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SUMMARY OF THE ENVIRONMENTAL OCCURRENCE, HUMAN EXPOSURE, TOXICITY, AND AVAILABLE REMEDIATION TECHNOLOGIES FOR PERFLUOROHEXANOIC ACID (PFHXA)

As summarized below, the body of scientific evidence does not support the listing of PFHxA as a substance of very high concern. Available toxicity information demonstrates that PFHxA is not carcinogenic, mutagenic or toxic for reproduction and poses no human health risk based on standard risk assessment methodology. Empirical data on PFHxA in the environment and in human serum from biomonitoring studies, all support a conclusion with high confidence that PFHxA is either not detected or is present at very low levels, indicating a high margin of safety for PFHxA from all potential sources and routes of exposure. Finally, recent advances in remediation technologies, including ion exchange resins and membrane filtration, have resulted in full-scale water treatment technologies currently able to effectively and efficiently remove short chain perfluoroalkyl acids, including PFHxA, from groundwater and drinking water.

Combined, PFHxA is not a substance of very high concern; human health toxicity and risk is low, exposure is low, and effective remediation technologies are available as needed.

A. Toxicological Data for PFHxA Demonstrates Low Human Health Risk

The full suite of standard laboratory assays are available for PFHxA and include:

- 2 year rodent cancer bioassay (Klaunig 2015)
- DNA mutation and genotoxicity *in vitro* assays (NTP 2018; Loveless 2009; Eriksen 2010)
- Chronic systemic toxicity rodent bioassay (Klaunig 2015)
- Reproductive/Developmental rodent bioassays (Loveless 2009; Iwai 2014)
- Sub-chronic systemic toxicity bioassays (Loveless 2009; Chengelis 2009; Iwai 2014)
- Analysis of endocrine disruption (Behr 2018; Borghoff in press, presented as poster at SETAC North America 2017)
- High-throughput molecular *in vitro* assays (EPA Tox21)
- Toxicokinetic assays in rats, mice, microminipigs, monkeys and humans (many, examples include Chengelis 2009; Iwai 2011; Russell 2013, 2015; Nilsson 2010, 2013; Fujii 2014; Guruge 2015; Gannon 2011, 2016)

1. *PFHxA does not exhibit carcinogenicity, mutagenicity, or genotoxicity. PFHxA is not an endocrine disruptor. Sensitive endpoints in rodent studies include effects on liver, thyroid, kidney, and hematology at high doses.*

PFHxA was not carcinogenic and has not exhibited any DNA mutation or genotoxic effects in several studies (NTP 2018, Klaunig 2015, Loveless 2009, Nobels 2010). A comprehensive review of both *in vitro* and *in vivo* studies evaluating PFHxA activity across endocrine pathways shows that PFHxA is not bioactive in estrogen, androgen, aromatase or thyroid receptor signaling pathways (Borghoff in prep.) and does not act as an estrogen or androgen receptor agonist or antagonist at environmentally relevant levels[1] (Behr 2018). Effects noted from high level exposure (more than 100 mg/kg) to PFHxA in subchronic and chronic noncancer rodent bioassays include liver, thyroid, kidney and hematologic effects (Loveless 2009, Chengelis 2009, Iwai 2014), with the lowest no-observed-adverse effect level (NOAEL) of 30 mg/kg-day from the chronic rat study (Klaunig 2015).

2. *PFHxA does not exhibit adverse effects on reproduction, and developmental effects are mixed and occur at higher doses than other endpoints (see above).*

PFHxA has not demonstrated any adverse reproductive effects in mice or rats, however, findings regarding developmental endpoints are mixed. PFHxA exposure did not cause any developmental effects in rats (Loveless 2009). A mouse study indicated some potential developmental concerns due to low incidences of increased stillbirths, pup death at postnatal days 1 to 4, and effects on the eye (Iwai 2014). However, when the full concurrent controls are included and when historical controls from the same mouse strain and lab are evaluated, it is clear that the low incidence of stillbirths is unrelated to PFHxA exposure (follow-on publication in preparation). Due to the inconsistency between studies and the questionable biological and statistical significance of the mouse effects, we do not believe that PFHxA is a developmental toxicant. However, even if these developmental endpoints were considered, the no-observed-adverse effect level from the 2-year rodent bioassay is more sensitive (i.e. lower) and, therefore, would be protective of any potential developmental effects in a quantitative risk assessment (see below for more detail).

3. *Epidemiologic data on PFHxA are limited and do not demonstrate consistency with adverse effects in animal toxicity studies.*

There are very few human observational studies that have included PFHxA due to the low frequency of detection and low levels detected. A study of Taiwanese children found no association with PFHxA and immunological markers or asthma in the children (Dong

[1] Specifically, PFHxA did not act as an agonist or antagonist to estrogen (alpha and beta) or androgen receptors, did not affect steroidogenesis, and did not impact estrogen or androgen responsive mRNA transcript levels in this study at concentrations of 10, 50, 100 or 500 μM. PFHxA only elicited statistically significant co-stimulatory effects on androgen receptor activation in the presence of dihydrotestosterone at high PFHxA levels of 100 μM and was negative in all other assays. 100 μM PFHxA equates to an exposure of over 31,000 μg/L,

2013). A study of the general population in China found that exposure to PFHxA was positively associated with two thyroid antibody markers often used as clinical markers for thyroid autoimmune diseases (Li 2017), however, this was inconsistent with the other PFAS included in the study (i.e. PFOS, PFHxS, PFOA, PFBS) and is inconsistent with the rat studies of thyroid effects (Loveless 2009, Iwai 2014). Furthermore, exposure to the general population in China is dominated by PFOS and PFOA, which accounted for approximately 70 - 90% of the total sum of blood PFAS in the Li et al. (2017) cohort. However, the study authors did not statistically account for multiple PFAS exposures in their analyses and thus, the specificity of the PFHxA results from Li et al. (2017) is unclear.

The currently available database for PFHxA is quite standard for environmental chemicals. Although some uncertainties within the data base remain, these uncertainties can be adequately accounted for by the use of the standard "database uncertainty factor" that is applied in a quantitative risk assessment (see Section D below for more detail).

In summary, PFHxA does not meet the criteria for classification as a substance of very high concern. PFHxA is not carcinogenic, mutagenic, toxic for reproduction, nor does it give rise to an equivalent level of concern; PFHxA does not have endocrine disrupting properties nor is there any evidence that exposure would result in serious effects to human health or the environment.

B. Environmental Occurrence and Human Exposure Is, and Will Likely Remain, Extremely Low for PFHxA

The available data consistently show extremely low frequency of detection, or low levels of detection for PFHxA in both environmental media and in the human population.

1. *Occurrence studies involving PFHxA have confirmed that PFHxA typically has a low frequency of detection or low level of detection. Some environmental and human monitoring programs no longer measure PFHxA for this reason.*

PFHxA has generally been excluded by environmental monitoring surveys and blood serum analyses due to the continual low frequency of detection (FOD) and low levels of detection compared to the associated method detection limit. This is the stated reason why PFHxA was not included in the United States Environmental Protection Agency's (USEPA) Unregulated Contaminant Monitoring Rule evaluation or the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey (NHANES). PFHxA is simply not found in the environment at levels that are of potential consequence to human health.

2. *Large-scale human biomonitoring studies in multiple countries within the past 10 years consistently demonstrate that PFHxA has an extremely low frequency of detection in human serum and, when detected, the range of concentrations is low relative to the detection limits.*

Biomonitoring surveys consistently demonstrate that PFHxA is infrequently detected in human serum, particularly compared with most other perfluoroalkyl acids. The following are examples of survey results for a wide range of countries and study populations, sorted by limit of detection (LOD) for PFHxA in serum:

Country / Study	Sample Size	LOD (ng/mL)	FOD (%)	Citation
U.S. / C8 Health Study	67,000	<0.5	**53%**	Frisbee (2009)
New Zealand / POP Study	747	<0.5	**0%**	New Zealand Ministry of Health (2013)
U.S. / American Red Cross	2,294	<0.02 – 0.1	**6%**	Olsen (2017)
South Korea	1,874	<0.11	**0%**	Lee (2017)
Canada / Health Measures Study	1,524	<0.1	**2%**	Health Canada (2013)
Japan / Exposure to Chemical Compounds	326	<0.1	**0%**	Japan Ministry of the Environment (2016)
China / General Population Study of Three Provinces	202	<0.01	**53%**	Li (2017)
Norway / A-Team Study	61	<0.045	**0%**	Poothong (2017)

Notes: FOD = frequency of detection of PFHxA; LOD = limit of detection of PFHxA; POP = persistent organic pollutant

Given the low frequency of detection for PFHxA in serum, the summary statistics (e.g., arithmetic mean, median) can be very sensitive to the method used to represent the PFHxA "nondetect level" (ND). ND concentrations may range from zero to the analytical detection limits, and a common approach is to substitute half the detection limit when calculating summary statistics, rather than zero. Even a study that represents an exposed community with higher levels of PFHxA in serum (Frisbee 2009), demonstrates that the way in which the ND is handled when calculating summary statistics can change the reported mean by almost 40%. The estimated arithmetic mean serum PFHxA levels from Frisbee et al. (2009) differs from 0.9 ng/mL using ND=LOD/2, to 1.4 ng/mL using ND=LOD, which is a 1.56 fold increase (or 36% change). Surveys representing the general U.S. population (e.g. Olsen et al. 2017) show a significantly lower frequency of detection for PFHxA nationwide, and

would therefore be even more sensitive to the method used to represent ND in summary statistic calculations. Careful review of the analytical quality control measures for PFHxA serum measurements are also warranted. For example, Frisbee et al. (2009) also reported the results of their quality assurance analysis, noting that PFHxA exhibited the least agreement among all PFAS for duplicate samples analyzed by the same lab and between two labs. In 1,180 samples evaluated, all duplicate quality assurance samples sent to a second lab were nondetect for PFHxA. It is not clear how to interpret this inconsistency, however, this highlights the importance of attention to analytical quality assurance.

3. *One study provides an estimate of exposure to PFHxA in infants in Spain from multiple routes of ingestion and finds that most infants have an estimated daily intake of less than 1 ng/kg-day – well below any risk level.*

A recent publication from Spain (Lorenzo 2016) investigated potential perfluoroalkyl substance (PFAS) exposure to infants by examining various PFAS, including PFHxA, in baby food containers, dry cereals, infant formula, and breast milk. PFHxA was not detected in the majority of samples. Reported frequency of detections are as follows:

- Baby food jars: 0%
- Dry cereals: 23%
- Infant formula: 25%
- Breast milk: 10% (from 10 women, at an average and median of 60 ng/L)[2]

Using the levels of PFHxA detected in each media and standard estimated daily consumption rates and body weights, the authors then calculated the estimated daily intake for infants up to two years. They found that potential exposure to infants up to 12 months of age from PFHxA in infant formula resulted in the highest estimated daily intake of 1 ng/kg-day. As discussed further below, these levels are well below any level of concern.

4. *The assumption that exposures to PFHxA are likely to increase due to the phase out of long-chain perfluoroalkyl acids (PFAAs) is unsubstantiated by any data and inconsistent with present-day industry manufacture, use, and improved best management practices.*

The FluoroCouncil members are committed to sound environmental stewardship of fluorotechnology. Short-chain PFAAs such as PFHxA and precursor fluorotelomers that degrade into PFHxA, such as 6:2 fluorotelomer alcohol, have been used within the fluorotechnology market since the 1970's. It has been stated that the industrial phase-out of

[2] The PFHxA frequency of detection and concentrations in breast milk samples from Lorenzo et al. (2016) shows that this smaller number of samples (N = 10) from Spain had a lower frequency of detection than seen in larger studies of Korean mothers, but the median concentration is consistent with other reports. Kang et al. (2016) report a frequency of detection of ~70% and median of 45 ng/L. Lee et al. (2018) report a 40% detection rate and an average concentration of 13 ng/L with a range of 10-129 ng/L. Conversely, Cariou et al. (2015), was unable to detect any PFHxA in samples from 61 lactating women from France.

long-chain PFAAs is resulting in rising levels of short-chain PFAAs (see discussion in Scheringer et al. 2014). In fact, the manufacturing of fluorochemicals and customer usage have both become more efficient, thus limiting environmental releases and potential future contamination levels. Furthermore, the FluoroCouncil has actively worked with industry partners, including the Fire Fighting Foam Coalition, to develop Best Management Practices that ensure that PFAS-based products are only used when necessary and only at levels that are necessary, that minimize the waste and emissions related to manufacture and product use, and that manufacturers and users dispose of all chemicals and PFAS-based products properly. Additionally, the dramatic change in fire-fighting training practices in the U.S. and Australian Departments of Defense, and elsewhere, have significantly decreased potential future PFAS contamination from Aqueous Film Forming Foam (AFFF) use by orders of magnitude.

In summary, the improvements within the various manufacturing processes, the significant changes in the fire-fighting foam industry (training and equipment calibration, as well as the switch to Fluorine Free Foams), and within the use and disposal of PFAS-based products is expected to result in reduced environmental levels of PFAS, including PFHxA, on a continuing basis over the next several years.

C. PFHxA Does Not Bioaccumulate and is Rapidly Eliminated from the Human Body

The nonpolymeric long-chain PFAAs such as PFOA and PFOS, are of significant concern to human health due to their long elimination half-lives. While the carbon-fluorine bonds within PFHxA make the chemical extremely stable, and physicochemical properties such as logKow and water solubility indicate that PFHxA will be mobile in water and soil, these properties do not suggest that PFHxA will be bioaccumulative. In fact, studies conducted thus far have indicated that PFHxA does not elicit the same high protein binding affinity as long-chain PFAAs such as PFOA and is rapidly eliminated from the human and mammalian body and is not bioaccumulative (Gannon 2011; Martin 2003a, 2003b; Russell 2013). The continued low-level frequency of detection and low levels in human serum, as discussed above, is further evidence that PFHxA does not bioaccumulate.

1. *PFHxA does not have as high a binding affinity for proteins as long-chain PFAAs, as demonstrated by numerous protein binding assays.*

Protein rich body compartments such as the liver, kidney and blood are the primary tissues for the retention of long-chain PFAAs such as PFOA and PFOS (Jones 2013). This is due to the high non-covalent binding affinity of long-chain PFAAs to serum proteins such as serum albumin (Bischel 2011). Furthermore, the extensive renal tubular reabsorption of long-chain PFAAs is mediated by high affinity binding to the organic anion transport proteins (OATs) located within the proximal tubular cell membranes (Yang 2010; Han

2011). However, although a wide range of association constants and affinity parameters have been reported for PFAAs and serum albumin and OATs, all studies have shown that the carbon-chain length and functional group directly influence the protein binding capacity; binding affinity is highest for PFAAs having at least eight carbon atoms. PFHxA with a carbon chain length of 6 has a reduced protein binding affinity (Han 2011; Fuji 2015). Using a fluorescence model for binding, Herbert et al. 2010 demonstrate that PFHxA does not appear to bind to the human serum albumin protein in the same manner as long-chain PFAAs. PFAA binding to liver proteins such as the liver fatty acid binding protein is also thought to be import for tissue distribution and liver effects (Zhang 2009; Han 2003), however, PFHxA has shown no binding affinity to the human liver fatty acid binding protein in several studies (Sheng 2014), further demonstrated a marked difference between long chain PFAA protein binding and PFHxA. Combined, these results suggest that PFHxA would not exhibit high distribution to protein-rich tissues and would not accumulate as a bound fraction to protein in blood serum.

2. *PFHxA is rapidly eliminated from all mammalian bodies.*

Renal elimination is the most significant route of elimination and a determining factor for PFAA-specific internal body concentrations/exposure and long elimination half-lives. Because PFAAs vary in their protein binding affinities, as discussed above, the elimination and bioaccumulation of PFAAs in mammalian systems is directly related to the fluorinated carbon chain length, functional group, and associated protein binding (Conder 2008; Han 2011). PFHxA is nearly 100% eliminated within the first day after dosing in rodents (Gannon 2011) and the elimination half-lives of PFHxA have been reported as between 0.5 to 1.7 hours in rats and 2.4 to 5.3 hours in monkeys (reviewed in Han 2011). The elimination kinetics for PFHxA have also been analyzed in humans (a cohort of professional ski was technicians) and the apparent half-life estimated at approximately 32 days (Russell 2013; note that this was not a formal pharmacokinetic study). The half-lives of PFHxA is mice, rats, monkeys and humans are proportional to body weight, with no differences observed between genders, suggesting similar elimination mechanisms (Russell 2013), and therefore, no additional concern related to higher human bioaccumulation compared to rodents, as is with long-chain PFAAs.

D. ANSES, the French Agency For Food Safety, Environment and Labor, Determined a Human-Health Threshold Level for PFHxA That Indicates There Is A High Margin Of Safety

The French agency for food safety, environment and labor, ANSES, issued an expert evaluation on the chronic risks of PFHxA for the French General Directorate of Health.

1. *ANSES converted the animal study findings to a human equivalent dose in order to develop a human health-based toxicity value comparison of exposure levels and levels that may be associated with a human health risk.*

ANSES derived a toxicity value for PFHxA based on kidney effects from the chronic rodent study (Klaunig 2015), which was deemed protective of all other potential health endpoints of concern. Given the extremely quick elimination of PFHxA from all species tested, the agency applied the standard allometric scaling based on body weights to convert the rodent administered dose to the human equivalent dose. This methodology has been shown to be appropriate for PFHxA specifically (Russell 2013). The agency also applied standard uncertainty factors to account for variability in humans and database uncertainty. In summary, the Agency concludes the following:

- PFHxA is rapidly excreted
- The hepatic effects (increase in absolute and relative liver weight associated with hepatocellular hypertrophy and statistically significant increase in aspartate aminotransferases and alanine aminotransferases) observed in two subchronic studies are not relevant to human health because the enzyme increases were not more than a factor of 2 or 3 (per USEPA (2002) guidance), and were not evident in the chronic study
- The kidney effects from Klaunig et al. (2015) were severe enough to be considered adverse and would be protective of other potential effects.

The final PFHxA oral chronic toxicity value is 0.32 mg/kg-day.

2. *The PFHxA toxicity value derived by ANSES is four orders of magnitude higher (less stringent) than the perfluorooctanoic acid (PFOA) toxicity value currently used by the USEPA.*

Compared to the most stringent toxicity value for PFOA derived by the USEPA (2016) (i.e., an oral reference dose of 0.00002 mg/kg-day), the comparable toxicity value for PFHxA is four orders of magnitude greater. Furthermore, when this toxicity value is applied to the standard USEPA drinking water health advisory calculation, the result is a drinking water health advisory of 2.2 mg/L (2.2 $x10^6$ parts per trillion (ppt)), which is almost 32,000 times higher than the USEPA health advisory for PFOA of 70 ppt[3]). This finding underscores the importance of evaluating PFHxA data rather than extrapolating findings from PFOA or other PFAAs.

3. *The margin of safety for potential daily intake of PFHxA from all routes of exposure in infants is more than 300,000.*

[3] USEPA (2016) did not use the standard drinking water equation when deriving the health advisory for PFOA. Their critical effect for PFOA was a developmental endpoint; they used a drinking water intake rate for lactating women rather than standard adult parameters.

As described above, Lorenzo et al. (2016) recently calculated the estimated daily intake for infants exposed to PFHxA from consumption of breast milk, formula, dry cereal, or baby foods. The highest estimated daily intake of 1 ng/kg/day is 320,000 times lower than the daily human threshold value derived by ANSES.

After a comprehensive review of the collective evidence, the potential for human health risks from PFHxA exposure at relevant levels is low. When the collective toxicological data are reviewed, the conclusion can be reached that PFHxA would "not [be] considered to cause serious damage to health" (NICNAS 2017, p.11).

E. There Are Multiple Full-Scale Treatment Technologies Available to Remove PFHxA From Water

The body of scientific evidence on treatment technologies[4] indicates there are currently multiple full-scale options to remove PFHxA from water, and several promising technologies are in development at the pilot- and bench-scale. Additionally, combinations of technologies into treatment trains could provide comprehensive removal of a wide array of per- and polyfluoroalkyl substances (PFAS). Finally, this discussion provides a comment regarding the ability of available technologies to meet current and potential future PFHxA water treatment goals.

1. Demonstrated full-scale water treatment technologies are available for the removal of PFHxA.

Proven full-scale water treatment technologies are currently available for the removal of PFHxA from water: ion exchange resins and membrane filtration. These *ex situ* treatment technologies have been applied to drinking water supplies, groundwater remediation, and industrial wastewater treatment.

Ion Exchange Resins

Ion exchange resins are an established treatment technology for many common contaminants in both municipal drinking water and groundwater, including sulfate, chromate, nitrate, chloride, and perchlorate. Full-scale ion exchange resin systems engineered to treat PFAS-impacted water are currently in operation in Australia and the United States (ITRC 2018). The resins utilize both adsorption and ion exchange, which effectively remove long and short-chained PFAS compounds by attraction of both the polar

[4] Whenever possible, peer-reviewed scientific literature were incorporated into this summary rather than company-sponsored documentation, brochures, and presentations. Please note that this summary does not provide an exhaustive review of all PFAS treatment technologies as there are many investigations at the bench-scale not represented by available literature. Additionally, please note that several potentially viable PFAS treatment technologies found in available literature do not present results for short-chain PFAS, as research to date has been largely focused on long-chain PFAS.

and non-polar properties of PFAS compounds (ECT2 2018a). Ion exchange resins designed to selectively remove PFAS are not subject to the same degree of fouling as carbon-based sorbents (ITRC 2018).

Ion exchange resins are designed to be regenerable or disposed of after breakthrough of target compounds (single use). Resin regeneration is typically performed within the ion exchange treatment vessel, and results in a highly concentrated regenerant waste that requires further treatment and disposal. Currently available literature regarding PFAS removal has focused on regenerable ion exchange resins, however, single use resins are gaining traction in the remedial market as they have lower initial capital costs and the used resin can be disposed of by incineration (ITRC 2018).

The regenerable ion exchange resin Sorbix LC1 was designed to treat an array of PFAS compounds, specifically short-chain PFAS, and is currently in use in multiple full-scale ion exchange groundwater treatment plants in Australia and the United States (ECT2 2018a,b). United States-based company Emerging Compounds Treatment Technologies (ECT2) developed designed, fabricated, and oversaw the installation of ion exchange resin groundwater treatment plants at two separate Australian Government Department of Defence (Defence) sites formerly used for fire-fighting training (ECT2 2018a,b). The two Australian plants have a similar design to one another: each are capable of operating at 192 liters per minute (50 gallons per minute), and each contain two vessels filled with Sorbix A3F resin followed by polish vessels containing Sorbix LC1 (ECT2 2018a,b). Influent PFAS concentrations range from 1-120 µg/L and both plants have demonstrated removal of three regulated target PFAS compounds, including short-chain PFAS perfluorohexane sulfonic acid (PFHxS), below reportable limits of 10 parts per trillion (ppt) (ECT2 2018 a,b; Defence 2018). ECT2 is currently building a second, larger PFAS removal and resin regeneration system capable of treating 750 liters per minute (200 gallons per minute) at an identified source area on one of the Defence sites (ECT2 2018a).

Additional commercially available ion exchange resins have demonstrated short-chain PFAS removal at the bench scale. Purolite Purofine® PFA694E is a single use resin being marketed for point of entry and point of use systems for removal of both long and short-chain PFAS (Purolite 2018). Bench-scale results from treatment of municipal well water with PFA694E showed 100% removal of PFHxA, reducing concentrations below 1 part per trillion, as compared with less than 10% by a bituminous granular activated carbon sorbent (Purolite 2018). Separately, bench-scale experiments tested the removal efficacy of PFHxA from synthetic and fluorochemical plant wastewater using five different commercially available Purolite resins; Purolite resin BA103 was found to have the highest PFHxA-adsorption capacity of the five tested resins, with removal rates ranging from 101-320 mg/g/hour (Karnwadee 2015).

<u>Membrane Filtration</u>

Two commercially available membrane filtration technologies, reverse osmosis and nanofiltration, have demonstrated effective removal of PFAS regardless of chain length (Dickenson 2016). In each of these technologies, impacted water is forced via high pressure through a filter membrane with a high contact area, producing a high concentration rejectate while allowing the treated filtrate to pass through. Dickenson and Higgins (2016) evaluated fifteen full-scale water treatment systems and concluded reverse osmosis was the most effective PFAS treatment method evaluated in the study: reverse osmosis systems at two California potable reuse treatment plants demonstrated removal of all PFAS analyzed, including PFHxA, to below reportable quantities (less than 0.50 ng/L for PFHxA) (Dickenson 2016). Additionally, reverse osmosis techniques have been designed for household under-sink and residential well water PFAS treatment with removal rates greater than 90% for PFHxA (AWWA 2016).

It is to be noted that though full-scale implementation of nanofiltration has not yet been demonstrated for PFAS removal, commercially available nanofiltration membrane systems could evolve to be just as effective as reverse osmosis (ITRC 2018). Nanofiltration was shown to reject PFHxA at greater than 95% removal rates in bench-scale testing of the Dow FILMTEC™ NF270, NF200, and NF90 membranes (Steinle-Darling 2008) and field pilot-scale testing of two NF270 membranes in series at a Swedish drinking water treatment plant (Lindegren 2015).

2. *Water treatment technologies capable of complete destruction of PFHxA are in development and may eventually evolve to commercial full-scale applications.*

Current commercially available treatment technologies (e.g. ion exchange resin, membrane filtration) do not destroy PFAS but rather concentrate PFAS in the spent media, rejectate water, or regenerant solution. Ongoing research is being performed to develop advanced chemical oxidation techniques that are capable of complete PFAS destruction. AECOM (2018) developed the DE-FLUORO™ electrochemical oxidation technology, a proprietary electrode capable of PFHxA destruction. The manufacturer is currently identifying trial sites for the treatment of groundwater and commercialization of this technology is underway (AECOM 2018). Heat-activated persulfate chemical oxidation has shown promise at the bench-scale for PFAS destruction in waters impacted by fire-fighting foams: at the start of the experiments PFHxA concentrations increased due to precursor degradation, but ultimately PFHxA further degraded and eventually mineralized (Bruton 2017).

3. *Combinations of remedial technologies into treatment trains show potential to be an efficient method for removal of a wide array of PFAS from water.*

The development of a treatment technology that can effectively treat the full suite of PFAS, including precursors, has been challenging given the varying physical and chemical characteristics within this class of compounds. Available scientific and product literature

highlight the possibility of combining remedial technologies in treatment trains for the efficient removal of a wide array of PFAS compounds, including short-chain PFAS such as PFHxA, from impacted waters.

Recent research has demonstrated the potential for electrochemical oxidation technologies to effectively treat highly-concentrated PFAS waste streams generated during remediation, such as the rejectate from membrane filtration or ion-exchange regenerant waste. Bench-scale testing for the electrochemical oxidation technology DE-FLUORO™ demonstrated a 99.66% removal rate of PFHxA from ozone oxidation treatment effluent (AECOM 2018). Separately, Soriano et al. (2017) performed a series of bench-scale experiments to remove and degrade PFHxA from industrial process waters using a combination of nanofiltration and electrochemical oxidation. Initial PFHxA concentrations ranged from 60 – 200 mg/L: under a range of operating pressures, the Dow FILMTEC™ NF270 membrane rejected PFHxA at a rate of 96.6 – 99.4%. The nanofiltration step concentrated PFHxA in the rejectate solution to 870 mg/L, which was then subjected to electrochemical degradation to reduce PFHxA by 98% (Soriano 2017).

Some companies are specifically marketing their remedial technologies for use in treatment trains for comprehensive PFAS removal. At an Australian demonstration treatment plant for a former fire-fighting training facility, Evocra verified the efficacy of its patented ozofractionation column technology combined with sorbent polishing steps (Evocra 2017). The ozofractionation columns were effective at removing PFOA and PFOS and precursors from influent wastewater, and subsequent polishing steps with engineered sorbent removed PFHxA and other residual PFAS. The overall PFHxA removal rate in the combined ozofractionation and sorbent treatment train was 99.8%, reducing influent wastewater PFHxA from 5.16 µg/L to 0.0114 µg/L (Evocra 2017).

4. *Given the lower toxicity of PFHxA as compared to long-chain PFAS, future PFHxA treatment goals based on toxicity data may be magnitudes higher (i.e., parts per billion (ppb)) than those currently in place for long-chain PFAS (i.e., ppt). PFHxA standards and guidance values in the ppb range would be more practicable and achievable for emerging treatment technologies discussed in the sections above.*

Several countries and states within the United States have issued guidance values for PFHxA in water (ITRC 2017); however, these values largely mirror existing values for bioaccumulative long-chain PFAS compounds and do not necessarily reflect human-health or ecological risks specific to PFHxA exposure. A review of available toxicity data provides insight as to potential future risk-based treatment goals for PFHxA. As summarized above, ANSES determined a human-health threshold level for PFHxA that is four orders of magnitude higher (less stringent) than the PFOA toxicity value currently used by the USEPA. When this toxicity value is applied to the standard USEPA drinking water health advisory calculation, the result is a drinking water health advisory of 2.2 mg/L (2.2×10^6 ppt), which is almost 32,000 times higher than the USEPA health advisory for PFOA of 70

ppt). Should PFHxA toxicity data guide the development of future promulgated PFHxA drinking water treatment standards and groundwater remediation goals, it is expected that these values will be in the ppb range, rather than ppt. PFHxA standards and guidance values in the ppb range are more practicable and achievable for the emerging treatment technologies discussed in the sections above.

F. CONCLUSIONS

Based on the information summarized above, the following can be concluded based on the scientific evidence regarding potential exposure and toxicity from PFHxA in the environment:

1. The levels of PFHxA in the environment and in human serum are extremely low.
2. PFHxA does not exhibit a potential to bioaccumulate in fish, wildlife or humans, nor to biomagnify in the food chain.
3. PFHxA is not carcinogenic, mutagenic or toxic for reproduction, nor does it exhibit endocrine disrupting properties or any evidence of serious effects to human health or the environment.
4. Using the recently calculated toxicity value from the French agency, ANSES, and published estimated daily intake rates, the margin of safety for PFHxA from all routes of exposure to the most sensitive population is over 300,000.
5. Ion exchange resins and membrane filtration are two demonstrated full-scale water treatment technologies currently available for the removal of PFHxA.
6. Water treatment technologies capable of complete destruction of PFHxA are in development and may eventually evolve to commercial full-scale applications.
7. Combinations of remedial technologies into treatment trains show potential to be an efficient method for removal of both short and long-chain PFAS from water.

The data do not support the listing of PFHxA as a substance of very high concern.

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