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Ministry of Agriculture, Nature and Food Quality

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To the Minister of Medical Care and Sports

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Advice on PFOA and GenX in food

Background

Perfluoroalkylated substances (PFASs) have been used, and are being used, in a range of industrial and chemical applications, e.g. as processing aids in impregnation agents for a wide range of products. The best known PFASs are perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA). PFASs are thermally and chemically stable and can be taken up and accumulate in organisms. Their chemical properties and the widespread use led to worldwide distribution in the environment and thus to human exposure. In many countries there is pressure on industry to reduce, or even ban, the use of PFASs and to find and apply alternatives.

GenX is such an alternative to the use of PFOA. It is a polymerisation aid that is used for the production of fluoropolymers, such as Teflon® and denotes two substances:

- ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoate (FRD-902) and
- 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoic acid (FRD-903).

Under environmental and physical conditions (e.g. in water or blood) FRD-902 and FRD-903 dissociate into the ion HFPO-DA (hexafluoropropyleneoxide dimer acid). The HFPO-DA ion is relevant for toxicological effects. In this advice the HFPO-DA ion is called GenX.

In the past, the companies DuPont/Chemours in Dordrecht and Custom Powders in Helmond emitted PFOA and GenX to the air. As a consequence, the areas around the sites of these companies have been polluted. In 2017 and 2018 the 'Expertisecentrum PFAS' has investigated the deposition of PFOA and GenX via air in the surroundings of DuPont Chemours in Dordrecht[1] and Custom Powders in Helmond[2]. PFOA and GenX were found to be present in soil and water due to air

[1]Report is available via https://www.ozhz.nl/fileadmin/uploads/bodeminformatie/PFOA_in_bodem/Onderzoek_Expertisecentrum_-_Maart_2018
[2]First report is available via https://www.helmond.nl/Media%20Helmond.nl/Documenten%20Helmond/Actueel/Nieuws/Nieuws%202018/2018-10-23%20VO%20GenX%20en%20PFOA%20Helmond%20definitief%20incl%20bijlagen.pdf
Second report is available via

deposition and may thus enter the food chain. Livestock might be exposed if polluted soil, grass or water is consumed[3]. Subsequently, consumers might be exposed via the consumption of products of animal origin (e.g. dairy products or meat), leading to a elevated risk for human health.

The Office for Risk Assessment & Research (BuRO) of the Netherlands Food and Consumer Product Safety Authority (NVWA), therefore, investigated in a pilot study in 2018 the presence of PFOA and GenX in feed and food. The results of this study were used for a preliminary assessment to answer the question:

> Is there a possible risk for human health due to exposure to PFOA and GenX in food?

Approach

The sites of the companies DuPont/Chemours in Dordrecht and Custom Powders in Helmond are two 'hot spots' related to PFOA and GenX emissions. BuRO requested the directorate Enforcement of the NVWA to collect egg, milk, cheese, yoghurt and silage samples at farms in the vicinity of DuPont/Chemours in Dordrecht and Custom Powders in Helmond. As a starting point, farms were selected based on locations where soil samples were taken for air deposition studies as performed by the 'Expertisecentrum PFAS'. Subsequently, the directorate Enforcement was requested to collect fish samples at a fishing pond in the close vicinity of the site of Custom Powders in Helmond.

The collected samples were sent to Wageningen Food Safety Research (WFSR, formerly known as RIKILT) for analysis. Next, BuRO sent the results of the analysis to the Front Office Food and Product Safety (FO) of the National Institute for Public Health and the Environment (RIVM) addressing the following questions:

1. Describe the toxicology of PFOA and GenX.
2. Estimate the intake of PFOA and GenX by consumers based on the measured concentrations of PFOA and GenX in dairy products, eggs and fish.
3. Perform a risk assessment of PFOA and GenX in contaminated food of animal origin.
4. Model the transfer of PFOA and GenX from ditch water to edible products from lactating cows and sheep (milk and meat).
5. Estimate the intake of PFOA and GenX by consumers based on the theoretical (modelled) concentrations in cow's milk and meat and sheep's milk and meat.
6. Calculate the possible concentrations of PFOA and GenX in ditch water when concentrations of PFOA and GenX occur at the analytical limit of quantification (LOQ) of 0.01 ng/g in milk (based on reversed dosimetry modelling).
7. Estimate the transfer of PFOA and GenX in silage to milk and meat from lactating cows and sheep.

FO divided their report in two parts. Part one addresses questions 1 – 3 and part two addresses questions 4 – 7. The FO risk assessments are added to this advice as appendices 1 and 2. BuRO used the FO risk assessments as a starting point for this advice. However, BuRO did not stick to the exposure assessment performed by the FO. BuRO compared the actual PFOA and GenX exposure via the

https://www.helmond.nl/Media%20Helmond.nl/Documenten%20Helmond/Actueel/Nieuws/Nieuws%202018/2019-03-14%20Definitief%20onderzoeksrapport%20fase%202%20inclusief%20bijlagen%20SECURED.pdf

[3] The NVWA received questions from farmers who wanted to know if they could let their livestock drink with PFOA or GenX contaminated ditch water.

consumption of products of animal origin to tolerable daily intakes (TDI)[4] of both PFOA and the GenX.

Regarding PFOA and GenX, FO used the TDI as derived by RIVM in its risk assessment. FO did not use the provisional TDI for PFOA as derived by the European Food Safety Authority (EFSA) in 2018. According to FO the risk assessments based on the TDI derived by RIVM should be considered provisional until EFSA has finalized their evaluation on PFOA.

In this advice BuRO uses the provisional TDI for PFOA provided by EFSA and the TDI's for PFOA and GenX provided by RIVM for the risk assessment. EFSA did not derive a health based guidance value for GenX.

Findings

Toxicology PFOA

- After oral administration PFOA is readily absorbed in the gastrointestinal tract in mammals, including humans, and distributed to plasma and liver. PFOA is not metabolized and is excreted unchanged in urine and faeces. PFOA crosses the placenta leading to prenatal exposure of the foetus. PFOA is also present in breastmilk. The estimated half-life for PFOA in humans is between 2 – 4 years.
- Short-term, subchronic and chronic oral PFOA toxicity studies using experimental animals report developmental effects, liver and kidney toxicity, immune effects and cancer (liver, testicular and pancreatic). Developmental effects observed in animals include decreased survival, delayed eye opening and reduced ossification, skeletal defects, altered puberty and altered mammary gland developments.

Toxicology GenX

- The biokinetics of GenX were studied in rats, mice and monkeys. The results indicate that GenX has lower potential for bioaccumulation compared to PFOA in these species (half-lives in experimental animals between hours and days for GenX and between hours and weeks for PFOA). Data on the half-life of GenX in humans are lacking. Toxicokinetic data indicate that GenX is mainly distributed to liver and blood.
- Apart from the tumorigenic response in rats, the main affected organs in rodents resulting from repeated exposure to GenX are liver, kidneys, haematological system and immune system.

Health based guidance values

- In 2016, RIVM derived a tolerable daily intake (TDI) for PFOA of 12.5 ng/kg body weight per day. Hepatotoxicity was considered by RIVM to be the critical effect. In 2018, the EFSA Panel on Contaminants in the Food Chain (CONTAM) derived a provisional TDI for PFOA of 0.8 ng/kg body weight per day. The increase of serum cholesterol was considered by EFSA to be the critical effect.
- For GenX, RIVM derived a provisional TDI of 21 ng/kg body weight per day. An increase in albumin and albumin/globulin ratio in male rats was considered the critical effect, possibly indicating immunotoxic effects.

Exposure assessment

- Table 1 provides an overview of the worst-case exposure of children (1-18 years old; average body weight 38.5 kg) and adults (19-79 years old; average body weight 81.9 kg) to PFOA and GenX via the consumption of contaminated milk (cow/sheep), meat (cow/sheep), cheese, yoghurt, egg, eel and carp. BuRO assumed a high intake (P95) of these foods based on the Dutch Food Consumption Survey 2012-2016. A further assumption

[4] A TDI estimates the amount of a potentially harmful substance or contaminant in food or water that can be ingested per day over a lifetime without risk of adverse health effects.

was that the PFOA or GenX concentration was equal to the quantification limit if a PFOA or GenX concentration was reported to be below the quantification limit.

Table 1. The exposure of children (1-18 years old) and adults (19-79 years old) to PFOA and GenX via the consumption of contaminated milk (cow/sheep), meat (cow/sheep), cheese, yoghurt, egg, eel and carp.

		Concentration (ng/g)		**P95 consumption rate of food or beverage (g/day)**	**Exposure (ng/kg body weight per day)**	
	Product	**PFOA**	**GenX**		**PFOA**	**GenX**
Children (1-18 years)	Milk (cow)[1]	0.06[2]	0.01[3]	446.1[7]	0.70	0.12
	Milk (cow)	0.01[5]	0.10[5]	446.1[7]	0.12	1.16
	Milk (sheep)[1]	0.2 – 0.7[4]	0.04 - 0.14[4]	446.1[7]	2.32 – 8.11	0.46 – 1.62
	Meat (cow)[1]	0.28[2]	0.06[3]	15.5[7]	0.11	0.02
	Meat (sheep)[1]	0.2[4]	0.04[4]	15.5[7]	0.08	0.02
	Cheese	0.10[5]	0.10[5]	44.1[7]	0.11	0.11
	Yoghurt	0.10[5]	0.10[5]	138.2[7]	0.36	0.36
	Egg	0.14[6]	0.25[5]	20.3[7]	0.07	0.13
	Eel	0.05[5]	0.01[5]	0[8]	0	0
	Carp	1.3[6]	4.7[6]	37[9]	0.87	3.15
Adults (19-79 years)	Milk (cow)[1]	0.06[2]	0.01[3]	365.5[10]	0.27	0.04
	Milk (cow)	0.01[5]	0.10[5]	365.5[10]	0.04	0.45
	Milk (sheep)[1]	0.2 – 0.7[4]	0.04 - 0.14[4]	365.5[10]	0.89 – 3.12	0.18 – 0.62
	Meat (cow)[1]	0.28[2]	0.06[3]	29.6[10]	0.10	0.02
	Meat (sheep)[1]	0.2[4]	0.04[4]	29.6[10]	0.07	0.01
	Cheese	0.10[5]	0.10[5]	68.7[10]	0.08	0.08
	Yoghurt	0.10[5]	0.10[5]	189.5[10]	0.23	0.23
	Egg	0.14[6]	0.25[5]	30.1[10]	0.05	0.09
	Eel	0.05[5]	0.01[5]	300[11]	0.18	0.37
	Carp	1.3[6]	4.7[6]	101[12]	1.48	5.35

[1]Based on exposure through contaminated ditch water;
[2]Concentration calculated by FO via an adjusted transfer model for PFOS in dairy cows;
[3]Concentration reasoned by FO;
[4]Concentration estimated by FO based on experimental data from literature;
[5]Concentration < LOQ;
[6]Positive concentration (>LOQ);
[7]Data on usual intake based on high consumption from the Dutch Food Consumption Survey 2012-2016 by children (1-18 years old; average body weight 38.5 kg). Assumption that the same amount of milk or meat is consumed regardless if it is from cow or sheep;
[8]Data on actual intake based on high consumption from the Dutch Food Consumption Survey 2012-2016 by children (1-18 years old; average body weight 38.5 kg);
[9]High consumption based on the Dutch Food Consumption Survey 2012-2016. Female consumers (9-18 years old; average body weight 55.2 kg);
[10]Data on usual intake based on high consumption from the Dutch Food Consumption Survey 2012-2016 by adults (19-79 years old; average body weight 81.9 kg). Assumption that the same amount of milk or meat is consumed regardless if it is from cow or sheep;
[11]Data on actual intake based on high consumption from the Dutch Food Consumption Survey 2012-2016 by adults (19-79 years old; average body weight 81.9 kg);

[12]High consumption based on the Dutch Food Consumption Survey 2012-2016. Male consumers (51-79 years old; average body weight 88.8 kg).

Risk assessment

- The exposure to PFOA via the consumption of sheep's milk and carp by children and adults exceeds the provisional EFSA-TDI (0.8 ng/kg body weight per day) for PFOA, indicating a possible risk for human health (see also table 5 in substantiation).
- Both the TDI's for PFOA and the TDI for GenX are not exceeded after the consumption of cow's milk, meat (cow/sheep), cheese, yoghurt, egg and eel by children and adults. The consumption of these products does not pose a risk for human health (see also table 5 in substantiation).
- A calculated PFOA concentration of 810 – 1100 ng/L in ditch water could lead to a PFOA concentration at the analytical limit of quantification (LOQ; being 0.01 ng/g) in milk of dairy cows after the consumption of contaminated ditch water (80 L or 110 L).

Answers to the questions

1. *Is there a possible risk for human health due to exposure to PFOA and GenX in food?*

Despite the fact that the exposure of children and adults to PFOA via the consumption of carp exceeds the provisional EFSA-TDI of 0.8 ng/kg body weight per day, the risk for human health is expected to be low. A TDI is a health based guidance value based on chronic (long term) exposure. The carp was caught in a fishing pond in the close vicinity of the factory of Custom Powders in Helmond. Fish from this pond will probably only, on occasion, be eaten by specific consumers (sport fishermen) leading to acute (short term) exposure. Furthermore, the risk assessment of carp was based on one fish and this fish does not provide an overview of the PFOA distribution in fish from the fishing pond.

Based on a comparison with the provisional EFSA-TDI of 0.8 ng/kg body weight per day, the exposure of children and adults to PFOA via the consumption of sheep's milk might pose a risk to human health. The risk assessment for sheep's milk is based on experimental transfer data from two sheep that do not show the same kinetics. Compared to dairy cows, the transfer of PFOA to milk in sheep is higher than one might expect. Therefore, no firm conclusion about the human health risk can be drawn.

The exposure of children and adults to PFOA and GenX via the consumption of cow's milk, meat (cow/sheep), cheese, yoghurt, egg and eel does not pose a risk for human health.

A calculated PFOA concentration of 810 – 1100 ng/L in ditch water would lead to a PFOA concentration at the analytical limit of quantification (LOQ; being 0.01 ng/g) in milk of dairy cows after the consumption of contaminated ditch water (intake of 80 L or 110 L). If the PFOA concentration is higher than 1100 ng/L contamination of milk with PFOA may occur.

As no transfer model for GenX was available, no maximum GenX concentration in ditch water that would lead to a GenX concentration in milk at the present analytical limit of quantification (LOQ; 0.1 ng/g) could be calculated.

Office for Risk Assesment & Research

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Advice

To the minister of Medical Care and Sports

Initiate additional toxicological research to investigate the risk caused by exposure to (mixtures of) PFAS substances; this because many PFAS substances are already on the market, new PFAS substances are being developed, while currently the main focus of regulatory and scientific authorities is on PFOS, PFAS and GenX.

To the Head of Agency

- Monitor the presence of PFAS in food of animal origin to allow assessment of the potential exposure of humans; this in spite of the fact that this preliminary assessment does not indicate increased risks for human health due to the current exposure to PFOA and GenX by food consumption in general
- However, inform the municipality of Helmond that increased health risk should not be excluded after regular consumption of fish from the specific fishing pond in the close vicinity of the factory of Custom Powders.

Yours sincerely,

Prof. dr. Antoon Opperhuizen
Director of the Office for Risk Assessment & Research

SUBSTANTIATION

Background

Perfluoroalkylated substances (PFASs) are compounds consisting of a hydrophobic alkyl chain of varying length and a hydrophilic end group (EFSA CONTAM Panel, 2018). PFASs are thermally and chemically stable. They have, therefore, been used since decades in a range of industrial and chemical applications as processing aids for impregnation of textiles, carpets, paper, packaging materials, furniture, shoes, cleaning agents, paints and varnish, wax, floor polishing agents, fire-extinguishing liquids, photo paper and insecticide formulations (EFSA, 2012; EFSA CONTAM Panel, 2018). This widespread use led to their global distribution in the environment including humans. The best known PFASs are perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA). PFOA has an anionic head group and belongs to the perfluoroalkyl carboxylic acids (PFCAs) (EFSA CONTAM Panel, 2018).

GenX is a polymerisation aid that is used for the production of fluoropolymers, such as Teflon®, without the use of PFOA (Beekman et al., 2016; Bokkers et al., 2018; FO, 2019a). GenX is used to denote two substances:

- ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoate (FRD-902) and
- 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoic acid (FRD-903).

Under environmental and physical conditions (e.g. in water or blood) FRD-902 and FRD-903 dissociate into the ion HFPO-DA (hexafluoropropyleneoxide dimer acid). The HFPO-DA ion is responsible for the observed toxicological effects (Bokkers et al., 2018; FO, 2019a). In this advice the HFPO-DA ion is called GenX.

In the Netherlands, the companies DuPont/Chemours in Dordrecht and Custom Powders in Helmond emitted PFOA and GenX in to the air. The emission of GenX by DuPont/Chemours is ongoing. Consequently, the area around the sites of these companies (soil, water and vegetation) is polluted (FO, 2019a).

Legislation

PFOA

Based on the REACH Regulation (Registration, Evaluation, Authorisation and Restriction of Chemicals; Regulation (EC) No 1907/2006[5]) PFOA is a persistent, bioaccumulative and toxic (PBT) substance. In 2013 PFOA was included in the Candidate List of Substances of Very High Concern (SVHC) for possible inclusion into Annex XVI of the REACH Regulation. Annex XVI describes a list of substances subject to authorisation.

Via Commission Regulation (EU) 2017/1000[6], PFOA was included in Annex XVII of the REACH Regulation. Annex XVII describes restrictions on the manufacture, placing on the market and use of certain dangerous substances, mixtures and articles. From July 4th 2020 PFOA substances shall not

- be manufactured or placed on the market as substances on their own;

[5] REGULATION (EC) No 1907/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC.
[6] COMMISSION REGULATION (EU) 2017/1000 of 13 June 2017 amending Annex XVII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards perfluorooctanoic acid (PFOA), its salts and PFOA-related substances.

- be used in the production of, or placed on the market in (a) another substance, as a constituent (b) a mixture (c) an article in a concentration equal to or above 225 ppb of PFOA including its salts or 1000 ppb of one or a combination of PFOA-related substances.

In the annex PFOA is specified as:

- PFOA (CAS No 335-67-1) and it salts
- Any related substance (including its salts and polymers) having a linear or branched perfluoroheptyl group with the formula C_7F_{15}- directly attached to another carbon atom, as one of the structural elements.
- Any related substance (including its salts and polymers) having a linear or branched perfluorooctyl group with the formula C_8F_{17}- as one of the structural elements, excluding:
  - C_8F_{17}-X, where X = F, Cl, Br.
  - C_8F_{17}-C(=O)OH, C_8F_{17}-C(=O)O-X′ or C_8F_{17}-CF_2-X′ (where X′ = any group, including salts).

There are a few exceptions where the restrictions will enter into force at a later point in time:

- equipment used to manufacture semi-conductors and latex printing inks (July 4th 2022).
- textiles for the protection of workers from risk to their health and safety, membranes intended for use in medical textiles, filtration in water treatment, production processes and effluent treatment and plasma nano-coatings (July 4th 2023).

There are also some exceptions that are not restricted:

- PFOS and its derivatives, which are listed in Part A of Annex I to Regulation (EC) No 850/2004[7].
- The manufacture of a substance where this occurs as an unavoidable by-product of the manufacture of fluorochemicals with a carbon chain equal to or shorter than six atoms.
- A substance that is to be used, or is used as a transported isolated intermediate, proved that the conditions in points (a) to (f) of Article 18(4) of the REACH Regulation are met.
- A substance, constituent of another substance or mixture that is to be used, or is used:
  - In the production of implantable medical devices within the scope of Directive 93/42/EEC[8].
  - In photographic coatings applied to films, papers or printing plates.
  - In photo-lithography processes for semiconductors or in etching processes for compound semiconductors
- Concentrated fire-fighting foam mixtures that were placed on the market before 4 July 2020 and are to be used, or are used in the production of other fire-fighting foam mixtures.

Commission Regulation (EC) No 10/2011[9] states that PFOA can be used as a polymer production aid only to be used in repeated use plastic articles that come into contact with food, sintered at high temperatures.

PFOA is not listed in Regulation (EC) No 1881/2006[10] setting maximum levels for certain contaminants in food.

[7] REGULATION (EC) No 850/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 29 April 2004 on persistent organic pollutants and amending Directive 79/117/EEC.
[8] COUNCIL DIRECTIVE 93/42/EEC of 14 June 1993 concerning medical devices.
[9] COMMISSION REGULATION (EU) No 10/2011 on plastic materials and articles intended to come into contact with food.
[10] COMMISSION REGULATION (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs.

GenX
The Netherlands (represented by the Dutch Ministry of Infrastructure and Water Management) proposed "2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid, its salts and its acyl halides (covering any of their individual isomers and combinations thereof)" to be identified as a SVHC. A dossier in accordance with the requirements set out in Annex XV to REACH was prepared. Comments on this dossier can be submitted by all interested parties before April 29th 2019[11]. When the public consultation is finalised and GenX is identified as a SVHC, it will be added to the Candidate List for eventual inclusion in the Authorisation List.

According to Commission Regulation (EC) No 10/2011[12] perfluoro[2-(n-propoxy)propanoic acid] or 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)-propanoic acid are only to be used in the polymerisation of fluoropolymers that are processed at temperatures at or above 265 °C and are intended for use in repeated use articles.

GenX is not listed in Regulation (EC) No 1881/2006[13] setting maximum levels for certain contaminants in food.

Toxicology
Below a short summary of toxicology of PFOA and GenX is presented, extracted from the report by the RIVM/RIKILT Front Office Food and Product Safety (FO). More detailed information on PFOA and GenX can be found in the FO report (Appendix 1)(FO, 2019a). Comprehensive reviews on the toxicity of PFOA are available (US EPA, 2016; DWQI, 2017; ATSDR, 2018; EFSA CONTAM Panel, 2018). The description of the GenX toxicology is mainly based on data available in the REACH registration dossier (Beekman et al., 2016; FO, 2019a).

PFOA
After oral administration PFOA is readily absorbed in the gastrointestinal tract in mammals, including humans, and distributed to plasma and liver. PFOA is not metabolized and is excreted unchanged in urine and faeces. PFOA crosses the placenta leading to prenatal exposure of a fetus. PFOA is also present in breastmilk. The estimated half-life for PFOA in humans is between 2 – 4 years (EFSA CONTAM Panel, 2018). This half-life is rather long compared to the period of several weeks which was reported for experimental animals (Zeilmaker et al., 2016). In contrast to classic lipophilic organic pollutants (e.g. dioxins) PFOA primarily binds to proteins instead of lipids (FO, 2019a).

Short-term, subchronic and chronic oral PFOA toxicity studies using experimental animals report developmental effects, liver and kidney toxicity, immune effects and cancer (liver, testicular and pancreatic). Developmental effects observed in animals include decreased survival, delayed eye opening and reduced ossification, skeletal defects, altered puberty and altered mammary gland developments (FO, 2019a).

Regarding PFOA toxicity, the liver is a target organ in rodents. PFOA is a ligand of the nuclear receptor peroxisome proliferator activated receptor-alpha (PPARα) and induces liver growth, proliferation of peroxisomes and inductions of peroxisomal β-oxidation in rodents. Elevated peroxisomal β-oxidation in rodents may lead to

[11] At https://echa.europa.eu/substances-of-very-high-concern-identification/-/substance-rev/22907/term
[12] COMMISSION REGULATION (EU) No 10/2011 on plastic materials and articles intended to come into contact with food.
[13] COMMISSION REGULATION (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs.

hepatic lipid peroxidation and subsequently to cell death and enhanced release of liver transaminases (EFSA CONTAM Panel, 2018).

PFOA has developmental neurotoxicity potential and widespread effects on the expression of genes relevant for signal transmission in the brain. Exposure of rodents to PFOA during pregnancy led to increased liver weight in pups and mothers (EFSA CONTAM Panel, 2018).

The International Agency for Research on Cancer (IARC) stated that there is limited evidence for carcinogenicity in experimental animals and moderate evidence for mechanisms of PFOA-associated carcinogenesis, including some evidence for these mechanisms being operative in humans. PFOA was assigned to group 2B as being possibly carcinogenic to humans (IARC, 2016; EFSA CONTAM Panel, 2018). From *in vitro* and *in vivo* genotoxicity studies, there is no evidence for a direct genotoxic mode of action of PFOA (FO, 2019a).

Human epidemiological studies report associations between PFOA exposure and a number of disorders and diseases. The National Institute for Public Health and the Environment (RIVM) reviewed these associations and concluded that the weight of evidence was variable and that uncertainty remains about the causality of the observed associations (Rijs & Bogers, 2017). In contrast, EFSA concluded that an association between PFOA exposure and adverse affected serum antibody response following vaccination in children is likely to be causal. For metabolic outcomes, human epidemiological studies provide strong support for causal associations between exposure to PFOA and increased serum levels of cholesterol and support for a causal association between exposure to PFOA and increased serum levels of the liver enzyme alanine transferase (ALT) (EFSA CONTAM Panel, 2018).

<u>GenX</u>
The majority of the toxicity studies using experimental animals are performed with FRD-902. Read-across of the toxicological properties of FRD-902 to FRD-903 is justified (Beekman et al., 2016; FO, 2019a). Under environmental and physical conditions (e.g. in water or blood) FRD-902 and FRD-903 dissociate into the ion HFPO-DA (hexafluoropropyleneoxide dimer acid). The HFPO-DA ion is responsible for the observed toxicological effects (Bokkers et al., 2018; FO, 2019a). In this advice the HFPO-DA ion is called GenX.

The biokinetics of GenX were studied in rats, mice and monkeys (Gannon et al., 2016). The results indicate that GenX has lower potential for bioaccumulation compared to PFOA in these species (half-lives between hours and days for GenX and between hours and weeks for PFOA) (FO, 2019a). Data on half-life on GenX in humans are lacking. The limited data available suggests that GenX binds to fatty acid-binding proteins in the liver (Sheng et al., 2018) and to serum proteins (albumin) in blood. Although no data are available on a direct interaction of GenX with albumin, toxicokinetic data illustrates that GenX mainly distributes to the liver and the blood. Overall, tissue and serum concentrations are higher in males compared to females, suggesting that females are able to eliminate GenX more effectively (FO, 2019a).

Apart from the tumorigenic response in rats, the main affected organs in rodents resulting from repeated exposure to GenX are the liver, the kidneys, the haematological system and the immune system (FO, 2019a). With regard to developmental toxicity, GenX crosses the placenta and distributes into the foetus and causes early deliveries and decreased birth weight in pups without causing severe parental toxicity at 100 mg/kg body weight per day. Information is inconclusive with respect to potential effects to the reproductive system (FO, 2019a). The observed liver effects are suggested to be (at least partly) explained (directly or indirectly) by activation of the peroxisome proliferator-activated receptor alpha (PPARα), a biological pathway mainly responsible for lipid metabolism (FO, 2019a). A recent study suggests that activation of PPAR signalling pathways is not solely responsible for the observed toxicity effects in pregnant rats and their offspring exposed to GenX (Conley et al., 2019).

Health based guidance values

PFOA

In 2016, RIVM derived a tolerable daily intake (TDI) for PFOA, at 12.5 ng/kg body weight per day (Zeilmaker et al., 2016). A TDI estimates the amount of a potentially harmful substance or contaminant in food or water that can be ingested per day over a lifetime without risk of adverse health effects. Hepatotoxicity was considered to be the critical effect. Male CrL:CD®BR rats were orally exposed to ammonium perfluorooctanoate concentrations of 0, 1, 10, 30 or 100 ppm (equivalent to 0, 0.06, 0.64, 1.94 and 6.5 mg/kg body weight per day) for 13 weeks (Perkins et al., 2004). After exposure for 4, 7 and 13 weeks increased liver weights (absolute and relative) and increased hepatocyte hypertrophy were observed at a dose of 10 ppm. When exposure was ceased the effects were reversible. From this rat study a lowest observed adverse effect level (LOAEL) and a no observed adverse effect level (NOAEL) can be derived, being 10 ppm (0.64 mg/kg body weight per day) and 1 ppm (0.06 mg/kg body weight per day). The PFOA serum concentration in rats related to the derived NOAEL was 7.1 µg/ml. RIVM translated the rat NOAEL to a Human Equivalent Dose for semi-chronic intake, being 0.001 mg/kg body weight per day. RIVM applied an assessment factor of 1 for interspecies differences, because rats are more sensitive to hepatotoxicity compared humans. RIVM also applied an assessment factor of 10 for intraspecies differences, resulting in a semi-chronic health based guidance value of 0.0001 mg/kg body weight per day (100 ng/kg body weight per day, corresponding to a human serum concentration of 710 ng/ml). An additional assessment factor of 8 was applied to translate the semi-chronic to a chronic health based guidance value of $12.5 * 10^{-6}$ mg/kg body weight per day (12.5 ng/kg body weight per day, corresponding to a human serum concentration of 89 ng/ml).

In 2018, the EFSA Panel on Contaminants in the Food Chain (CONTAM) derived a provisional tolerable weekly intake (TWI) for PFOA, being 6 ng/kg body weight per week (EFSA CONTAM Panel, 2018). A TWI estimates the amount of a potentially harmful substance or contaminant in food or water that can be ingested per week over a lifetime without risk of adverse health effects. A TWI is usually calculated for substances that are persistent (i.e. having a long half-life).
The increase of serum cholesterol is considered to be the critical effect. EFSA used the data of two studies (Steenland et al., 2009; Eriksen et al., 2013) on serum cholesterol to perform benchmark dose (BMD) modelling. The BMD modelling resulted in an estimated chronic daily intake of about 0.8 ng/kg body weight per day. This was considered to be an appropriate reference point for the establishment of the TWI (6 ng/kg body weight per week = 0.8 * 7). EFSA decided not to apply any additional uncertainty factor because the BMD modelling was based on large epidemiological studies from the general population, including potentially sensitive subgroups. EFSA also took into account that the BMD modelling was performed on risk factors for disease rather than disease (EFSA CONTAM Panel, 2018). How this was done is not further substantiated in the opinion.

Instead of the EFSA approach RIVM, ECHA[14] (European Chemicals Agency) and Danish EPA[15] have used a different approach for deriving a health based guidance value for PFOA (Danish EPA, 2015; ECHA, 2015; Zeilmaker et al., 2016). These different approaches were discussed during an expert meeting (EFSA, 2018). With regards the derived TWI by EFSA, RIVM identified three main issues:

- The suitability of the information in the epidemiological studies available for deriving a Point of Departure (PoD).
- The assumptions made in the derivation of the PoD.
- The inconsistency of the applied BMD analysis with the existing EFSA guidance.

In general, RIVM follows the health based guidance values set by EFSA. However, due to the above mentioned difference and the ongoing evaluation by EFSA, RIVM maintains its own TDI for PFOA presently. Risk assessments based on this value should be considered provisional until the EFSA evaluation is finalised (FO, 2019a).

<u>GenX</u>
RIVM derived a provisional TDI of 0,000021 mg/kg body weight per day (i.e. 21 ng/kg body weight per day). A NOAEL of 0,1 mg/kg body weight per day was considered as the point of departure (POD). The NOAEL, for a chronic oral gavage study in rats, is based on an increase in albumin and the albumin/globulin ratio in male rats. This effect indicates possible immunotoxic effects (Beekman et al., 2016). In agreement with the REACH guidance RIVM applied the following assessment factors to the oral NOAEL (Janssen et al., 2017):

- Standard interspecies for differences in kinetics	4
- Additional factor for potential kinetic differences	66
- Interspecies remaining toxicodynamic differences	1,8
- Intraspecies factor human	10

Livestock exposure
<u>PFOA and GenX in ditch water and silage</u>
Single samples of ditch water were taken at five different sites within a distance (radius) of four kilometres from the Dupont/Chemours factory in Dordrecht (van Poll, 2018). The average concentrations PFOA and GenX at these sites are given in table 1.

[14] In 2015, the committee for risk assessment (RAC), established a 'Derived No Effect Level' (DNEL) of 800 ng/mL serum for PFOA for the general population (ECHA, 2015). The DNEL was based on a study with mice where a decreased pup growth rate in the order of 25-30% during post-natal days 13-23 was observed at doses of 3 mg/kg/day and higher, leading to a NOAEL of 1 mg/kg/day. The corresponding NOAEL in serum was approximately 20,000 ng/mL. RAC used a total assessment factor of 12.5 (2.5 x 5), resulting in a worker DNEL of 1600 ng/mL serum. The corresponding DNEL for the general population was 800 ng/mL serum, using an intraspecies assessment factor of 10 (total assessment factor 2.5 x 10).
[15] The Danish EPA referred to the 2014 assessments by the US EPA (US EPA 2014a,b) to establish TDIs for PFOS and PFOA. The endpoint of liver toxicity in rats was used to derive TDIs of 0.03 µg/kg bw per day and 0.1 µg/kg bw per day for PFOS and PFOA, respectively. Human studies were considered in the Danish EPA 2015 assessment, however they were not considered to be adequate.

Table 1. Average PFOA- and GenX-concentrations in ditch water (ng/L) at five different locations around the factory in Dordrecht.

Location number	Distance (km)	PFOA (ng/L)	GenX (ng/L)
8	< 1	4670	956.5
6	1-2	660.5	133.5
4	1-2	556	97.5
3	2-3	172.5	24.5
10	3-4	40.5	9.7

The Netherlands Food and Consumer Product Safety Authority (NVWA) took ten samples of silage at farms in the vicinity of Dordrecht and Helmond. No GenX could be detected in these samples (<250 ng/kg). PFOA could only be detected in two samples in the vicinity of Dordrecht, concentrations were 540 and 600 ng/kg (measurements on basis of whole product).

Exposure of lactating cows
FO calculated the average intake of PFOA and GenX via ditch water by lactating cows (600 kg) assuming:

1. Maximum exposure – highest PFOA (4670 ng/L) and GenX (956.5 ng/L) concentration.
2. A maximum drinking water consumption of 110 L per day for mature lactating cows (weight 600 kg; milk yield 35 kg per day)
3. Cows solely consume contaminated ditch water.

The average intake of PFOA by lactating cows is approximately 510,000 ng PFOA per day (≈110 * 4670) and the average intake of GenX is approximately 110,000 ng GenX per day (≈110 * 956.5).

FO also calculated the average intake of PFOA via silage by lactating cows assuming:

1. Silage intake during winter time (worst case scenario). An average of 25 to 38.5 kg (grass) silage per day wet weight is consumed.
2. Cows solely consume contaminated silage.

The average intake of PFOA by lactating cows based on a worst case scenario is approximately 23,000 ng PFOA per day (≈38.5 * 600).
FO did not calculate the average intake of GenX via silage by lactating cows as GenX was not detected (<250 ng/kg).

Exposure of lactating sheep
FO calculated the average intake of PFOA and GenX via ditch water by lactating sheep (60 kg) assuming:

1. Maximum exposure – highest PFOA (4670 ng/L) and GenX (956.5 ng/L) concentration.
2. A daily drinking water consumption of 6 L per day.
3. Sheep solely consume contaminated ditch water.

The average intake of PFOA by lactating sheep is approximately 28,000 ng PFOA per day (≈6 * 4670) and the average intake of GenX is approximately 5700 ng GenX per day (≈6 * 956.5).

FO also calculated the average intake of PFOA via silage by lactating sheep assuming:

1. Daily silage intake of 2.7 kg wet weight grass silage daily.
2. Sheep solely consume contaminated silage.

The average intake of PFOA by lactating sheep based on the scenario above is approximately 1600 ng PFOA per day (≈2.7 * 600).

FO did not calculate the average intake of GenX via silage by lactating sheep as GenX was not detected is silage (<250 ng/kg).

Human exposure via food of animal origin

Dairy products, meat, egg and eel

FO modelled the PFOA concentration in milk and meat of cows exposed to ditch water and silage by using the adjusted transfer model for PFOS in dairy cows (van Asselt et al., 2013; FO, 2019b). The GenX concentrations (due to the absence of a transfer model) were reasoned by FO. FO did not scale the PFOA/PFOS transfer model from dairy cows to sheep. Allometric scaling does not apply, because renal clearance of PFOS/PFOA differs between animal species. Consequently one does not know if the PFOS/PFOA concentration in tissues of different animals is the same. Instead the experimental transfer of PFOA from contaminated feed into milk and meat of two sheep was used to estimate the PFOA concentration in milk of sheep exposed to contaminated ditch water (Kowalczyk et al., 2012; FO, 2019b). Table 2 provides an overview of the PFOA and GenX concentration in milk and meat of cows and sheep exposed to contaminated ditch water and silage.

Table 2. The PFOA and GenX concentration (ng/g) in milk and meat of cows and sheep exposed to contaminated ditch water or silage.

Animal	**Product**	**PFOA (ng/g)**		**GenX (ng/g)**	
		Ditch water	Silage	Ditch water	Silage
Cow	Milk	0.06[1]	0.003[1]	<0.01[2]	X[3]
	Meat	0.28[1]	0.01[1]	<0.06[2]	X[3]
Sheep	Milk	0.2 - 0.7[4]	0.01 – 0.04[4]	0.04 - 0.14[2]	X[3]
	Meat	0.2[4]	0.01[4]	0.04[2]	X[3]

[1]Modelled; [2]Reasoned assumption; i.e. assuming less efficient transfer of GenX relative to PFOA at comparable exposure; [3]X: negligible; [4]Estimated based on a pilot experiment (N=2)(Kowalczyk et al., 2012).

Samples of dairy products (milk, cheese and yoghurt), eggs and fish were taken by the NVWA from farms in the vicinity of Dordrecht and Helmond. One fish sample was taken from a fishing pond closely to Custom Powders in Helmond. Table 3 provides an overview of the PFOA- and GenX-concentrations in these samples.

Table 3. Analyzed PFOA- and GenX-concentrations in dairy products, egg and fish sampled near the companies DuPont/Chemours in Dordrecht and Custom Powders in Helmond.

Location	**Product**	**Concentration (ng/g)**		
		N	**PFOA**	**GenX**
Dordrecht	Dairy products			
	Milk[1]	15	<0.01[4]	<0.10
	Cheese[2]	1	<0.10	<0.10
	Yoghurt[2]	1	<0.10	<0.10
	Egg[3]	1	0.14	<0.25
Helmond	Dairy products			
	Milk[2]	2	<0.01	<0.10
	Egg[3]	1	<0.025	<0.25
	Fish			
	Eel (farmed)	1	<0.05	<0.10
	Carp	1	1.3	4.7

[1]Cow (N=14) and goat (N=1); [2]Cow; [3]Chicken; [4]< means <LOQ

Subsequently, BuRO took the PFOA and GenX concentrations in the products mentioned in tables 2 and 3 and calculated the worst-case exposure of children (1-18 years old) and adults (19-79 years old) (Table 4) by assuming:

1. That the PFOA or GenX concentration was equal to the quantification limit if a PFOA or GenX concentration was reported to be below the quantification limit.
2. High consumption (P95) based on the Dutch Food Consumption Survey 2012-2016.
    a. One consumes the same amount of milk or meat regardless if it is from a cow or sheep, as no consumption data for sheep's milk or meat are available in the Dutch Food Consumption Survey 2012-2016.
    b. Data on usual intake of milk, cheese, yoghurt, egg and beef.
    c. Data on the acute intake of eel, as no usual intake could be calculated in the Dutch Food Consumption Survey.
    d. No consumption data for carp were available in the Dutch Food Consumption Survey, therefore fish consumption was used as an alternative. See also the FO rapport (FO, 2019a).
3. Average body weight of 38.5 kg (children) and 81.9 kg (adults).

BuRO did not follow the exposure assessment performed by the FO. BuRO compared the actual PFOA and GenX exposure via the consumption of products of animal origin to both PFOA TDI's and the GenX TDI.

Table 4. The exposure of children (1-18 years old) and adults (19-79 years old) to PFOA and GenX via the consumption of contaminated milk (cow/sheep), meat (cow/sheep), cheese, yoghurt, egg, eel and carp.

		Concentration (ng/g)		**P95 consumption rate of food or beverage (g/day)**	**Exposure (ng/kg body weight per day)**	
	Product	**PFOA**	**GenX**		**PFOA**	**GenX**
Children (1-18 years)	Milk (cow)[1]	0.06[2]	0.01[3]	446.1[7]	0.70	0.12
	Milk (cow)	0.01[5]	0.10[5]	446.1[7]	0.12	1.16
	Milk (sheep)[1]	0.2 – 0.7[4]	0.04 - 0.14[4]	446.1[7]	2.32 – 8.11	0.46 – 1.62
	Meat (cow) [1]	0.28[2]	0.06[3]	15.5[7]	0.11	0.02
	Meat (sheep) [1]	0.2[4]	0.04[4]	15.5[7]	0.08	0.02
	Cheese	0.10[5]	0.10[5]	44.1[7]	0.11	0.11
	Yoghurt	0.10[5]	0.10[5]	138.2[7]	0.36	0.36
	Egg	0.14[6]	0.25[5]	20.3[7]	0.07	0.13
	Eel	0.05[5]	0.01[5]	0[8]	0	0
	Carp	1.3[6]	4.7[6]	37[9]	0.87	3.15
Adults (19-79 years)	Milk (cow)[1]	0.06[2]	0.01[3]	365.5[10]	0.27	0.04
	Milk (cow)	0.01[5]	0.10[5]	365.5[10]	0.04	0.45
	Milk (sheep)[1]	0.2 – 0.7[4]	0.04 - 0.14[4]	365.5[10]	0.89 – 3.12	0.18 – 0.62
	Meat (cow) [1]	0.28[2]	0.06[3]	29.6[10]	0.10	0.02
	Meat (sheep) [1]	0.2[4]	0.04[4]	29.6[10]	0.07	0.01
	Cheese	0.10[5]	0.10[5]	68.7[10]	0.08	0.08
	Yoghurt	0.10[5]	0.10[5]	189.5[10]	0.23	0.23
	Egg	0.14[6]	0.25[5]	30.1[10]	0.05	0.09
	Eel	0.05[5]	0.01[5]	300[11]	0.18	0.37
	Carp	1.3[6]	4.7[6]	101[12]	1.48	5.35

[1]Based on exposure through contaminated ditch water;
[2]Concentration calculated by FO via an adjusted transfer model for PFOS in dairy cows;
[3]Concentration reasoned by FO;
[4]Concentration estimated by FO based on experimental data from literature;
[5]Concentration < LOQ;
[6]Positive concentration (>LOQ);
[7]Data on usual intake based on high consumption from the Dutch Food Consumption Survey 2012-2016 by children (1-18 years old; average body weight 38.5 kg). Assumption that the same amount of milk or meat is consumed regardless if it is from cow or sheep;
[8]Data on actual intake based on high consumption from the Dutch Food Consumption Survey 2012-2016 by children (1-18 years old; average body weight 38.5 kg);
[9]High consumption based on the Dutch Food Consumption Survey 2012-2016. Female consumers (9-18 years old; average body weight 55.2 kg);
[10]Data on usual intake based on high consumption from the Dutch Food Consumption Survey 2012-2016 by adults (19-79 years old; average body weight 81.9 kg). Assumption that the same amount of milk or meat is consumed regardless if it is from cow or sheep;
[11]Data on actual intake based on high consumption from the Dutch Food Consumption Survey 2012-2016 by adults (19-79 years old; average body weight 81.9 kg);
[12]High consumption based on the Dutch Food Consumption Survey 2012-2016. Male consumers (51-79 years old; average body weight 88.8 kg).

Risk assessment
Table 5 provides an overview of the percentages PFOA and GenX covering the TDI's of both substances, being 0.8 ng/kg body weight per day (provisional by EFSA) or 12.5 ng/kg body weight per day (RIVM) for PFOA and 21 ng/kg body weight per day for GenX. If the percentage is higher than 100%, the TDI is exceeded and consumption of the related products might pose a risk for human health.

Table 5. Overview of the percentages PFOA and GenX covering the TDI's of both substances, being 0.8 ng/kg body weight per day (provisional by EFSA) or 12.5 ng/kg body weight per day (RIVM) for PFOA and 21 ng/kg body weight per day for GenX.

		Exposure (ng/kg body weight per day)		**%TDI**		
	Product	**PFOA**	**GenX**	**PFOA[2]**	**PFOA[3]**	**GenX**
Children (1-18 years)	Milk (cow)[1]	0.70	0.12	87	6	1
	Milk (cow)	0.12	1.16	14	1	6
	Milk (sheep)[1]	2.32 – 8.11	0.46 – 1.62	290 – 1014[4]	19 – 65	2 – 8
	Meat (cow) [1]	0.11	0.02	14	1	0
	Meat (sheep) [1]	0.08	0.02	10	1	0
	Cheese	0.11	0.11	14	1	1
	Yoghurt	0.36	0.36	45	3	2
	Egg	0.07	0.13	9	1	1
	Eel	0	0			
	Carp	0.87	3.15	109	7	15
Adults (19-79 years)	Milk (cow)[1]	0.27	0.04	33	2	0
	Milk (cow)	0.04	0.45	6	0	2
	Milk (sheep)[1]	0.89 – 3.12	0.18 – 0.62	111 – 390	7 – 25	1 – 3
	Meat (cow) [1]	0.10	0.02	13	1	0
	Meat (sheep) [1]	0.07	0.01	9	1	0
	Cheese	0.08	0.08	10	1	0
	Yoghurt	0.23	0.23	29	2	1
	Egg	0.05	0.09	6	0	0
	Eel	0.18	0.37	23	1	2
	Carp	1.48	5.35	185	12	25

[1]Based on exposure through contaminated ditch water; [2]Based on a provisional EFSA-TDI of 0.8 ng/kg body weight per day; [3]Based on a RIVM-TDI of 12.5 ng/kg body weight per day; [4]Red numbers indicate an exceedance of the TDI.

Table 5 shows that the consumption of sheep's milk and carp by children and adults exceeds the provisional EFSA-TDI (0.8 ng/kg body weight per day) for PFOA, indicating a possible risk for human health. Both TDI's for PFOA and the TDI for GenX are not exceeded after the consumption of cow's milk, meat (cow/sheep), cheese, yoghurt, egg and eel by children and adults. The consumption of these products does not pose a risk for human health.

Maximum PFOA and GenX concentration in ditch water
FO calculated the maximum PFOA concentration in ditch water that would lead to a PFOA concentration in milk at the present analytical limit of quantification (LOQ; being 0.01 ng/g = 0.01 ng/mL). In literature a transfer model for PFOS in dairy cows is available (van Asselt et al., 2013), which was adjusted to PFOA by FO (FO, 2019b). For their calculation FO assumed that no additional exposure occurs from

other sources than ditch water. Using a PFOA concentration of 0.01 ng/g in milk as input, a theoretical intake of 89,000 ng per day was calculated. This results in a calculated PFOA concentration in ditch water of approximately 1100 ng/L (≈89,000/80) or 810 ng/L (≈89,000/110) depending on the ditch water intake (80 L or 110 L).

As no transfer model for GenX was available, FO could not calculate the maximum GenX concentration in ditch water that would lead to a GenX concentration in milk at the present analytical limit of quantification (LOQ; 0.1 ng/g).

Discussion

The exposure assessment and subsequently the risk assessment performed by BuRO are based on a very limited number of samples of possible contaminated foods, such as milk, cheese and eggs. This explorative sample strategy was chosen by BuRO to obtain an indication of the possible risk for human health due to exposure to PFOA and GenX in foods.

In interpreting the sheep transfer calculations it should be noted that the transfer to milk was observed in only two sheep showing quite different PFOA kinetics. The available transfer data in dairy cattle and lactating sheep indicate that PFOA transfer to organs and tissues is comparable in both species, but transfer to milk is not. Regarding the latter, the limited available data suggest a much higher transfer (i.e. up to 6 – 20 fold) of PFOA from the blood to milk in lactating sheep than from the blood to milk in dairy cattle. Therefore, FO concluded that the observed transfer of PFOA in lactating sheep to milk needs to be confirmed beyond the pilot experiment in which it was assessed in order to draw a more definitive conclusion on the relevance of such transfer for human risk assessment (FO, 2019b).

Due to the absence of consumption amounts of fish by persons fishing in the fish pond in Helmond, the consumption rates of fish by the general Dutch population were used in the risk assessment. Persons fishing in this pond possibly consume fish more frequently than the general population. They may also consume fish in larger amounts when eating fish. By using the consumed amount at the 95^{th} percentile of the consumption distribution, this was partly addressed (FO, 2019a).

People living in the vicinity of either of the two sites are not only exposed to PFOA and GenX through the consumption of dairy products, egg and fish. As a result of emissions from the DuPont/Chemours site in Dordrecht and Custom Powders in Helmond, PFOA and GenX have been emitted into the environment via the air. As a consequence, these substances may have been deposited at a vegetable garden in the vicinity of the sites and local authorities were concerned whether it is safe to eat their home-grown vegetables. Therefore, RIVM performed a risk assessment of PFOA and GenX in vegetable garden crops in Dordrecht (including Papendrecht and Sliedrecht) and Helmond. In both assessments RIVM assumed that the persons in question would eat exclusively home-grown vegetables every day throughout their life. As a worst-case scenario, the calculated exposure is therefore probably higher than the actual exposure to PFOA and GenX of vegetable garden owners in the vicinity of the factories. Information about the amount and frequency in which the vegetables and potatoes are consumed was obtained from the Dutch food consumption survey (Mengelers et al., 2018; Boon et al., 2019).

<u>Dordrecht, Papendrecht and Sliedrecht</u>
RIVM concludes that the TDI for PFOA and the TDI for GenX are not exceeded via food. However, residents are also exposed to these substances via air and drinking water. Therefore, RIVM advises that vegetable garden crops grown within

a radius of one kilometer from the company should be consumed in moderation (not too often or too much). Outside this area, the concentrations were so low that the crops can be safely consumed even if one takes into account the two other sources of exposure (Mengelers et al., 2018).

<u>Helmond</u>
RIVM concludes that persons with a vegetable garden near the company Custom Powders in Helmond can safely eat their home-grown vegetables. In the past, this company emitted the substances PFOA and GenX into the air. However, RIVM-TDI's of PFOA and Genx for exposure were not exceeded by oral intake (Boon et al., 2019).

Other relevant sources of exposure in the vicinity of both companies are drinking water and air (Mengelers et al., 2018; Boon et al., 2019) and possibly sheep meat and milk (FO, 2019b). In Helmond, also swimming water was identified as a potential source of exposure (Beekman, 2018; Muller & te Biesebeek, 2018). These sources need also to be considered to determine whether there is a health risk related to the exposure to PFOA and GenX.

In 2011, Noorlander and colleagues calculated the high level intake (99^{th} percentile) of PFOA via food (flour, fatty fish, lean fish, pork, eggs, crustaceans, bakery products, vegetables/fruit, cheese, beef, chicken/poultry, butter, milk, vegetable oil and industrial oil) and drinking water for the Dutch population, being 0.6 ng/kg body weight per day (Noorlander et al., 2011). This concentration is lower than the EFSA-TDI of 0.8 ng/kg body weight per day.

Conclusion
Despite the fact that the exposure of children and adults to PFOA via the consumption of carp exceeds the provisional EFSA-TDI of 0.8 ng/kg body weight per day, the risk for human health is expected to be low. A TDI is a health based guidance value based on chronic (long term) exposure. This carp was caught in a fishing pond in the close vicinity of the factory of Custom Powders in Helmond. Fish from this pond will probably only, on occasion, be eaten by specific consumers (sport fishermen) leading to acute (short term) exposure. Furthermore, the risk assessment of carp was based on one fish and this fish does not provide an overview of the PFOA distribution in fish from this fishing pond in general.

Based on a comparison with the provisional EFSA-TDI of 0.8 ng/kg body weight per day, the exposure of children and adults to PFOA via the consumption of sheep's milk might pose a risk to human health. The risk assessment for sheep's milk is based on experimental transfer data from two sheep that do not show the same kinetics. Compared to dairy cows, the transfer of PFOA to sheep's milk is higher than one might expect. Therefore, no firm conclusion about the human health risk regarding sheep's milk can be drawn.

The exposure of children and adults to PFOA and GenX via the consumption of cow's milk, meat (cow/sheep), cheese, yoghurt, egg and eel does not pose a risk for human health.

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Appendix 1: Risk assessment of GenX and PFOA in food
Part 1: Toxicity of GenX and PFOA and intake through contaminated food of animal origin

Office for Risk Assesment & Research

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Appendix 2: Risk assessment of GenX and PFOA in food
Part 2: Transfer of GenX and PFOA in ditch water and silage to edible products of food producing animals