clarify whether the risk identified in the first step is significant.

6.2 Method

The risk assessment follows the principles of "Notes of Guidance" (SCCS, 2016), and is based on a calculation of Margin of Safety (MoS). Margin of Safety (MoS) is a safety margin that expresses the relationship between the No Observed Adverse Effect level (NOAEL) expressed as an internal value for the critical effect, and the theoretical, expected, or estimated internal exposure dose or concentration.

In order to conclude that there is little or no risk, MoS must be greater than the assessment factor that would be used if a risk assessment, for instance as under REACH, was performed. This factor is used to account for extrapolation from data from experimental animals to an average human being (also called interspecies differences") and extrapolation from average humans to sensitive subpopulations ("intraspecies differences"), as well as possible other uncertainties in the database. Notes of Guidance sets a default value of 100 (covering default factors of 10 for intraspecies differences and 10 for interspecies differences). Therefore, as a rule of thumb, if the calculated margin of safety is less than 100, this indicates a risk to consumers.

The REACH guidance uses the same default assessment factors for inter- and intraspecies when assessing the risk of consumers. Both the REACH Guidance, as well as Notes of Guidance, prescribes that these default factors may be either enhanced or reduced when the specific data base gives rise to it or otherwise takes into account differences in-between humans or between humans and animals. This is assessed on a case by case basis.

For the two dose-approach scenarios described in section 4.2.6.5, MoS is calculated from the following equation:

$$MoS = \frac{NOAEL_{sys}}{SED}$$

where $NOAEL_{sys}$ is the systemic (internal) NOAEL value and SED is the systemic (internal) exposure dose of the substance as described and estimated above in section 5.2.3.

For the third scenario described in section 4.2.6.5 (based on serum concentration), MoS is calculated as:

$$MoS = \frac{NOAEL\ (as\ serum\ concentration)}{Estimated\ serum\ concentration\ as\ a\ result\ of\ exposure}$$

Three NOAEL values for PFOA are used (see Table 20), as explained in section 4.2.6.5. The calculation will be made for the concealer, as the exposure is greatest for this product.

Table 20 NOAEL values used for the risk assessment (see section 4.2.6.5 for further explanation)

Substance name	Scenario	Applied NOAEL value (mg/kg bw/day)
Perfluorooctanoic acid (PFOA)	Scenario 1 (internal dose)	0.056 mg/kg bw/day
	Scenario 2 (internal dose)	0.93 mg/kg bw/day.
	Scenario 3 (serum concentration)	20,000 ng/mL

6.3 Calculation of MoS

As previously described, the MoS calculation will be performed for both situations: assuming 2% dermal absorption (assumed worst case absorption for PFOA as salt (APFO)), and 70% dermal absorption (assumed worst case absorption for PFOA as acid).

For total PFAS content, assuming 2% absorption, for the selected product, MoS is as follows:

Scenario1:

$$MoS_{concealer} = \frac{0.056\ mg/kg\ bw/day}{8.45\ \times\ 10^{-7}\ mg/kg\ bw/day} = 66{,}012$$

Scenario 2:

$$MoS_{concealer} = \frac{0.93\ mg/kg\ bw/day}{8.45\ \times\ 10^{-7}\ mg/kg\ bw/day} = 1{,}100{,}201$$

Scenario 3:

$$MoS_{concealer} = \frac{20{,}000\ ng/ml}{16.6\ ng/ml} = 1{,}207$$

For total PFAS content, assuming 70% absorption, for the selected product, MoS is as follows:

Scenario1:

$$MoS_{concealer} = \frac{0.056\ mg/kg\ bw/day}{2.96\ \times\ 10^{-5}\ mg/kg\ bw/day} = 1{,}886$$

Scenario 2:

$$MoS_{concealer} = \frac{0.93\ mg/kg\ bw/day}{2.96\ \times\ 10^{-5}\ mg/kg\ bw/day} = 31{,}434$$

Scenario 3:

$$MoS_{concealer} = \frac{20{,}000\ ng/ml}{580\ ng/ml} = 34$$

As described in section 6.2, Notes of Guidance sets a default value of 100. The calculated MoS are much larger than 100 in the scenarios based on NOAEL and exposure expressed as dose (Scenario 1 and 2). This applies to both the situation where 2 and 70 % dermal absorption is assumed.

In scenario 3, where NOAEL and exposure as serum concentrations is used, the highly significant interspecies difference (between humans and experimental animals) in serum elimina-

tion/clearance has been accounted for. RAC uses the specified NOAEL (20,000 ng/l) as a basis for their assessments and operates for this NOAEL with an overall assessment factor of 25 for the general population, of which the interspecies factor (difference between animal and human) is reduced from a default of 10 to a factor of 2.5. As previously described (see section 6.2), the use of default factors can be diverged in accordance with the principles of Notes of Guidance. Applying the same assumption as RAC - that a part of the interspecies differences has been accounted for in scenario 3, MoS should be above 25 to conclude that there are no indications of consumer risk. It is seen that the calculated MoS in scenario 3 of 1,207 and 34, respectively, for the concealer is higher than 25.

The above calculations cover the use of the individual cosmetic products. In the same way, MoS can be calculated, assuming that the three products (body lotion no. 21a, concealer no. 4a and foundation no. 14a) are used at the same time. This can in principle be done by calculating a total SED for the three products (sum of SED for each of the three products in Table 18 and Table 19) and following the method for calculating MoS in section 6.2. However, it should be noted that a smaller amount of concealer will typical be used if a person is also using foundation as described in Table 16. There is no value for the estimated daily exposure of concealer in Notes of guidance. However, in scenario 3 (based on serum concentrations) with 70 % dermal absorption, a MoS of less than 25 can be calculated if a person covers more than 1/10 of the face with the concealer (No. 4a) while the estimated daily exposure to body lotion (No. 21a) and foundation (No. 14a) is assumed to be as in Table 16. It should, however, be emphasized that in this scenario all other parameters than the estimated daily exposure (dermal absorption, total PFAS as PFOA and total clearance) was set to worst case in the calculation. This calculation is therefore considered as a conservative/extreme worst case.

Doing a similar calculation with 25 % dermal absorption (as in Franko *et al*., 2012 cf. Section 5.2.2) for the three products used at the same time a MoS above 25 is found - even if it is assumed that the entire face is covered with the concealer while the estimated daily exposure to body lotion and foundation is assumed to be as in Table 16. This scenario, as mentioned, is not considered to be realistic, as one will normally not apply a large amount of concealer while also using foundation.

7. Conclusion and discussion

As seen in section 6.3, the calculated MoS for the individual cosmetic products is well over 100 in the scenarios based on NOAEL and exposure expressed as dose (Scenario 1 and 2) when assuming both 2 and 70% dermal absorption. The same is true for scenario 3, when operating with NOAEL and exposure as serum-concentrations, when 2% absorption is considered.

In contrast, scenario 3 with an assumption of 70% absorption gives an estimated MoS of 34. It should be mentioned that in this scenario, by operating with NOAEL and exposure as serum concentrations, the highly significant interspecies difference (between humans and experimental animals) in serum elimination/clearance has been accounted for. RAC uses the specified NOAEL (20,000 ng/l) as a basis for their assessments and operates for this NOAEL with an overall assessment factor of 25 for the general population, of which the interspecies factor (difference between animal and human) is reduced from a default of 10 to a factor of 2.5. As previously described (see section 6.2), the use of default factors can be diverged in accordance with the principles of Notes of Guidance. Applying the same assumption as RAC - that a part of the interspecies differences has been accounted for in scenario 3, MoS should be above 25 to conclude that there are no indications of consumer risk. It is seen that the calculated MoS of 34 is higher than 25, which indicates that there is no risk for consumers in scenario 3 when using the individual cosmetic products.

A MoS below 25 and thus a risk in the most conservative (extreme worst case scenario) scenario cannot be ruled out if a consumer uses the three cosmetic products at the same time. This is the case if the concealer is used in more than 1/10 of the face and body lotion and foundation is used as assumed in section 6.2.

However, it should be emphasized once more that the assessment should be considered very conservative/extreme worst case for the following reasons:

- Dermal absorption is set conservatively at 70%. As mentioned earlier, the value is based on a study (Franko *et al*., 2012) which showed that approximately 25% PFOA (as acid) was absorbed through the skin and that 45% of the substance was retained in the epidermis. If using the situation of 70% dermal absorption, it is assumed that the proportion of PFOA retained in the epidermis would be systemically available, a highly conservative assumption. If instead 25% dermal absorption is assumed, MoS would be 97 in scenario 3 for the individual cosmetic product. If the concealer is used in 1/10 of the face and body lotion and foundation is used as assumed in section 6.2 while 25% dermal absorption is assumed, MoS will be 70 in scenario 3.
- It is assumed that all PFAS measured in the chemical analyses will occur as PFOA, which on the basis of the available data is assumed to be the most toxic PFAS and the PFAS which is eliminated most slowly from the human body. Again, this is a very conservative assumption. If the calculations instead are conducted for PFOA concentration alone or using an 'average' NOAEL for the selected substances (which will be higher than that for PFOA alone), MoS would be significantly larger.

All in all, based on highly conservative scenarios and the no-effect values used by the regulatory authorities within the EU, it is assessed that the measured concentrations of PFCA in cosmetic products themselves do not pose a risk to consumers. However, in the most conservative scenario a risk cannot be completely ruled out if several cosmetic products contain-

ing PFAS are used at the same time - this very conservative scenario is, however, not considered to be particularly realistic.

As mentioned above, the above conclusion is based on studies which are currently considered relevant for quantitative risk assessment in the EU. It should be mentioned that a number of studies of PFOA indicate that there may be effects at lower levels. However, these studies were considered unsuitable for quantitative risk assessment in RAC opinion (ECHA, 2015 a,b).

Another uncertainty is the fact that PFOA and other PFCA is eliminated much more slowly from serum in humans than from serum in experimental animals. It was attempted to take this factor into account in scenario 3.This scenario is uncertain because i) the external dose is theoretically converted to an internal concentration, and ii) the scenario does not directly account for differences in deposition in human or animal organs.

Despite the fact that the risk assessment, based on the measured concentrations of PFCA, shows that the individual cosmetic product in itself is unlikely to pose a risk for consumers, the concentrations in products 4 and 17 exceed both the upcoming EU limit value of 25 ng/g for PFOA and the proposed EU sum limit for C_9-C_{14} PFCA of 25 ng/g. Product No. 10, 16, 21 and 23 also exceeds the proposed EU sum limit value for C_9-C_{14} PFCA. PFOA, its salts and

PFOA-related substances are banned from 4 July 2020. On 6 October 2017, a proposal has been submitted to ECHA to ban the manufacture and use of C_9-C_{14} PFCA, salts thereof and C_9-C_{14} PFCA-related substances. C_9-C_{14} PFCA, PFOA, PFHpA, PFHxA, PFPeA, PFBA and other perfluoroalkyl acids are extremely persistent substances. Any emission of these substances or their precursors will contribute to an accumulation in the environment and thus potentially also to an increased exposure of humans via the environment.

Furthermore, it should be mentioned that cosmetic products may contain lipophilic PFAS precursors, which could potentially be absorbed through the skin and which, after exposure, could be metabolised to PFAS in an unknown extent. These precursors are not quantified in the chemical analyses. The analysis of total organic fluorine (TOrF) gives an indication of the amount of total organic fluorine in the cosmetic products, but it is still unknown how much of the measured content consists of lipophilic precursors that can be metabolised to PFAS in the body after dermal uptake. Therefore, from the chemical analyses it cannot be determined the extent to which lipophilic precursors could contribute to the PFAS blood concentration of the consumer using the cosmetic products.

All in all, the above uncertainties could be taken into account if biomonitoring of consumers using the cosmetic products in question was performed. However, such a study would be costly and it might be difficult to find a relevant control group.

It has been assumed, on the basis of the available knowledge, that PFOA is the most toxic of the five assessed PFCAs. At the present time, too little is known about the other PFCAs with different chain-lengths to rule out that, in some cases, these substances may be as or more hazardous to health as PFOA. There is particular concern that some PFAS accumulates to a greater extent in human brain tissue than PFOA. There are no data to elucidate possible effects of this, but the overall surfactant properties of the substances, which may result in undesirable changes in the functioning of the cell membranes in the brain, are worrying.

Finally, it should be mentioned that many toxicity studies are based on the PFAS salts, which cannot be assumed to have the same toxicological profile as the acids. However, it is a common regulatory approach to use these studies to assess both the salts and the acids.

The above risk assessments and considerations apply to systemic effects. Several PFAS, especially when they appear as acids, may be irritating, a possibility also reflected in the available data for the classification and labelling of the substances. Since cosmetic products are applied to the skin and several products around the eyes, it is relevant to consider whether they could be irritating. In addition, the measured PFAS concentrations in the products are very low and well below the classification limit of the products. There is no identified information indicating that PFAS should be sensitizing, either in itself or as a constituent of cosmetic products.

Finally, it should be mentioned that this study focused on PFAS in cosmetic products, and that only the individual PFAS, preferably PFCA, for which there are commercial analytical methods were analysed. Thus, eventual exposure of PFCA from other sources or other substances with the same mode of action is not considered. As seen from the results from the chemical analyses, the total organic fluorine content is greater than the content of PFAS. This finding can be explained by the fact that most of the fluoroalkyl substances which, according to the survey (Appendix 1), have been added to the cosmetic products have not been specifically analysed. These substances are usually larger and more lipophilic molecules which, after possible skin uptake, can break down in the body and release PFAS. The extent to which this process happens has not been investigated in this report, but there is a possibility of greater exposure to PFAS from this process than from the simple PFCA measured in the products. These substances are probably not being used themselves, but are believed to be primarily derived from impurities in the raw materials or formed during the production processes.

Hazard and risk associated with other organic fluorinated compounds are not evaluated in this report as there is still a lack of knowledge about these substances.

Abbreviations

APFO	Ammonium perfluorooctanoate
BMDL	Benchmark dose
bw	Body weight
CAS	Chemical Abstract Service
CLP	Classification, Labelling and Packaging (EU regulation)
DNEL	Derived No Effect Level
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
ERK	Extracellular signal-regulated kinase
FTOH	Fluorotelomer alcohols
4:2 FTS	4:2 Fluorotelomer sulfonate
6:2 FTS	6:2 Fluorotelomer sulfonate
8:2 FTS	8:2 Fluorotelomer sulfonate
HPFHpA	7H-Dodecafluoroheptanoic acid
IARC	International Agency for Research on Cancer
JNK	c-Jun N-terminal kinase
INCI	International Nomenclature of Cosmetic Ingredients
LOAEL	Lowest Observed Adverse Effect Level
LOD	Limit of Detection
LOQ	Limit of Quantification
MoS	Margin of Safety
MTD	Maximal Tolerable Dose
NaPFHx	Sodium perfluorohexanoate
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level
PAP	Polyfluoroalkyl phosphate esters
PBPK	Physiologically-Based PharmacoKinetic (modelling)
PBT	Persistent, Bioaccumulative and Toxic
PF-3,7-DMOA	Perfluoro-3,7-dimethyloctanoic acid
PFAA	Perfluoroalkyl acids
PFAS	Entire group of perfluoroalkyl and polyfluoroalkyl substances
PFBA	Perfluorobutanoic acid
PFBS	Perfluorobutane sulfonic acid
PFCA	Perfluoroalkanoic acids
PFDA	Perfluorodecanoic acid
PFDoA/PFDoDA	Perfluorododecane acid
PFDS	Perfluorodecane sulfonic acid
PFHpA	Perfluoroheptanoic acid
PFHpS	Perfluoroheptane sulfonic acid
PFHxA	Perfluorohexanoic acid
PFHxS	Perfluorohexane sulfonic acid
PFNA	Perfluorononanoic acid
PFPeA	Perfluoropentanoic acid
PFPrA	Perfluoropropionic acid
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctane Sulfonic Acid
PFOSA	Perfluorooctane sulphonamide
PFPeA	Perfluoropentanoic acid
PFTeDA/PFTeA	Perfluorotetradecanoic acid

PFTrA/PFTrDA	Perfluorotridecanoic acid
PFUnDA/PFUnA	Perfluoroundecanoic acid
PPARα	Peroxisome proliferator–activated receptor-α
PTFE	Polytetrafluoroethylene
RAC	The Committee for Risk Assessment
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals (EU Regulation)
SCCS	Scientific Committee for Consumer Safety
SED	Systemic Exposure Dosage
SPT	Association of Danish Cosmetics, Toiletries, Soap and Detergent Industries
SVHC	Substances of Very High Concern
T4	Thyroxin
TBG	Thyroxine-binding globulin
TDI	Tolerable Daily Intake
TOrF	Total organic fluorine
TTR	Transthyretin
UN no.	United Nations number
VKH	The Association of Danish Detergents and Cosmetics Industries
vPvB	Very persistent and very bioaccumulative

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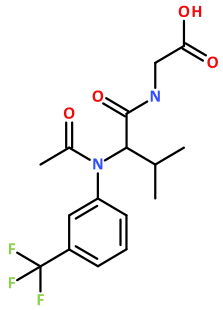
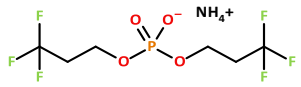
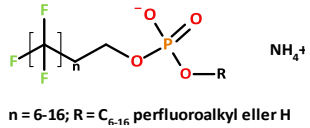
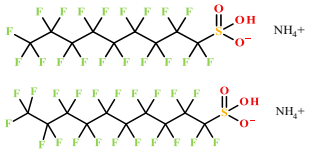
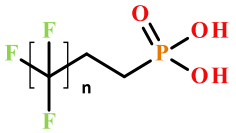
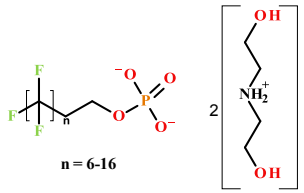
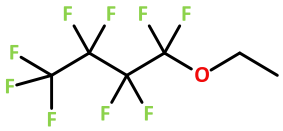
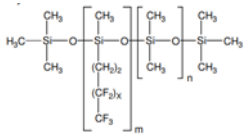
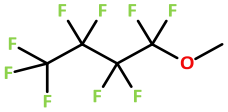
Appendix 1 Overview of results from the survey

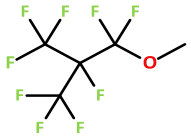
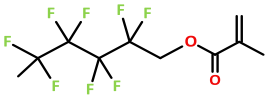
Table A1: Overview of the results of survey, including information on the chemical structure of the ingredients, any PFAS degradation products, and information about PFAS substances found in products with the substance declared in previous studies.

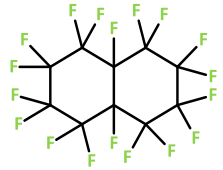
INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Acetyl trifluoromethylphenyl valylglycine	379685-96-8, 609-497-4	 [2] $C_{16}H_{19}F_3N_2O_4$	BB/CC cream, cream/lotion [1]	Contains a single carbon atom with fluorine (trichloromethyl), but is not a normal PFAS.	None	

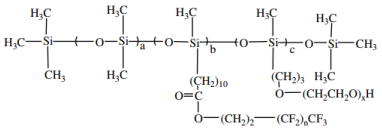
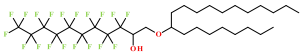
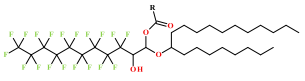
INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Ammonium C_{6-16} perfluoralkylethyl phosphate	65530-70-3, 65530-71-4, 65530-72-5	 65530-70-3 Structure $C_7H_9F_3O_2$  n = 6-16; R = C_{6-16} perfluoroalkyl eller H	Foundation [4,9]	Complex mixture of phosphoric acid esters and C_{6-16} perfluoroalkyl ethyl alcohol. PFAS, fluorotomers	6:2 FTOH (can (secondary) degrade to PFBA) 8:2 FTOH 10:2 FTOH 12:2 FTOH 14:2 FTOH PFPeA PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, etc.	PFOA, PFNA, PFDA [9]
Ammonium C_{9-10} perfluoroalkylsulfonate [5]	999999-35-7 (bl.) 17202-41-4 (C_9) 67906-42-7 (C_{10})		(Products with the ingredient are not confirmed on the Danish market)	Long chain perfluoroalkyl sulfonate. Is PFAS. May contain impurities with shorter/longer chains	PFNS PFDS	

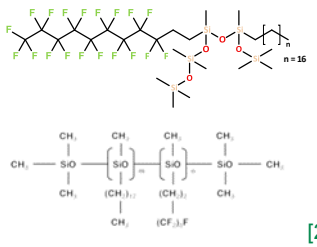
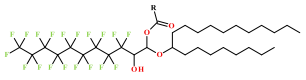
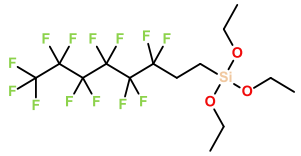
INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
C4-18 Perfluoroalkylethyl thiohydroxypropyltrimonium chloride	70983-60-7; 275-091-5		Conditioner [4]	Mixture of fluorothioethers. PFAS, fluorotomers	Depending on the alkyl chain length, PFCA can be formed	
C_{9-15} Fluoroalcohol phosphate	223239-92-7		Foundation, concealer, BB/CC cream, powder, sun screen with SPF >30, eyeliner, facial cream, Anti-aging cream, skin lightning product [1,4,9]	Mixture of many substances, which probably is PFAS	Degrades to FTOH and long chained PFCA	PFOA, PFNA, PFDA [9]
DEA-C_{8-18} Perfluoroalkylethyl phosphate	65530-63-4		[4] (Products with the ingredient are not confirmed on the Danish market)	PFAS. Diethanolamine (DEA) salt of a complex mixture of phosphoric acid esters and a perfluoroalkyl ethyl alcohol with C_{8-18} carbon chains.	Degrades to different FTOH and PFCA	

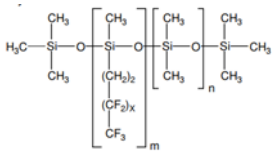
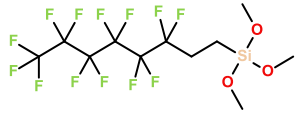
INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Ethyl perfluorobutyl ether	163702-05-4	 $C_6H_5F_9O$	[4] (Products with the ingredient are not confirmed on the Danish market)	Mixed ether. Not really PFAS	Ethers are stable and Cannot be degraded into PFAS	
Fluoro C_{2-8} alkyl-dimethicone		 X = 3	[4] (Products with the ingredient are not confirmed on the Danish market)	Fluorinated siloxane polymer. Not PFAS.	Cannot be degraded into PFAS	
Methyl perfluorobutyl ether	163702-07-6		Primer/fixer, lip product, mask [1]	Mixed ether. Not really PFAS	Ethers are very stable and cannot normally be oxidized to PFCA, although the possibility is mentioned in Wang *et al.* (2014)	

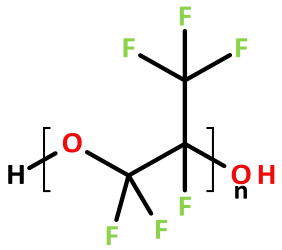
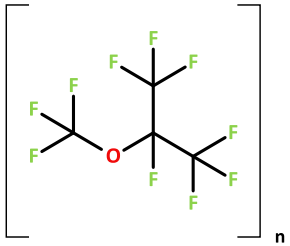
INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Methyl perfluoroisobutyl ether	163702-08-7		Primer/fixer [1]	Mixed ether. Not really PFAS	Ethers are stable and cannot normally break down/oxidize to PFCA	
Octafluoropentyl methacrylate	355-93-1/ 206-596-0	$C_9H_8F_8O_2$ 	Hair spray, conditioner, shampoo, hair care/-serum, mask, hair styling [4]	Polyfluoro compound and acrylate. Not PFAS, because the alkyl chain lacks an F	Hydrolysed to polyfluoro pentyl alcohol and pentanoic acid. Alcohol may be oxidized to PFBA	
PEG-8 trifluoropropyl dimethicone copolymer			Liquid foundation (sun screen) [10] (not confirmed on the Danish market)d)	Fluorinated siloxane polymer. Not PFAS.	Side chain can probably be broken down to PFAS. However, the found substances can also be residues of starting materials	PFHxA,, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA [10]

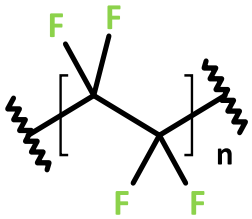
INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Perfluoroalkyl ethoxydimethicone			Liquid foundation, primer [10] (Products with the ingredient are not confirmed on the Danish market)	Fluorinated siloxane polymer. Not PFAS.	Side chain can probably be broken down to PFAS. However, the found substances can also be residues of starting materials	PFHxA,, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA [10]
Perfluorodecalin	306-94-5, 206-192-4	 $C_{10}F_{18}$	Nail polish/ nail care, cleansing wipes, cream/lotion, hair spray, moisturizer, anti-aging, facial cream, facial cleansing, eye cream, lip balm, acne treatment, mask, scrub [1,4]	Very stable perfluoro compound, but without alkyl and functional group, not PFAS.	Cannot be broken down to PFAS.	
Perfluorodecalin, Polyperfluoromethylisopropyl ether	Blanding		Cream/lotion [1]	Mixture of two substances that are not PFAS	Cannot be broken down to PFAS.	

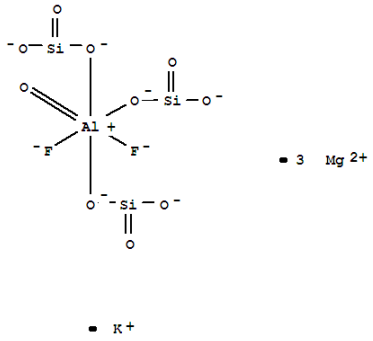
INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Perfluorononyl dimethicone, crosspolymer			Lip stick [3] (Products with the ingredient are not confirmed on the Danish market)	Unknown structure		
Perfluorononyl ethyl carboxydecyl peg-10 dimethicone;	500208-75-3	 [7]	Scrub/peeling, Sun protection, shampoo, hair care, products for showering, skin cream and skin lotion, shaving products, lip stick and make-up [1,4]	Fluorinated siloxane polymer. Not PFAS.	May release FTOH by hydrolysis of the side chain. Can be further degraded to PFCA.	
Perfluorononyl octyldodecyl glycol			[4] (Products with the ingredient are not confirmed on the Danish market)	Alkylated and perfluoroalkylated propylene glycol, PFAS derivatives	May be broken down into PFDA, PFNA	
Perfluorononyl octyldodecyl glycol grapeseedate			Blush [4] (Products with the ingredient are not confirmed on the Danish market)	Alkylated acylated and perfluoroalkylated propylene glycol PFAS derivatives	May be broken down into PFDA, PFNA	

INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Perfluorononylethyl stearyl dimethicone,	882878-48-0, 1858250-39-1	$C_{39}H_{71}F_{19}O_4Si_5$  [20]	Lip gloss, lip stick [4] (Products with the ingredient are not confirmed on the Danish market)	Siloxane with 9:2 fluorotomer group	Can probably be decomposed into PFDA, PFNA	
Perfluorononyl octyldodecyl glycol meadowfoamat			Blush [4,3]	Alkylated acylated and perfluoroalkylated propylene glycol, PFAS derivatives	May be broken down into PFDA, PFNA	
Perfluoroctyl triethoxysilane	51851-37, 257-473-3	 $C_{14}H_{19}F_{13}O_3Si$	Foundation, BB/CC cream [1,4,9]	6:2 fluorotomer silane derivative. PFAS	Can probably be broken down into PFDA, PFNA	PFOA, PFNA [9]

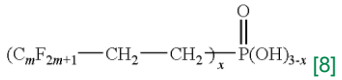
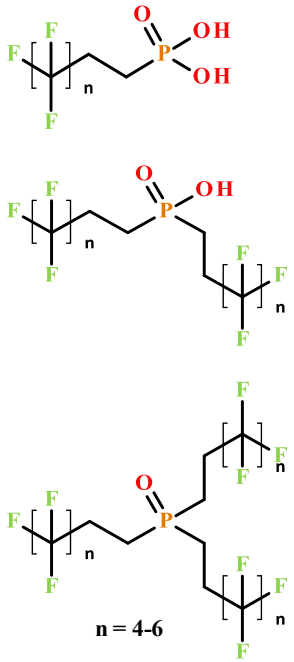
INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Perfluorononyl dimethicone;	259725-95-6	 [7]	Eyeliner, eye shadow, lip conditioner, shaving cream, hair spray [1,4]	Fluorinated siloxane polymer. Not PFAS.	Side chain can probably be broken down to PFAS/PFCA	
Perfluoroalkylsilyl mica		Unknown structure	Foundation [10] (Products with the ingredient are not confirmed on the Danish market)			PFHxA,, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA [10]
Polyfluorooctylmethyl trimethoxysilane (probably analogous to perfluoroctyl triethoxysilane)	85857-16-5/ 288-657-1	 $C_{11}H_{13}F_{13}O_3Si$	Powder, foundation [10] (Products with the ingredient are not confirmed on the Danish market)	6:2 fluorotomer silane derivative. PFAS	May be broken down into PFHxA and PFPeA	PFHxA,, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA [10]
Polyperfluoroethoxymethoxy difluoroethyl peg phosphate	200013-65-6		Hair spray, hair mousse, powder, sun screen [1,4,9]	Polyethylene glycol perfluoroalkyl ether, unknown structure	Short perfluoroalkyl ether chains. Ethers break down difficult. What has been found is probably impurities	PFOA, PFNA [9]

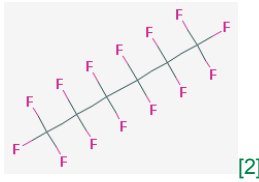
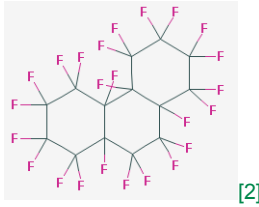
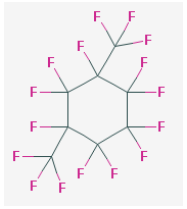
INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Polyperfluoroisopropyl ether			Cream/lotion [1]	Poly perfluoroalkyl ether, short chain <C_4. Not normal PFAS	Short perfluoroalkyl ether chains are difficult to break down.	
Polyperfluoromethyl isopropyl ether	69991-67-9		Cream/lotion [1,9,6]	Poly perfluoroalkyl ether, short chain <C_4. Not normal PFAS	Short perfluoroalkyl ether chains. Ethers break down difficult. What has been found is probably impurities	PFOA [9]

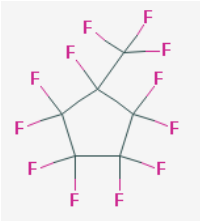
INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Polytetrafluoroethylene (PTFE) acetoxypropyl betaine	123171-68-6		Shaving foam [4]		PTFE is not degraded.	
PTFE (Polytetrafluoroethylene)	9002-84-0		Shaving foam/-gel, blush/highlighter, body lotion/-cream, brows, concealer, cream/lotion, foundation, lip balm, mascara/lashes, powder, eye cream, eye shadow, make up with SPF, anti-aging, bronzer/highlighter [1,9]	Fully fluorinated (perfluoro) polyethylene	Very stable and inert polymer. Only degrade at temperatures > 300 °C. What has been found must be impurities from the production process where ammonium salts of PFOA or PFNA are used	PFOA, PFNA, PFDA [9]

INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Synthetic fluorphlogopite.	12003-38-2/ 234-426-5		Foundation [1]	Not PFAS		

INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Tetradecyl aminobutyroylvalylaminobutyric urea trifluoroacetate(TAUT)	934368-60-2		Cream/lotion, body lotion [1]	TAUT is a synthetic tripeptide. Trifluoroacetate contains only 1 fluorinated carbon and is not PFAS	Cannot form PFAS	
Trifluoromethyl C_{1-4} alkyl dimethicone			Hair conditioner, skin care [4] (Products with the ingredient are not confirmed on the Danish market)	Siloxane polymer with trifluoromethyl C_{1-4} alkyl groups.	Cannot form PFAS	

INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
2-(Perfluoralkyl) ethyl alcohol phosphate C_{6-18} Fluoroalcohol phosphate (NB – not INCI names) (see also C_{9-15} Fluoroalcohol phosphate)		 [8] m = 4-6, x =1-3  n = 4-6	Powder [8] (Products with the ingredient are not confirmed on the Danish market)	Fluorotomer phosphate, PFAS. May contain residues of starting materials	May be degraded into various 4:2 and 6:2 FTOH and short-chain PFCA	

INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Perfluorohexane	355-42-0/ 206-585-0	 [2]	Eye cream, facial cream, mask, CC cream, anti-aging products [4,3]	Not PFAS		
Perfluoroperhydrophenanthrene	306-91-2/ 400-470-0	 [2]	Eye cream, facial cream, mask, anti-aging products [4,3]	Not PFAS		
Perfluorophenanthrene			Anti-aging products, lip gloss, facial mask [3]	Not PFAS		
Perfluorodimethylcyclohexane	335-27-3/206-386-9	 [2]	Eye cream, facial cream, mask, anti-aging products [4,3]	Not PFAS		

INCI name	CAS/EC no.	Potential formulas (molecular/structural)	Occurrence in cosmetic product type	+/- PFAS substance?	Potential PFAS degradation products	PFAS substances found in products with the substance declared in previous studies
Perfluoromethylcyclopentane	1805-22-7		Shaving foam [4,3]	Not PFAS		
Perfluorophenyl dimethicone			Eyeliner [3]	Not PFAS		

Appendix 2 Results from chemical analysis

Table A2: Results from the chemical analyses (Eurofins, 2017)

Product	Per-fluoroundecanoic acid (PFUnA)	Per-fluoro-dodec-ane acid (PFDoA)	Per-fluoro-tetra-decanoic acid (PFTeA)	Per-fluorodecane sul-fonate (PFDS)	Perfluoro-3,7-dime-thyloctanoic acid (PF-3,7-DMOA)	*7H*-Dode-cafluoro-heptanoic acid (HPFHpA)	6:2 Fluorote-lomer sul-fonate (6:2 FTS)	Per-fluoro-buta-noic acid (PFBA)	Per-fluoro-pentano-ic acid (PFPeA)	Per-fluorotri decanoic acid (PFTrA)	Perfluo-rohep-tane sul-fonate (PFHpS)	8:2 Fluorote-lomer sul-fonate (8:2 FTS)	4:2 Fluorote-lomer sulfonate (4:2 FTS)
Facial cream no 22	1	0.75	0.72	-	-	-	-	1.5	1.2	-	-	-	-
Facial cream no 22a	0.91	0.53	0.51	-	-	-	-	2.3	1.6	-	-	-	-
Facial cream no 23	6.4	7.2	8.2	-	-	-	-	4.2	2.9	10	-	-	-
Facial cream no 23a	6.2	6.5	7.8	-	-	-	-	4.3	2.8	10	-	-	-
Facial scrub no 5	-	-	-	-	-	-	-	2.4	3.1	-	-	-	-
Facial scrub no 5a	-	-	-	-	-	-	-	2.6	4	-	-	-	-
Shaving foam no 15	*Not analysed*												
Shaving foam no 15a	*Not analysed*												
Shaving foam no 9	*Not analysed*												
Shaving foam no 9a	*Not analysed*												
BB cream no 7	-	-	-	-	-	-	-	51	9.2	-	-	-	-
BB cream no 7a	-	-	-	-	-	-	-	16	8.7	-	-	-	-
Body lotion no 19	0.86	1.5	0.5	-	-	-	-	3.4	3.2	-	-	1.1	-
Body lotion no 19a	0.83	1.4	0.48	-	-	-	-	3.4	2.7	-	-	0.93	-
Body lotion no 21	8.6	10	12	-	-	-	-	4.8	4.2	13	-	-	-
Body lotion no 21a	9.1	9.8	12	-	-	-	0.78	4.9	4.2	14	-	-	-
CC cream no 2	-	-	-	-	-	-	-	35	8.2	-	-	-	-
CC cream no 2a	-	-	-	-	-	-	-	35	7.7	-	-	-	-

Product	Perfluoroundecanoic acid (PFUnA)	Perfluorododecane acid (PFDoA)	Perfluorotetradecanoic acid (PFTeA)	Perfluorodecane sulfonate (PFDS)	Perfluoro-3,7-dimethyloctanoic acid (PF-3,7-DMOA)	*7H*-Dodecafluoroheptanoic acid (HPFHpA)	6:2 Fluorotelomer sulfonate (6:2 FTS)	Perfluorobutanoic acid (PFBA)	Perfluoropentanoic acid (PFPeA)	Perfluorotridecanoic acid (PFTrA)	Perfluoroheptane sulfonate (PFHpS)	8:2 Fluorotelomer sulfonate (8:2 FTS)	4:2 Fluorotelomer sulfonate (4:2 FTS)
CC cream no 20	-	-	-	-	-	-	-	146	39	-	-	-	-
CC cream no 20a	-	-	-	-	-	-	-	149	40	-	-	-	-
Concealer no 24	*Not analysed*												
Concealer no 24a	*Not analysed*												
Concealer no 4	440	842	369	-	-	4	270	180	190	470	-	240	4.6
Concealer no 4a	440	840	330	-	-	3.9	260	180	190	450	-	260	4.1
Eyeliner no 6	-	-	0.7	-	-	-	-	-	1.2	-	-	-	-
Eyeliner no 6a	-	-	-	-	-	-	-	-	-	-	-	-	-
Foundation no 1	*Not analysed*												
Foundation no 1a	*Not analysed*												
Foundation no 13	-	-	-	-	-	-	-	-	-	-	-	-	-
Foundation no 13a	-	-	-	-	-	-	-	-	-	-	-	-	-
Foundation no 14	-	0.78	-	-	-	-	24	280	450	-	-	-	-
Foundation no 14a	0.49	0.51	-	-	13	-	23	290	470	-	-	-	-
Foundation no 17	17	17	NA	-	-	-	43	22	20	NA	-	NA	-
Foundation no 17a	17	18	NA	-	-	-	42	21	20	NA	-	NA	-
Foundation no 8	-	-	-	-	-	-	-	86	30	-	-	-	-
Foundation no 8a	-	-	-	-	-	-	-	89	32	-	-	-	-
Highlighter no 10	25	29	43	-	-	-	-	36	20	47	-	-	-
Highlighter no 10a	24	26	39	-	-	-	-	35	20	40	-	-	-
Hair spray no 12	-	-	-	-	-	-	-	-	-	-	-	-	-
Hair spray no 12a	-	-	-	-	-	-	0.69	-	-	-	-	-	-
Powder no 3	-	-	-	-	#	#	-	84	32	-	-	-	#
Powder no 3a	-	-	-	-	-	-	-	87	29	-	-	-	-
Eye shadow no 16	8	9.2	9.9	-	-	-	-	8.3	4.9	11	-	-	-
Eye shadow no 16a	8.2	8.1	9.2	-	-	-	-	8.3	5.4	8.9	-	-	-

Product	Per-fluoround ecanoic acid (PFUnA)	Per-fluoro-dodec-ane acid (PFDoA)	Per-fluoro-tetra-decanoic acid (PFTeA)	Per-fluorode cane sul-fonate (PFDS)	Perfluoro-3,7-dime-thyloctanoic acid (PF-3,7-DMOA)	*7H*-Dode-cafluoro-heptanoic acid (HPFHpA)	6:2 Fluorote-lomer sul-fonate (6:2 FTS)	Per-fluoro-buta-noic acid (PFBA)	Per-fluoro-pentano-ic acid (PFPeA)	Per-fluorotri decanoic acid (PFTrA)	Perfluo-rohep-tane sul-fonate (PFHpS)	8:2 Fluorote-lomer sul-fonate (8:2 FTS)	4:2 Fluorote-lomer sulfonate (4:2 FTS)
Body lotion no 18	-	-	-	-	-	-	-	-	-	-	-	-	-
Body lotion no 18a	-	-	-	-	-	-	-	-	-	-	-	-	-
Foundation no 11	-	-	-	-	-	-	-	-	-	-	-	-	-
Foundation no 11a	-	-	-	-	-	-	-	-	-	-	-	-	-

Product	Perfluorobutane sulfonate (PFBS)	Perfluorohex-ane sulfonate (PFHxS)	Perfluo-rooctane sulfonate (PFOS)	Perfluoro-hexanoic acid (PFHxA)	Perfluoro-heptanoic acid (PFHpA)	Perfluo-rooctanoic acid (PFOA)	Perfluoro-nonanoic acid (PFNA)	Per-fluorode canoic acid (PFDA)	Perfluo-rooctane sulfona-mide (PFOSA)	Total PFOS/ PFOA excl. LOQ	Total PFAS content excl. LOQ¤	TOrF [ng/g]
Facial cream no 22	-	-	-	1.1	0.96	1.1	1.1	1	-	1.1	11	740,000
Facial cream no 22a	-	-	-	1.5	1	1.1	0.87	0.85	-	1.1	12	
Facial cream no 23	-	-	-	2.6	2.6	3.1	3.9	5	-	3.1	56	130,000
Facial cream no 23a	-	-	-	2.8	2.6	3.2	3.7	4.9	-	3.2	55	
Facial scrub no 5	-	-	-	5.4	1.3	-	-	-	-	ND	12	3,300
Facial scrub no 5a	-	-	-	6.3	1.2	-	-	-	-	ND	14	
Shaving foam no 15	*Not analysed*											
Shaving foam no 15a	*Not analysed*											
Shaving foam no 9	*Not analysed*											
Shaving foam no 9a	*Not analysed*											
BB cream no 7	-	-	-	15	-	-	-	-	-	ND	76	37,000
BB cream no 7a	-	-	-	18	-	-	-	-	-	ND	43	
Body lotion no 19	-	-	-	24	5.1	20	1.4	6.3	-	20	68	8,600
Body lotion no 19a	-	-	-	24	5.1	22	1.3	6.1	-	22	68	
Body lotion no 21	-	-	-	4.5	4.6	5.2	6.4	7.5	-	5.2	81	280,000

Product	Perfluorobutane sulfonate (PFBS)	Perfluorohexane sulfonate (PFHxS)	Perfluorooctane sulfonate (PFOS)	Perfluorohexanoic acid (PFHxA)	Perfluoroheptanoic acid (PFHpA)	Perfluorooctanoic acid (PFOA)	Perfluorononanoic acid (PFNA)	Perfluorodecanoic acid (PFDA)	Perfluorooctane sulfonamide (PFOSA)	Total PFOS/ PFOA excl. LOQ	Total PFAS content excl. LOQ¤	TOrF [ng/g]
Body lotion no 21a	-	-	-	4.5	4.8	5.4	6.2	7.8	-	5.4	83	
CC cream no 2	-	-	-	-	0.93	-	-	-	-	ND	45	33,000
CC cream no 2a	-	-	-	12	-	-	-	-	-	ND	56	
CC cream no 20	-	-	-	383	35	-	-	-	-	ND	602	69,000
CC cream no 20a	-	-	-	397	34	-	-	-	-	ND	619	
Concealer no 24	*Not analysed*											
Concealer no 24a	*Not analysed*											
Concealer no 4	2	-	-	1,930	860	2,300	830	1,640	-	2,300	10,600	230,000
Concealer no 4a	2	-	-	1,940	860	2,370	820	1,710	-	2,370	10,700	
Eyeliner no 6	-	-	-	-	-	-	-	-	-	ND	1.9	200,000
Eyeliner no 6a	-	-	-	-	-	-	-	-	-	ND	ND	
Foundation no 1	*Not analysed*											
Foundation no 1a	*Not analysed*											
Foundation no 13	-	-	-	-	-	-	-	-	-	ND	ND	69,000
Foundation no 13a	-	-	-	-	-	-	-	-	-	ND	ND	
Foundation no 14	-	-	-	3,220	830	3.9	0.53	1.8	-	3.9	4,820	160,000
Foundation no 14a	-	-	-	3,340	827	4.3	0.58	1.8	-	4.3	4,970	
Foundation no 17	-	-	-	80	48	64	35	43	-	64	390	79,000
Foundation no 17a	-	-	-	81	44	66	33	40	-	66	380	
Foundation no 8	-	-	-	276	16	-	-	-	-	ND	409	59,000
Foundation no 8a	-	-	-	284	18	-	-	-	-	ND	423	
Highlighter no 10	-	-	-	18	17	17	22	23	-	17	300	310,000
Highlighter no 10a	-	-	-	17	18	17	21	22	-	17	280	
Hair spray no 12	-	-	-	-	-	-	-	-	-	ND	ND	
Hair spray no 12a	-	-	-	-	-	-	-	-	-	ND	0.69	
Powder no 3	-	-	-	34	4.6	NA	-	NA	-	ND	155	180,000

Product	Perfluorobutane sulfonate (PFBS)	Perfluorohexane sulfonate (PFHxS)	Perfluorooctane sulfonate (PFOS)	Perfluorohexanoic acid (PFHxA)	Perfluoroheptanoic acid (PFHpA)	Perfluorooctanoic acid (PFOA)	Perfluorononanoic acid (PFNA)	Perfluorodecanoic acid (PFDA)	Perfluorooctane sulfonamide (PFOSA)	Total PFOS/ PFOA excl. LOQ	Total PFAS content excl. LOQ¤	TOrF [ng/g]
Powder no 3a	-	-	-	30	2.7	NA	-	NA	-	ND	150	
Eye shadow no 16	-	-	-	5.4	5.3	6	7.1	7.8	-	6	83	190,000
Eye shadow no 16a	-	-	-	5.5	4.6	6	6.6	7.6	-	6	78	
Body lotion no 18	-	-	-	-	-	-	-	-	-	ND	ND	-
Body lotion no 18a	-	-	-	-	-	0.7*	-	-	-	0.696	0.696	
Foundation no 11	-	-	-	-	-	-	-	-	-	ND	ND	67,000
Foundation no 11a	-	-	-	-	-	-	-	-	-	ND	ND	-

-: Below "Limit of Quantification" (LOQ)

#: Unable to report. LOQ was increased due to disturbances from the matrix.

NA: It was not possible to analyse for this substance due to various interferences and matrix disorders.

ND: Not detected.

* 0.7 ng/g is identical to LOQ for this product. It cannot be excluded that the product contains PFOA as background contamination. However, the average of the double determinations gives a concentration below LOQ.

Risk assessment of fluorinated substances in cosmetic products

Perfluoroalkyl and polyfluoroalkyl substances (PFAS), also known as fluoroalkyl substances (or the short term 'fluorinated substances'), are a large group of substances used in a wide range of consumer products to make them water-, grease- and dirt-repellent. PFAS and other fluorinated compounds are used in cosmetic products because they are surfactants and therefore make creams etc. penetrate the skin more easily, make the skin brighter, make the skin absorb more oxygen, or make the makeup more durable and weather resistant. Fluoroalkyl substances and other fluorinated compounds are used, for example, in foundation, moisturizer, eye-shadow, powder and lipstick, shaving cream etc. The purpose of the project was to build knowledge of fluoroalkyl substances in cosmetic products and to clarify whether the use of cosmetic products containing certain fluoroalkyl substances presents a health risk to consumers. In the report 17 different cosmetic products with declared content of Perfluoroalkyl and polyfluoroalkyl substances (PFAS) or other fluorinated compounds were tested for the content of total organic fluorine and specific PFAS. The report also contains a risk assessment of the selected cosmetic products based on the analysis of specific PFAS.

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