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Perfluoroalkyl Compounds (PFCs) in the Village of Hoosick Falls, Rensselaer County, New York: Health Risks and Successive Approximation Toward Enforceable National Regulations

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Abstract

Perfluoroalkyl compounds (PFCs) such as perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) are surfacing in a lengthening list of drinking water systems in the U. S. These most recently include the Village of Hoosick Falls in Rensselaer County, New York and several other Northeast locations. The ability to detect these 'emerging contaminants' in the parts-per-trillion concentration range, combined with emerging evidence of their public health significance in that range, together reveal the need for routine monitoring, aggressive cleanup, and promulgation of enforceable regulations to control human exposure, prevent disease, and help to clarify accountability, thereby preventing similar incidents elsewhere. Accordingly, the New York State Department of Health is offering blood serum analysis at no charge to Hoosick residents and former residents, and is evaluating possible cancer clustering.

The predominant PFC in the Village of Hoosick Falls is PFOA, which exhibits a 'perfect storm' of troubling properties: essentially infinite lifetime in the environment, resistance to human metabolism, bioconcentration in the food chain, transmissibility to infants via breastfeeding, years-long excretion half-time in the human body, and causation of human cancer and non-cancer effects. These properties, together with widespread use in manufacturing Teflon and other widely used products, have resulted in PFCs becoming ubiquitous contaminants in the global environment and in human blood serum. PFCs have been phased out of U. S. commerce, but persist in the environment, regulated mainly by unenforceable health 'advisories'. Recent U. S. EPA promulgation of a new health advisory, 70 ng/L (parts per trillion) for lifetime exposure to the sum of PFOA and PFOS in drinking water, is supported by description of, at best, an uncertain and lengthy pathway toward enforceable regulation. The present investigation concludes that EPA has failed to show that this latest advisory, even if enforced, is sufficiently stringent to protect public and environmental health.

Introduction

PFCs include PFOA and PFOS, which have been subjects of recent revelations about public health consequences arising from industrial releases in the manufacture of widely used commercial products of modern society. Common examples are Teflon used in cookware and fire retardants used in consumer fire extinguishers. The revelations, newsworthy for their human interest and exposé values, are of special scientific and regulatory significance because they suggest the need to regulate environmental residues of some substances down to the parts-per-trillion[1] range, which usually has been dismissed as insignificant for public health.

Routine monitoring of PFCs in environmental media such as air and water, and in biological media such as blood serum and milk, in the ppt concentration range only recently has become feasible. To illustrate, EPA's standard Method 537 for measurement of PFCs in water was published in 2009, whereas PFOA was introduced into commerce decades earlier, in the 1940s. Analysis for PFCs in drinking water can be performed by only a small number of laboratories in the U. S., certified by the U. S. EPA Environmental Laboratory Accreditation Program (ELAP), and still remains time-consuming and expensive. Monitoring in serum and milk has become possible, but still is not routine (ATSDR 2015)[2].

In the U. S. PFCs are regulated mainly via unenforceable, provisional health 'advisories'. PFCs with such advisories include PFOA and PFOS, issued by the U. S. EPA and the states of New Jersey and Vermont; and perfluorononanoic acid (PFNA), by New Jersey. Such advisories, however, apply to only some PFCs. This weak regulatory status raises two issues: whether more PFCs should be regulated more stringently and, if so, determination of safe PFC levels in environmental media that might suggest appropriate regulatory enforcement targets.

Recent findings enhance the relevance to New York: PFOA and perfluorobutanoic acid (PFBA) now have been detected in Hudson River water[3], which is a drinking water source.

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[1] **Units used:** parts per trillion (ppt) = nanograms per liter (ng/L) = 10^{-12};
parts pert billion (ppb) = micrograms per liter (ug/L) = 10^{-9};
parts per million (ppm) = milligrams per liter (mg/L) = 10^{-6};
Conversion: ug/mL = mg/L = ppm.

[2] **ATSDR.** *Draft Toxicological Profile for Perfluoroalkyls.* Atlanta, Georgia; U. S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 574 pages including appendices, http://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf, supersedes May 2009 draft profile and *"any previously released draft or final profile,"* August 2015;

[3] **Pochodylo, Amy; and Demian E. Helbling.** *Target Screening for Micropollutants in the Hudson River Estuary During the 2015 Recreational Season.* Ithaca, Cornell University, College of Agriculture and Life Sciences, New York State Water Resources Institute, http://www.riverkeeper.org/wp-content/uploads/2016/07/Appendix-A-2015-progress-report.pdf, 10 pages including Appendix, 2016;

PFOA was detected in 15 of 24 samples, and PFBA in 11 of 24 samples, together taken at eight Hudson River locations, from the confluence with the Mohawk River to the Tappan Zee Bridge.

Accordingly, the present investigation assesses public health risks potentially posed by PFCs, and evaluates their possible management via regulation and implementation technologies. Assessment of PFC risks includes documenting environmental residues of PFCs and elucidating physical, chemical, and biological properties that give rise to their environmental and clinical dynamics. These 'pharmacokinetic' and 'pharmacodynamic' properties result in potential risks being posed to public and environmental health. A related issue is historical: how did environmental regulation fail to prevent PFOA and PFOS from attaining ubiquity as residues detectable in human blood serum globally?

Some substances placed in commerce before regulation under modern national and international environmental statutes have been disseminated globally, and some of these exhibit essentially infinite persistence in the environment. Most of the latter are heavy metals such as lead (Pb), until recent decades widely used in gasoline, and (the metalloid) arsenic (As), until recent decades widely used in (arsenical) pesticides. Several of the persistent substances are organic, including DDT, PAHs, PCBs, PFCs, and chlorinated dibenzo-p-dioxins, many of which also tend to bioconcentrate, meaning that they may attain concentrations in organisms that are higher, possibly orders of magnitude higher, than the concentrations in environmental media from which they originated.

Modern regulation of chemicals in U. S. commerce was codified under the Toxic Substances Control Act (TSCA, Public Law 94-469, 15 USC 53) enacted in 1976 and updated in 2016. TSCA required testing to demonstrate the safety of substances for their commercial uses. Under TSCA, EPA inventoried nearly 100,000 chemicals in U. S. commerce, but many were 'grandfathered' because of longstanding usage, notwithstanding potential risks that substances such as PFOA and PFOS might pose to public and environmental health. Most grandfathered substances were exempt from safety testing requirements.

Some substances that were safety tested and found to be too toxic for use were replaced by structural analogs that had not been tested. Structural analogs often exhibit similar properties (structure-activity relationships; SARs), making them useful commercially, and likewise often exert similar toxic effects, making them dangerous to introduce into commerce without prior safety testing. Modernization of TSCA may improve this situation, but the U. S. and other societies must grapple with the legacy of multiple substances such as PFCs (including PFOA, PFOS, and PFNA) having been introduced into commerce in recent decades.

Methods

This assessment is based upon critical examination of available environmental and biomonitoring data as well as scientific, technical, and regulatory literature. It is meant to be general, not encyclopedic. Accordingly, it highlights concepts via examples, most notably relating to PFOA and PFOS rather than to an exhaustive list of all PFCs. Methods applied are generally those of scientific peer review and synthesis of published findings to draw new conclusions. The main example from which more broadly applicable conclusions are drawn is the Village of Hoosick Falls.

Findings

PFC Levels in Drinking Water

Perfluorinated compounds, most notably including PFOA and PFOS, have been detected in water in multiple locations, including widely publicized events in West Virginia and Ohio. Post, *et al.* (2013)[4] report PFC levels detected in public water supplies (PWSs) at multiple locations in New Jersey. Sampling in New Jersey occurred over multiple studies and years; results, presented in detail in the report, are too complex to present in similar detail here. The authors concluded that: *"PFCs were frequently found at greater than or equal to 5 ng/L in raw water from NJ PWSs. At least 1 PFC was detected at 21 (70%) of 30 intakes (18 groundwater and 12 surface water) from 29 NJ PWSs. Multiple PFCs (up to 8 at one site) were found in 13 of these 21 samples. Although PFOA was the most commonly detected PFC (57% of samples) and was found at the highest maximum concentration (100 ng/L), relatively high levels of other PFCs were found in some samples with little or no PFOA."*

Additional locations of PFC contamination have emerged recently in New York and New England States. Concentrations of PFOA and other PFCs in water sampled from drinking water supply wells in the Village of Hoosick Falls in Rensselaer County, New York were reported by Attorney David G. Servadi (law firm of Keller and Heckman, LLC; Washington, DC) on behalf of client Saint-Gobain Performance Plastics Corporation (SGPP; Saint-Gobain, 2014).[5] SGPP is a subsidiary of Saint-Gobain, S. A., a historic French multinational corporation founded in 1665

[4] **Post, Gloria B.; *et al.*** *Occurrence of perfluorinated compounds in raw water from New Jersey public drinking water systems.* Environmental Science & Technology, 47, 13,266−75, dx.doi.org/10.1021/es402884x, 2013;

[5] **Saint-Gobain.** *Submission of information concerning allegations of environmental contamination.* Letter from Attorney David G. Servadi, Keller and Heckman, LLC (Washington, DC) to TSCA Confidential Business Information Center (Washington, DC) on behalf of Saint-Gobain Performance Plastics Corporation (SGPP; Village of Hoosick Falls, Rensselaer County, New York), 2 pages plus attachments (8 pages), 30 December 2014;

and headquartered in Paris. Prior owners of the SGPP site include Honeywell International, which sold the site to Saint-Gobain, S. A. in 1996, as well as former Oak Industries and Dodge Industries. In view of the PFOA detections and holistic consideration of available evidence, the New York State Department of Environmental Conservation (NYS DEC) instructed SGPP and Honeywell to enter into a consent agreement to fund site investigation and remediation[6].

PFOA first was detected in the Village of Hoosick Falls in August 2014[7], though the Village's 2014 Water Quality Report[8] included neither PFOA nor other PFCs. PFOA is the predominant PFC that has been detected, though two water samples also contained perfluoroheptanoic acid (PFHPA, Supply Well 7, Table 2). The issue was addressed the Village Newsletter in 2015[9]. Results of public water supply sampling on 2014.10.02 and 2014.11.04 are presented for all three Village supply wells (Well 3, Well 6, and Well 7), and for post-treatment finished-water with respect to PFOA (Table 1) and all sampled PFCs (Table 2).

Water samples were analyzed via EPA Method 537 (US EPA 2009)[10], consisting of solid-phase extraction with sample concentration, followed by liquid chromatography and tandem mass spectroscopy for sensitivity in the ppt range. The geographic relationship of SGPP to the Village's water treatment plant on Waterworks Road is depicted in Figure 1. Results of ongoing private well sampling current to 18 May 2016 are depicted graphically in Figure 2, showing 1006 sample results as follows: less than 2 ppt, 500 samples (49.7 percent); less than 70 ppt, 384 samples (38.2 percent); and more than 70 ppt, 122 samples (12.1 percent).

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[6]**French, Marie J.** *New York State: Saint-Gobain, Honeywell International responsible for Hoosick Falls water contamination.* New York; The Albany Business Review, http://www.bizjournals.com/albany/news/2016/02/11/new-york-statesays-saint-gobain-honeywell.html, 11 February 2016: *"The agency did not rule out holding other companies liable as the investigation moves forward."*

[7]**Village of Hoosick Falls.** Village web site, http://www.villageofhoosickfalls.com/Water/;

[8]**Village of Hoosick Falls.** *Annual Drinking Water Quality Report for 2014.* New York, Village of Hoosick Falls, 5 pages, 2014(?);

[9]**Village of Hoosick Falls.** *Village Water Quality Update,* page 3 of 14 pages*;* 14 September 2015;

[10]**US EPA: Shoemaker, J. A.; P. E. Grimmett, and B.K. Boutin.** *Method 537. Determination of selected perfluorinated alkyl acids in drinking water by solid phase extraction and liquid chromatography/tandem mass spectrometry (LC/MS/MS).* Cincinnati, Ohio; U. S. Environmental Protection Agency, National Exposure Research Laboratory Office Of Research And Development; Document No. EPA/600/R-08/092; Version 1.1, 50 pages, September 2009;

Table 1. Perfluorooctanoic Acid (PFOA) in the Village of Hoosick Falls, New York*

		Well 3	**Well 6**	**Well 7**
		(nanograms per liter, ng/L = parts per trillion, ppt)		
Sample 1	pre-treated	230	280	540
Sample 2	pre-treated	170	280	450
Sample 1	treated	…	…	440
Sample 2	treated	…	…	to be determined

***Saint-Gobain.** *Submission of information concerning allegations of environmental contamination.* Letter, Attorney David G. Servadi, Keller and Heckman, LLC (Washington, DC) to TSCA Confidential Business Information Center (Washington, DC) on behalf of Saint-Gobain Performance Plastics Corp. (Village of Hoosick Falls, New York), 2 pages plus attachments (8 pages), 30 December 2014.

Table 2. Perfluorinated Compounds in Water: Village of Hoosick Falls, New York*

CAS No.	perfluorinated alkyl compound	Minimum Reporting Level (MRL)**	sample no.	date in 2014	Supply Well 3	Supply Well 6	Supply Well 7
…	…	(ng/L = pptr)	…	…	(ng/L = pptr)		
			pre-treatment				
375-73-5	perfluorobutanesulfonic acid (PFBS)	90	1	2-Oct	<90	<90	<90
			2	4-Nov	<90	<90	<90
375-85-9	perfluoroheptanoic acid (PFHPA)	10	1	2-Oct	<10	<10	10
			2	4-Nov	<10	<10	10
355-46-4	perfluorohexanesulionic acid (PFHxS)	30	1	2-Oct	<30	<30	<30
			2	4-Nov	<30	<30	<30
375-95-1	perfluorononanoic acid (PFNA)	20	1	2-Oct	<20	<20	<20
			2	4-Nov	<20	<20	<20
1763-23-1	perfluorooctane sulfonate (PFOS)	40	1	2-Oct	<40	<40	<40
			2	4-Nov	<40	<40	<40
335-67-1	perfluorooctanoic acid (PFOA)	20	1	2-Oct	230	280	540
			2	4-Nov	170	280	450
			post-treatment (water plant finished water)				
375-73-5	perfluorobutanesulfonic acid (PFBS)	90	…	4-Nov	…	…	<90
375-85-9	perfluoroheptanoic acid (PFHPA)	10	…	4-Nov	…	…	10
355-46-4	perfluorohexanesulionic acid (PFHxS)	30	…	4-Nov	…	…	<30
375-95-1	perfluorononanoic acid (PFNA)	20	…	4-Nov	…	…	<20
1763-23-1	perfluorooctane sulfonate (PFOS)	40	…	4-Nov	…	…	<40
335-67-1	perfluorooctanoic acid (PFOA)	20	…	4-Nov	…	…	440

***Saint-Gobain.** *Submission of information concerning allegations of environmental contamination.* Letter from Attorney David G. Servadi, law firm of Keller and Heckman, LLC (Washington, DC) to TSCA Confidential Business Information Center (Washington, DC) on behalf of Saint-Gobain Performance Plastics Corporation (SGPPC; Village of Hoosick Falls, New York), 2 pages plus attachments (8 pages), 30 December 2014

****US EPA: Shoemaker, J. A.; P. E. Grimmett, and B.K. Boutin.** *Method 537. Determination of selected perfluorinated alkyl acids in drinking water by solid phase extraction and liquid chromatography/tandem mass spectrometry (LC/MS/MS).* Cincinnati, Ohio; U. S. Environmental Protection Agency, National Exposure Research Laboratory Office Of Research And Development; Document No. EPA/600/R-08/092; Version 1.1, 50 pages, September 2009;

Figure 1. Geographic Relationship of Saint-Gobain Performance Plastics and the Water Treatment Plant on Water Works Road, Village of Hoosick Falls, New York

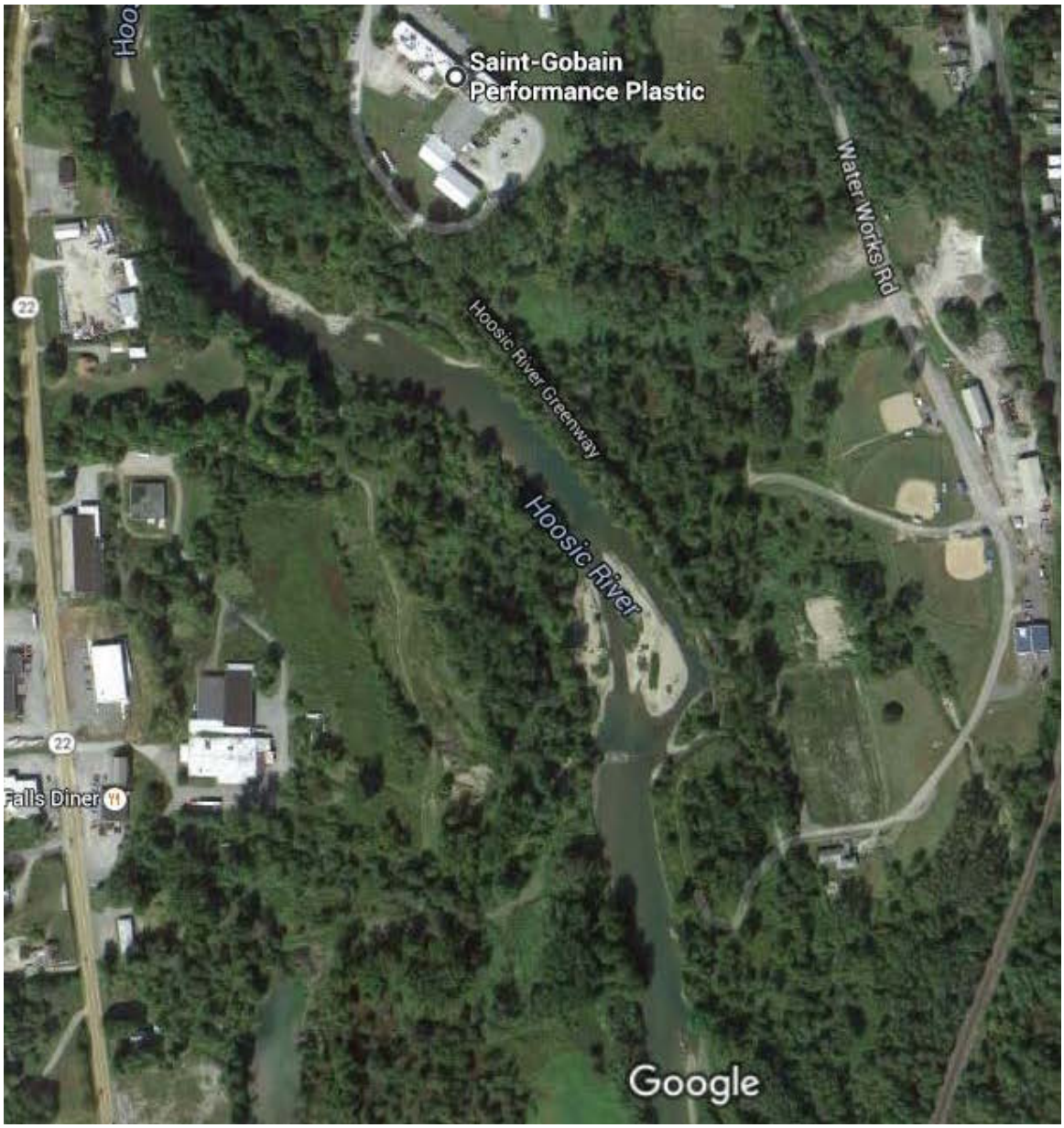
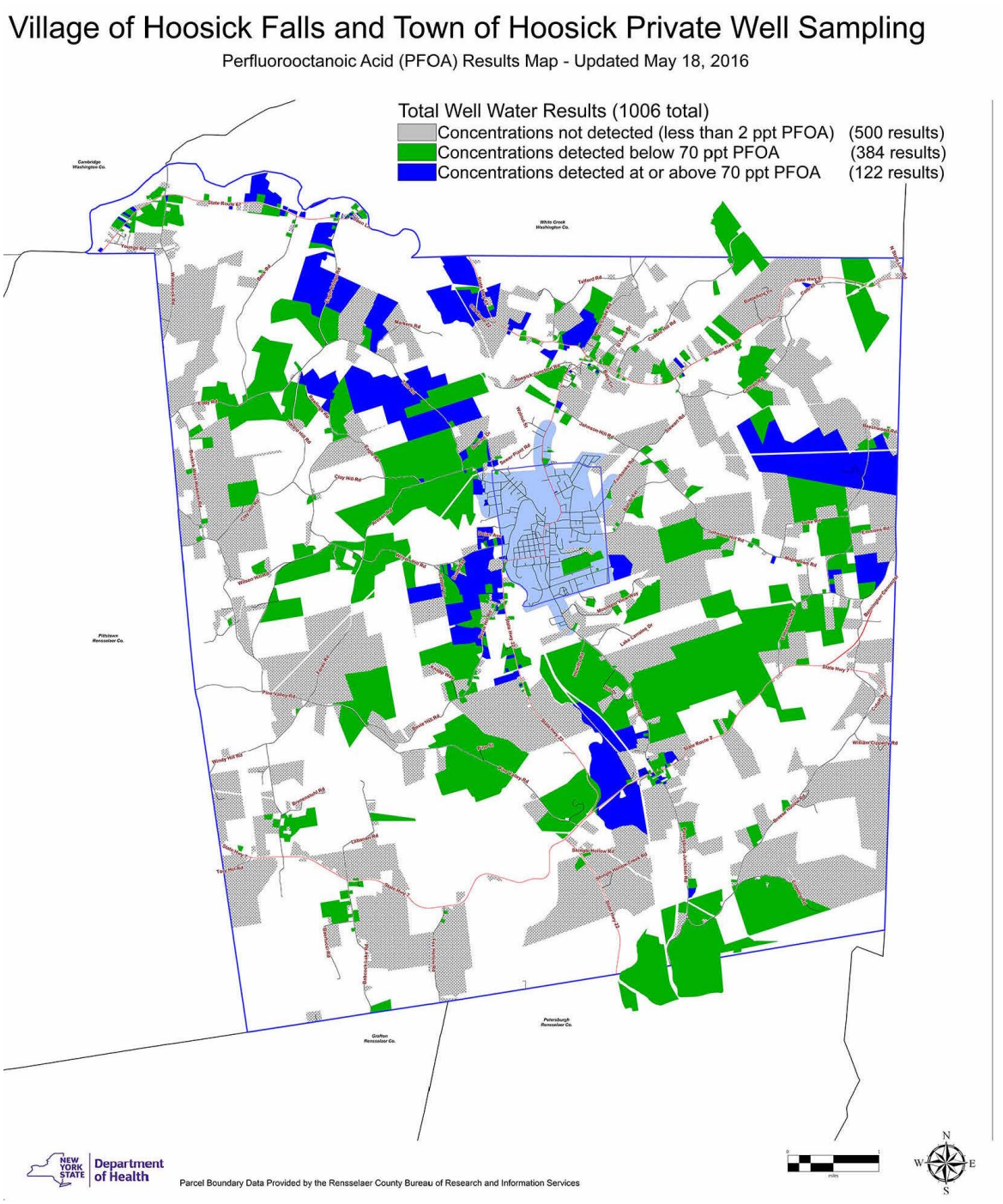


Figure 2. PFOA Results for Private Wells in the Village and the Town of Hoosick Falls*



***NYS DOH.** *Village of Hoosick Falls and Town of Hoosick Private Well Sampling, Perfluorooctanoic Acid (PFOA) Results Map.* Albany, New York State Department of Health, https://www.health.ny.gov/environmental/investigations/hoosick/images/results_dist.jpg, updated 18 May 2016.

Physical and Chemical Properties

PFOA and PFOS are structurally similar (Figure 3). PFOA, used in manufacture of other PFCs, has a carboxylic (organic) acid group (COOH or O=C-OH) at the terminal carbon, with all other hydrogen atoms substituted by fluorine (F), producing the formula F_3C-$(CF_2)_6$-COOH. PFC manufacture may involve the ammonium salt of PFOA (O=C-O^- NH_4^+ instead of O=C-OH), ammonium perfluorooctanoate (APFO)[11], rather than PFOA itself. PFOA has Chemical Abstract Service Registration Number (CASRN) 335-67-1. Selected physical and chemical properties of PFOA are set forth in Table 3.

A comprehensive but general explication of physical and chemical properties of PFCs including PFOA serves as a preamble justifying subsequent recommendations for comprehensive international action in the 'Madrid Statement' (Blum, *et al.,* 2015).[12] The Madrid Statement highlights several environmental and toxicologically significant properties of PFCs, including the following:

--man-made, ubiquitous, globally distributed, and highly persistent;

--residues, which are found everywhere, eventually enter groundwater, surface water, and drinking water; and

--with high bioaccumulation potential, PFCs are listed by the UN Environment Programme Stockholm Convention as persistent organic pollutants.

[11] **US EPA.** *Health Effects Support Document for Perfluorooctanoic Acid (PFOA).* Washington, DC; U. S. Environmental Protection Agency, Office of Water, EPA 822-R-16-003, 322 pages, May 2016;

[12] **Blum, A.; *et al.*** *The Madrid Statement on Poly- and Perfluoroalkyl Substances (PFCs).* Environmental Health Perspectives, 123(5):A107-11, **http://dx.doi.org/10.1289/ehp.1509934**, May 2015;

Figure 3. Chemical Structure of Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS)*

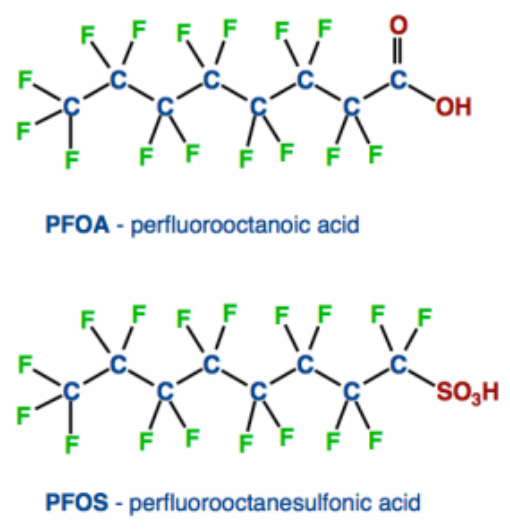


*__Image source:__

http://charlestonwaterkeeper.org/watershed-facts/toxic-pollutants-1-in-general-and-sources/pfoa-pfos-285x300/

Table 3. Physical and Chemical Properties of Perfluorooctanoic Acid (PFOA)*

Property	Perfluorooctanoic Acid
Chemical Abstracts Registry (CAS) No.	335-67-1
Synonyms	PFOA; Hexanoyl fluoride, 3,3,4,4,5,5,6,6,6-nonafluoro-2-oxo-; Pentadecafluoro-1-octanoic acid; Pentadecafluoro-n-octanoic acid; Octanoic acid, pentadecafluoro-; Perfluorocaprylic acid; Pentadecafluoroocanoic acid; Perfluoroheptanecarboxylic acid;
Chemical Formula	$C_8HF_{15}O_2$
Molecular Weight	414.09
Color/Physical State	White powder
Boiling Point	189°C
Melting Point	45-50 °C
Density (at 20°C)	1.7921 g/cm^3
Vapor Pressure:	4.2 (25°C) 2.3 (20°C) 128 (59.3°C)
pKa	2.5 2.8 1.5-2.8
pH value	2.6, 1 g/L (20°C)
K_{oc}	27,000 estimated
Solubility in water (g·L^{-1})	9.5 (25°C) 4.1 (22°C)
Solubility in organic solvents	-
Conversion Factors for vapor phase	1 ppm = 17.21 mg/m^3

Sources: HSDB (2006); SIAR (2006), EFSA (2008); RTECS (2008)

*Derived from: **US EPA.** *Health Effects Document for Perfluorooctanoic Acid (PFOA).* Washington, DC; U. S. Environmental Protection Agency, EPA 822R14001, 268 pages, February 2014.

Pharmacokinetics

'Pharmacokinetics' and 'pharmacodynamics' (next section) are, respectively (and very generally), the effects of the body on substances, and the effects of substances on the body. Pharmacokinetics includes intake (absorption), distribution, metabolism, and excretion (subsections below). Principal routes of exposure to substances generally include inhalation, ingestion ('oral exposure'), and dermal contact. Routes are subdivided into pathways, for example, food vs. drinking water for oral exposure. Thus, body burdens depend upon the intensity and duration of exposure, the efficiency of absorption via all routes and pathways, the targets of substance distribution and possible storage, the efficiency and nature of metabolic breakdown and substance transformation, and the efficiency and time course of excretion.

Most generally, therefore, body burdens of substances depend upon the net result of processes of increase and processes of decrease, as well as the nature of storage and possible accumulation. Storage may include organs that metabolize and/or sequester substances out of harm's way. Substances may be stored in fat, for example, where they may be metabolically inactive; this may change in the event of fat metabolism, for example as a result of metabolic challenges such as starvation or migration in which fat stores may be metabolized and fat-sequestered substances mobilized. These concepts are addressed in the subsections below.

Most generally, therefore, body burdens of substances depend upon the net result of processes of increase and processes of decrease, as well as the nature of storage and possible accumulation. Storage may include organs that metabolize and/or sequester substances out of harm's way. Substances may be stored in fat, for example, where they may be metabolically inactive; this may change in the event of fat metabolism, for example as a result of metabolic challenges such as starvation or migration in which fat stores may be metabolized and fat-sequestered substances mobilized. These general concepts are addressed below.

Absorption. *"Perfluoroalkyls… are readily absorbed following inhalation or oral exposure"* (ATSDR, 2015).[15]

Distribution. PFOA is highly cumulative once assimilated into the body. PFOA and PFOS tend to concentrate in the liver of animals[16]. *"Absorbed perfluoroalkyls distribute from*

[15]**ATSDR.** *Draft Toxicological Profile for Perfluoroalkyls.* Atlanta, Georgia; U. S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 574 pages including appendices, http://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf, supersedes May 2009 draft profile and *"any previously released draft or final profile,"* August 2015;

plasma to soft tissues, with the highest extravascular concentrations achieved in liver" (ATSDR, 2015)[17]. In pregnant women PFCs are distributed to the fetus via the placenta and, after birth, to the breastfeeding infant via milk.[18]

Metabolism. *"Perfluoroalkyls… are not metabolized in the body"* ATSDR (2015)[19].

Excretion. *"Elimination half-times in humans of 3.8 years, 5.4 years, 8.5 years, 665 hours, and 72 hours have been estimated for PFOA, PFOS, PFHxS, PFBuS, and PFBA, respectively"* (ATSDR, 2015;[20] acronyms defined in Table 2 above).

Biomarkers, Serum Levels, and Body Burdens

Biomarkers are indicators of signal events in biologic systems or samples. They include markers of exposure, markers of effect, and markers of susceptibility.[21] In the case of PFCs, the compounds themselves, detected in blood serum, are accepted markers of exposure. Specific biomarkers of effect, however, are unavailable, as are specific biomarkers of susceptibility.

Virtually all people have been exposed to PFOA and PFOS, resulting in non-zero background body burdens and the absence of a strictly unexposed control group for use in

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[16] **Gallo, V.** *Serum perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) concentrations and liver function biomarkers in a population with elevated PFOA exposure.* Environmental Health Perspectives, 120(5):655-60, May 2012;

[17]**ATSDR.** *Draft Toxicological Profile for Perfluoroalkyls.* Atlanta, Georgia; U. S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 574 pages including appendices, http://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf, supersedes May 2009 draft profile and *"any previously released draft or final profile,"* August 2015;

[18]**Needham, L. L.; P. Grandjean, B. Heinzow, *et al.*** *Partition of environmental chemicals between maternal and fetal blood and tissues.* Environmental Science and Technology, 45:1121–6, 2011;

Loccisano, A. E.; M. P. Longnecker, J. L. Campbell, Jr, *et al.* *Development of PBPK models for PFOA and PFOS for human pregnancy and lactation life stages.* Journal of Toxicology and Environmental Health A, 76:25–57, 2013;

[19]**ATSDR.** *Draft Toxicological Profile for Perfluoroalkyls.* Atlanta, Georgia; U. S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 574 pages including appendices, http://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf, supersedes May 2009 draft profile and *"any previously released draft or final profile,"* August 2015;

[20]**Ibid.**;

[21]**Ibid.**;

epidemiology studies (Kerger, Copeland, and DeCaprio 2011)[22]. Ingelido, *et al.* (2010)[23] determined serum concentrations of PFOA and PFOS in 230 members of the Italian general population, in three age ranges: 20-35 years, 36-50 years, and 51-65 years. Median concentrations of all participants were 6.31 ng/g for PFOS and 3.59 ng/g for PFOA. The 90th percentiles were 12.38 and 6.92 ng/g, respectively. Men had higher concentrations of PFOS and PFOA than women, regardless of age. PFOS and PFOA concentrations in serum also increased with age. The strong correlation between PFOS and PFOA concentrations, according to the authors, suggests the same or similar exposure routes.

The New York State Department of Health (NYS DOH) offered residents and former residents of the Village and the Town of Hoosick Falls blood tests at no charge to determine PFOA levels in their serum[24]. Results from 2081 participants tested from February to April 2016 are reported in Table 4. Results are placed in the context of the general U. S. population and other affected populations in Table 5. The median (50^{th}-percentile) serum level of PFOA was 28.3 ug/L (ppb) in Hoosick Falls (Table 4), about 11.3 times higher than the 50^{th} percentile nationally, which was 2.08 ug/L (ppb, Table 5). In Hoosick Falls and nationally, PFOA levels were higher in males than in females, and higher in adults than in children. NYS DOH blood tests can quantify other PFCs besides PFOA, but other PFCs in serum were not reported.

Pharmacodynamics

Acute Toxicity. Acute toxicity refers to toxic effects resulting from short-term exposure of up to one day (24 hours). Acute toxicity of PFCs including PFOA may occur in special circumstances such as accidental exposures in industrial settings where PFCs may be manufactured, packaged, and stored. In contrast, environmental levels of PFCs including PFOA typically have been reported in the ppt to parts-per-billion (ppb) range. Acute toxicity typically is unassociated with such environmentally realistic concentrations.

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[22] **Kerger, B. D.; T. L. Copeland, and A. P. DeCaprio.** *Tenuous dose-response correlations for common disease states: case study of cholesterol and perfluorooctanoate/sulfonate (PFOA/PFOS) in the C8 Health Project.* Drug Chemistry and Toxicology, 34(4):396-404, October 2011;

[23] **Ingelido, A. M.; *et al.*** *Perfluorooctanesulfonate and perfluorooctanoic acid exposures of the Italian general population.* Chemosphere, 80(10): 1125-30, August 2010;

[24] **NYS DOH.** *Hoosick Falls and Town of Hoosick Questions and Answers About PFOA Blood Testing Program.* Albany, New York; New York State Department of Health, 6 pages, http://www.villageofhoosickfalls.com/Water/Documents/HealthMonitoringFact_sheet-06022016.pdf, June 2016;

Table 4. Serum PFOA in Hoosick Falls Residents Tested Voluntarily, To April 2016*

PFOA blood test results by gender and age group: Hoosick Falls area participants Participants tested February – April, 2016			
	Number of participants	PFOA level in µg/L	
		Geometric mean	50th percentile
Total	2081	23.5	28.3
By gender			
Females	1146	21.3	26.7
Males	935	26.6	30.7
By age group			
0-17	353	16.3	19.8
18-39	458	18.7	22.6
40-59	700	25.7	32.8
60 and older	570	31.7	43.4

Source: **NYS DOH.** *Information Sheet, PFOA Biomonitoring Group-Level Results, Table 1,* page 1 of 2 pages; Albany, New York State Department of Health, http://www.villageofhoosickfalls.com/Water/Documents/HealthMonitoringFactSheet-06022016.pdf, 2 June 2016.

Table 5. Serum PFOA in Hoosick Falls Residents Tested Voluntarily, To April 2016*

PFOA Levels in Blood from Other Studies: Other communities with PFOA contamination in drinking water, people who worked with PFOA, and general U.S. population		
PFOA RESULTS FOR COMPARISON	Results in µg/L	
Other communities with PFOA in drinking water:	**Average level**	
Little Hocking, Ohio	228	N.A.
Lubeck, West Virginia	92	N.A.
Tuppers Plains, Ohio	42	N.A.
Mason County, West Virginia	16	N.A.
People who worked with PFOA:	**Average level**	
3M workers, Decatur, Alabama	1125	N.A.
DuPont workers, Parkersburg, West Virginia	410	N.A.
General U.S. population:	**Middle level (50th percentile)**	**High level (95th percentile)**
U.S. population age 12 and up	2.08	5.68
Males only	2.38	5.62
Females only	1.78	5.68
Young people age 12-19	1.74	3.59

NOTES FOR TABLE 2:

µg/L = micrograms per liter: A microgram per liter equals one part per billion, about one drop of liquid in an Olympic-size swimming pool.

Middle level (50th percentile): Half the people had a result below and half had a result above this level.

High level (95th percentile): 95 of every 100 people had results below this level.

Average level: The average is usually very similar to the middle level. In the published community studies, the average level is used.

N.A.: These levels are not available in the published studies about these communities.

References:

1. General U.S. population: National Health and Nutrition Examination Survey (NHANES), National Report on Human Exposure to Environmental Chemicals, U.S. Centers for Disease Control and Prevention (CDC), 2011-12.218.
2. Ohio/West Virginia communities: Paustenbach DJ, Panko JM, Scott PK et al (2007). A methodology for estimating human exposure to perfluorooctanoic acid (PFOA): a retrospective exposure assessment of a community (1951-2003). J Toxicol Environ Health 70:28-57.
3. Workers: Olsen GW (2015) "PFAS biomonitoring in higher exposed populations," in DeWitt JC (ed.) Toxicological effects of perfluoroalkyl and polyfluoroalkyl substances. Humana Press, Springer.

FOR MORE INFORMATION: NYS DOH, Center for Environmental Health, Bureau of Environmental and Occupational Epidemiology, Corning Tower, Albany NY 12237 518-402-7950 or BEOE@health.ny.gov

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Source: **NYS DOH.** *Information Sheet, PFOA Biomonitoring Group-Level Results, Table 2,* page 2 of 2 pages; Albany, New York State Department of Health, http://www.villageofhoosickfalls.com/Water/Documents/HealthMonitoringFactSheet-06022016.pdf, 2 June 2016.

Mutagenicity. Studies of PFC genotoxicity to humans were absent from available literature (ATSDR 2015)[26]. ATSDR, summarizing mutagenicity studies, concluded that *"in vitro studies provide evidence that PFOA and PFOS are not mutagenic at non-cytotoxic concentrations."* At cytotoxic concentrations, greatly exceeding typical environmental levels, PFOA has been reported to cause DNA damage including DNA strand breaks, induction of micronuclei (small cell nuclei visible after extrusion of the main cell nucleus, relevant to potential carcinogenicity), and increases in reactive oxygen species.

Carcinogenicity: Animal studies. In rats PFOA has been associated causally with liver, testicular, and pancreatic tumors[27].

Carcinogenicity: Epidemiology studies. Studies of PFOA have involved the general population, populations exposed residentially to PFOA from an industrial source, and populations exposed to PFOA occupationally. Eriksen, *et al.* (2009) investigated potential association between plasma levels of PFOA and PFOS and cancer risk within a prospective Danish cohort of 57,053 participants 50-65 years of age with no previous cancer diagnosis at enrollment[28]. They found no association of PFOA or PFOS plasma concentrations in the general Danish population apparently with risk of prostate, bladder, pancreatic, or liver cancer.

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[26] **ATSDR.** *Draft Toxicological Profile for Perfluoroalkyls.* Atlanta, Georgia; U. S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 574 pages including appendices, http://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf, supersedes May 2009 draft profile and *"any previously released draft or final profile,"* August 2015; regarding possible PFOA mutagenicity ATSDR also found (pages 240-1):

"A significant increase in mutation frequencies was observed in hamster-human hybrid cells exposed to 200 µM PFOA for 1–16 days; a 79% decrease in cell viability was also observed at this concentration (Zhao et al. 2011). Concurrent treatment with a ROS inhibitor significantly decreased the mutagenic potential, indicating that ROS may play an important role in mediating the genotoxic effects of PFOA. PFOA induced DNA damage in Paramecium caudatum following exposure to 100 µM for 12 and 24 hours (Kawamoto et al. 2010). Intracellular ROS was significantly increased and DNA damage was not reversed by the application of glutathione, a ROS-inhibitor, indicating that intracellular ROS may not be the cause of PFOA-induced DNA damage. PFOS did not induce DNA damage in this study. In contrast, no increases in DNA damage or micronuclei formation were found in human hepatoma HepG2 cells following a 24-hour exposure to PFOA concentrations as high as 800 µM (Florentin et al. 2011); cytotoxicity was observed at ≥200 µM. Eriksen et al. (2010) also found no evidence of DNA damage in HepG2 cells incubated with 100 or 400 µM PFOA for 24 hours."

[27] **Barry, Vaughn; Andrea Winquist, and Kyle Steenland.** *Perfluorooctanoic Acid (PFOA) Exposures and Incident Cancers among Adults Living Near a Chemical Plant.* Environmental Health Perspectives, 121(11/12):1313-8, http://dx.doi.org/10.1289/ehp.1306615, November/December 2013;

[28] **Eriksen, Kirsten T.**; ***et al.*** *Perfluorooctanoate and perfluorooctanesulfonate plasma levels and risk of cancer in the general Danish population.* Journal of the National Cancer Institute, 101 (8): 605-609. doi: 10.1093/jnci/djp041, jnci.oxfordjournals.org, first published online April 7, 2009;

In contrast, *Barry, Winquist, and Steenland* (2013)[29] reported that PFOA exposure of 32,254 residents of the mid-Ohio Valley, exhibiting 2,507 validated cases of cancer of 21 different types, was causally associated with renal (kidney) and testicular cancers. They also concluded that*: "Because this is largely a survivor cohort, findings must be interpreted with caution, especially for highly fatal cancers such as pancreatic and lung cancer."* That is, these cancers might be caused by PFOA but not represented in the 'survivor cohort' because of the brief time people have them before dying.

Vieira, *et al.* (2013)[30] studied the relationship between exposure to PFOA and cancer among residents living near the duPont Teflon-manufacturing plant in Parkersburg, West Virginia. The authors analyzed incidence data on 18 cancers diagnosed from 1996 through 2005, including 7,869 cases in five Ohio counties and 17,238 in eight West Virginia counties. They concluded that their *"results suggest that higher PFOA serum levels may be associated with testicular, kidney, prostate, and ovarian cancers and non-Hodgkin lymphoma. Strengths of this study include near-complete case ascertainment for state residents and well-characterized contrasts in predicted PFOA serum levels from six contaminated water supplies."*

The United Nations International Agency for Research on Cancer (UN IARC, 2014)[31] convened a Working Group on PFOA. Based upon consideration of available animal and human data the Working Group concluded that *"[o]n the basis of limited evidence in humans that PFOA causes testicular and renal cancer, and limited evidence in experimental animals, the working group classified PFOA as possibly carcinogenic to humans (Group 2B)."*

Teratogenicity. Available data on possible PFOA teratogenicity is limited but negative. ATSDR (2015)[32] addressed this issue in its holistic review of PFOA toxicology. With respect to oral exposure ATSDR reported that *"no fetal toxicity or teratogenicity was reported in offspring*

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[29] **Barry, Vaughn; Andrea Winquist, and Kyle Steenland.** *Perfluorooctanoic Acid (PFOA) Exposures and Incident Cancers among Adults Living Near a Chemical Plant.* Environmental Health Perspectives, 121(11/12):1313-8, http://dx.doi.org/10.1289/ehp.1306615, November/December 2013;

[30] **Vieira, Verónica M.; *et al.*** *Perfluorooctanoic acid exposure and cancer outcomes in a contaminated community: a geographic analysis.* Environmental Health Perspectives, 121(3):1-7, http://ehp.niehs.nih.gov/1205829/, DOI:10.1289/ehp.1205829, March 2013;

[31] **UN IARC.** *Carcinogenicvity of perfluorooctanoic acid, tetrafl uoroethylene, dichloromethane, 1,2-dichloropropane, and 1,3-propane sultone.* The Lancet, 15:924-5, www.thelancet.com/oncology, August 2014;

[32] **ATSDR.** *Draft Toxicological Profile for Perfluoroalkyls.* Atlanta, Georgia; U. S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 574 pages including appendices, http://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf, supersedes May 2009 draft profile and *"any previously released draft or final profile,"* August 2015;

of rabbits exposed to up to 50 mg/(kg d) PFOA on GDs [gestation days] 6-18…" No data on teratogenicity was presented in connection with either inhalation or dermal exposure.

Reproductive Effects. Studies of potential reproductive effects of PFOA and PFOS in people have been motivated by laboratory bioassays reporting reduced birth weight, increased postnatal mortality, and decreased postnatal growth in rats and mice (Olsen, Butenhoff, and Zobel, 2009)[33]. Olsen, Butenhoff, and Zobel reviewed eight epidemiological studies, together involving six general (non-occupational) populations and two occupational populations. In the five general population studies that measured PFOA and PFOS, inconsistent associations were obtained with respect to birth outcomes including birth weight, birth length, head circumference, and 'ponderal index' (a measure of leanness, relating body length and body mass).

Infertility. Infertility attributable to endocrine disruptors including PFOA was studied epidemiologically via comparison of serum PFOA levels of fertile vs. infertile women,[34] but the authors concluded that *"no significant difference was found between the groups with regard to perfluorooctane sulfonate (PFOS)* [and] *perfluorooctanoic acid (PFOA)…"* In contrast, La Rocca, *et al.* (2011)[35] reported that PFOS levels were associated positively with infertility among a group including fertile and infertile couples in an unspecified metropolitan community in Italy.

Fecundity. A study by Fei, *et al.* (2009) involving 1240 women from the Danish National Birth Cohort focused on fecundity based upon women's reported time to pregnancy[36]. The study revealed that high plasma levels of PFOA and/or of PFOS were associated with longer times to pregnancy. The authors concluded that their *"findings suggest that PFOA and PFOS exposure at plasma levels seen in the general population may reduce fecundity; such exposure levels are common in developed countries."*

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[33] **Olsen, G. W.; J. L. Butenhoff, and L. R. Zobel.** *Perfluoroalkyl chemicals and human fetal development: an epidemiologic review with clinical and toxicological perspectives.* Reproductive Toxicology, 27(3-4):212-30, June 2009;

[34] **Caserta, D.; *et al.*** *The influence of endocrine disruptors in a selected population of infertile women.* Gynecology and Endocrinology, 29(5):444-7, May 2013;

[35] **La Rocca, C.; *et al.*** *Exposure and effective dose biomarkers for perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) in infertile subjects: preliminary results of the PREVIENI project.* International Journal of Hygiene and Environmental Health, 215(2):206-11, February 2012;

[36] **Fei, Chunyuan; *et al.*** *Maternal levels of perfluorinated chemicals and subfecundity.* Human Reproduction, doi:10.1093/humrep/den490, 1(1):1–6, 2009;

Birth outcomes. A study of birth outcomes of women exposed to PFOA and PFOS in the mid-Ohio Valley revealed that both were associated positively with pregnancy-induced hypertension (preeclampsia)[37]. Apelberg, *et al.* (2007) studied women living near a chemical plant; they quantified fetal exposure via PFOA concentrations measured in maternal blood serum sampled from umbilical cords. PFOA concentrations in cord serum was found to be negatively correlated with size and weight of infants at birth[38]. Fei, *et al.* (2007) conducted a general population study involving the national cohort of women in Denmark. Despite being a general population study, it likewise revealed a negative association of PFOA (though not of PFOS) levels in blood plasma with infant birth weight[39].

In contrast, Hamm, *et al.* (2010) studied a cohort of 252 pregnant women,[40] and reported that maternal exposure to perfluorinated acids including PFOA and PFOS exerted *"no substantial effect on fetal weight and length of gestation at the concentrations observed in this population."* Likewise, Savitz, *et al.* (2013)[41] studied 11,737 pregnancies in a community highly exposed to PFOA. They reported *"no associations between estimated serum PFOA levels and adverse pregnancy outcomes other than possibly preeclampsia."*

Onset of puberty and mammary gland development. Tucker, *et al.* (2015)[42] investigated the effects of PFOA on female mouse pubertal development at doses ≤1 mg/kg. Female offspring from CD-1 and C57Bl/6 dams were exposed to PFOA prenatally, creating serum concentrations similar to serum concentrations in people. The onset of puberty, including mammary gland development, was delayed in both mouse strains, in a dose-dependent manner.

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[37] **Darrow, Lyndsey A.; Cheryl R. Stein, and Kyle Steenland.** *Serum perfluorooctanoic acid and perfluorooctane sulfonate concentrations in relation to birth outcomes in the mid-Ohio Valley, 2005–2010.* Environmental Health Perspectives, 121(10):1207–13, http://dx.doi.org/10.1289/ehp.1206372, 1 October 2013;

[38] **Apelberg, Benjamin J.; *et al.*** *Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth.* Environmental Health Perspectives, 115(11): 1670–76, November 2007; Published online, doi: 10.1289/ehp.10334, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2072847/, Jul 31, 2007.

[39] **Fei C.; *et al.*** *Perfluorinated chemicals and fetal growth: a study within the Danish National Birth Cohort.* Environmental Health Perspectives, 115(11):1677-82, November 2007;

[40] **Hamm, M. P.; *et al.*** *Maternal exposure to perfluorinated acids and fetal growth.* Journal of Exposure Science and Environmental Epidemiology, 20(7):589-97, November 2010;

[41] **Savitz, David A.; *et al.*** *Perfluorooctanoic Acid Exposure and Pregnancy Outcome in a Highly Exposed Community.* Epidemiology, 23(3):386-92, May 2012;

[42] **Tucker, Deirdre K.; *et al.*** *The mammary gland is a sensitive pubertal target in CD-1 and C57Bl/6mice following perinatal perfluorooctanoic acid (PFOA) exposure.* Reproductive Toxicology, 54:26–36, 2015;

Other reproductive effects. Hines, *et al.* (2009)[43] reported that PFOA *"is a proven developmental toxicant in mice, causing pregnancy loss, increased neonatal mortality, delayed eye opening, and abnormal mammary gland growth in animals exposed during fetal life."* They investigated fetal exposure of CD-1 mice to PFOA, and possible PFOA effects on birth weight, serum insulin, and leptin, a protein produced by fat that evidently is involved in fat storage. Their investigation revealed increased body weight, serum insulin, and leptin in mid-life of mice exposed developmentally. They concluded that their research revealed *"an important window of exposure for low-dose effects of PFOA on body weight* [BW] *gain, as well as leptin and insulin concentrations in mid-life, at a lowest observed effect level of 0.01mg PFOA/kg BW."*

Other Chronic Effects. The presence of PFOA in water has been recognized as a potential chronic exposure risk to human health, not only in the scientific literature, but in litigation[44]. In the scientific arena, ATSDR undertook a 'health consultation' relating to populations exposed to releases of PFCs including PFOA from an industrial facility in Cottage Grove, Minnesota[45]. As early as 2005 ATSDR concluded that *"PFCs have a long half-life in humans and animal studies indicate a potential for toxicity to the liver and effects on reproduction and development."*

Cholesterol. Eriksen, *et al.* (2013)[46] reported that PFOA and PFOS may affect serum cholesterol levels, mainly in highly exposed populations. They conducted a cross-sectional study of the plasma PFOA and PFOS vs. total cholesterol in a general middle-aged Danish population. They found positive associations of total cholesterol with both substances but, as in many epidemiology studies, theirs was unable to determine clearly whether the association was

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[43] **Hines, E. P.; *et al.*** *Phenotypic dichotomy following developmental exposure to perfluorooctanoic acid (PFOA) in female CD-1 mice: Low doses induce elevated serum leptin and insulin, and overweight in mid-life.* Molecular and Cellular Endocrinology, 25:304(1-2), 97-105, May 2009; doi: 10.1016/j.mce.2009.02.021. Epub 9 March 2009;

[44] **Delaware Riverkeeper.** *A duPont legacy: PFOA pollution,* 4 pages; http://www.delawareriverkeeper.org/sites/default/files/resources/Factsheets/fact%20sheet.pfoa.final%205.09.pdf, final, May 2009;

Associated Press., Andrew Welsh-Huggins. *Woman awarded $1.6 million over DuPont chemical in water,* 1 page, 7 October 2015;

Kary, Tiffany; and Denise Trowbridge. *Dupont, Chemours handed another loss in Teflon chemical case.* Bloomberg News, http://www.bloomberg.com/news/articles/2016-07-06/dupont-loses-third-case-over-teflon-toxin-chemours-to-pay, 4 pages, 6 July, 2016;

[45] **ATSDR.** *Health Consultation: 3M Chemolite, Perfluorochemical Releases at the 3M – Cottage Grove Facility; City of Cottage Grove, Washington County, Minnesota; EPA Facility ID: MND006172969,* page 27 of 43 pages, 18 February 2005;

[46] **Eriksen, Kirsten T.**; ***et al.*** *Association between plasma PFOA and PFOS levels and total cholesterol in a middle-aged Danish population.* PLoS ONE 8(2): e56969. doi:10.1371/journal.pone.0056969, 2013;

causal. Likewise, Kerger, Copeland, and DeCaprio (2011)[47] reported a trend of increasing blood cholesterol with increasing PFOA concentrations among 46,294 adult West Virginia residents who lived, worked, or went to school for at least one year in a C8 (PFOA and PFOS) contaminated drinking-water district.

Liver function. PFOA and PFOS tend to concentrate in the liver of animals.[48] As studies involving human exposure to PFOA have reported associations with liver function enzymes only inconsistently, Gallo, *et al.* (2012) undertook a massive study involving 69,030 persons (47,092 adults) to examine possible association of PFOA and PFOS with alanine transaminase (ALT), g-glutamyltransferase (GGT), and direct bilirubin (blood levels of bilirubin, a component of bile). Statistical analysis revealed associations of PFOA and PFOS with the liver function enzyme ALT, and inconsistent evidence of association with GGT and bilirubin.

Endocrine disruption. A recent concern is that low environmental levels of substances including PFOA other PFCs have been found to affect the endocrine system. The effects may include causing obesity and the autoimmune disease ulcerative colitis. Such substances may act by mimicking or blocking endogenous hormones (ATSDR 2015)[49].

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[47] **Kerger, B. D.; T. L. Copeland, and A. P. DeCaprio.** *Tenuous dose-response correlations for common disease states: case study of cholesterol and perfluorooctanoate/sulfonate (PFOA/PFOS) in the C8 Health Project.* Drug Chemistry and Toxicology, 34(4):396-404, October 2011;

[48] **Gallo, V.** *Serum perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) concentrations and liver function biomarkers in a population with elevated PFOA exposure.* Environmental Health Perspectives, 120(5):655-60, May 2012;

[49] **ATSDR.** *Draft Toxicological Profile for Perfluoroalkyls.* Atlanta, Georgia; U. S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 574 pages including appendices, http://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf, supersedes May 2009 draft profile and *"any previously released draft or final profile,"* August 2015:

> *"The available data from epidemiology and animal studies are inconclusive to evaluate whether the toxicity of perfluoroalkyls is mediated through the neuroendocrine axis or whether they have the ability to mimic or block endogenous hormones… The effects observed in humans and/or animals exposed to perfluoroalkyls that may be related to a disruption of the endocrine system include alterations in reproductive hormone levels, infertility, development of the reproductive system, alterations of the endometrium or mammary gland, and alterations in the function of endocrine glands such as the thyroid."*

Ulcerative colitis. Ulcerative colitis was strongly associated with exposure to PFOA measured via concentrations in blood serum (Steenland, *et al.,* 2013).[50] Ulcerative colitis is an autoimmune disease, in which the immune system of affected individuals has been compromised in a manner that reduces its ability to distinguish 'self' from 'non-self' targets of action. The Steenland study involved interviews with 32,254 adults highly exposed to PFOA as community members and occupationally exposed individuals living near a chemical plant in the mid-Ohio valley. Interviewees were people with high serum PFOA levels (median 28 ng/mL = 28 ug/L). The authors found that *"the incidence of ulcerative colitis was significantly increased in association with PFOA exposure, with adjusted rate ratios by quartile of exposure of 1.00 (referent)* ['referent' was first quartile, against which the three higher quartiles were compared], 1*.76 (95% CI: 1.04, 2.99), 2.63 (95% CI: 1.56, 4.43), and 2.86 (95% CI: 1.65, 4.96) (ptrend < 0.0001)."*

Obesity. As reported above, exposure of developing embryonic mice to low doses of PFOA via their mothers (dams) has been associated with increased weight and with increased fat ('adiposity') in postpubertal females.[51] This finding has been replicated in humans. Halldorsson, *et al.* (2012) undertook a prospective study of Danish women, and found that PFOA levels in blood serum sampled at pregnancy week 30 were correlated with obesity indicators in their daughters at 20 years of age.

PFOA has been identified as an endocrine disruptor capable of producing obesity via maternal exposure as described above. Skinner, *et al.* (2013), studying the pesticide DDT, reported that this endocrine disruption effect may occur, not only within a single generation, but extending into future generations.[52] Indeed, citing Newbold (2008), Halldorsson, *et al.* (2013), reported that endocrine disruptors *"may lead to permanent changes in metabolic pathways that regulate body weight."*[53] Grens (2015)[54] outlined the history of the broadening

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[50] **Steenland. Kyle; Liping Zhao, Andrea Winquist, and Christine Parks.** *Ulcerative colitis and perfluorooctanoic acid (PFOA) in a highly exposed population of community residents and workers in the mid-Ohio valley.* Environmental Health Perspectives, 121:900–5, http://dx.doi.org/10.1289/ehp.1206449 [Online 4 June 2013], 2013;

[51] **Hines, E. P.; *et al.*** *Phenotypic dichotomy following developmental exposure to perfluorooctanoic acid (PFOA) in female CD-1 mice: Low doses induce elevated serum leptin and insulin, and overweight in mid-life.* Molecular and Cellular Endocrinology, 25:304(1-2), 97-105, May 2009; doi: 10.1016/j.mce.2009.02.021. Epub 9 March 2009;

[52] **Skinner, MK; *et al.*** *Ancestral dichlorodiphenyltrichloroethane (DDT) exposure promotes epigenetic transgenerational inheritance of obesity.* BMC Medicine, 11:228, 2013;

[53] **Halldorsson, Thorhallur I.; *et al.*** *Prenatal exposure to perfluorooctanoate and risk of overweight at 20 Yyears of age: a prospective cohort study.* Environmental Health Perspectives, 120(5): 668-73, May 2012; published online, DOI:10.1289/ehp.1104034, 3 February 2012;

of this observation involving DDT and animal studies to other endocrine disruptors ('obesogens'), associating (speculatively) the current human epidemic of obesity with increased environmental dissemination of endocrine disruptors in recent decades.

Immunosuppression. Immunosuppression by PFCs at low serum levels has been reported in multiple studies revealing reduced antibody response in adults, and in children following routine administration of childhood vaccines (US EPA 2016)[55]: *"…three studies have reported decreases in response to one or more vaccines (e.g., measured by antibody titer) in relation to higher exposure to PFOA in children (Grandjean et al. 2012; Granum et al. 2013) and adults (Looker et al. 2014). In the two studies examining exposures in the background range (i.e., general population exposures, <0.010 µg/ml), the associations with PFOA also were seen with other correlated PFCs. This limitation was not present in the study in adults in the high-exposure C8 community population. Serum PFOA levels in this study population were approximately 0.014–0.090 µg/mL"* (pages 3-24 to 3-25).

Newbold, RR; *et al.* *Effects of endocrine disruptors on obesity.* International Journal of Andrology, 31:201-8, 2008;

[54]**Grens, Kerry.** *Obesogens – Low doses of environmental chemicals can make animals gain weight. Whether they do the same to humans is a thorny issue.* The Scientist, http://www.the-scientist.com/?articles.view/articleNo/44278/title/Obesogens, 10 pages, 1 November 2015;

[55] **US EPA.** *Health Effects Support Document for Perfluorooctanoic Acid (PFOA).* Washington, DC; U. S. Environmental Protection Agency, Office of Water, EPA 822-R-16-003, 322 pages, May 2016:

"Antibody responses to diphtheria and tetanus toxoids following childhood vaccinations were assessed in context of exposure to five perfluorinated compounds (Grandjean et al. 2012). The prospective study included a birth cohort of 587 singleton births during 1999–2001 from the National Hospital in the Faroe Islands. Serum antibody concentrations were measured in children at age 5 years prebooster, approximately 4 weeks after the booster, and at age 7 years. Prenatal exposures to perfluorinated compounds were assessed by analysis of serum collected from the mother during week 32 of pregnancy (PFOA geometric mean 0.0032 µg/mL; IQR 0.00256–0.00401); postnatal exposure was assessed from serum collected from the child at 5 years of age (PFOA geometric mean 0.00406 µg/mL; IQR 0.00333–0.00496). Multiple regression analyses with covariate adjustments were used to estimate the percent difference in specific antibody concentrations per twofold increase in PFOA concentration in both maternal and 5-year serum. Maternal PFOA serum concentration was negatively associated with antidiphtheria antibody concentration (-16.2%) at age 5 before booster. The biggest effect was found in comparison of antibody concentrations at age 7 with serum PFOA concentrations at age 5 where a twofold increase in PFOA was associated with differences of -36% (95% CI, -52%–-14%) and -25% (95% CI, -43%–-2%) for tetanus and diphtheria, respectively. Additionally at age 7, a small percentage of children had antibody concentrations below the clinically protective level of 0.1 international unit (IU) /mL. The ORs of antibody concentrations falling below this level were 4.20 (95% CI, 1.54–11.44) for tetanus and 3.27 (95% CI, 1.43–7.51) for diphtheria when age 7 antibody levels were correlated with age 5 PFOA serum concentrations. Maternal and child PFOS levels also were negatively associated with antibody titers…"

Sensitive Subpopulations

Sensitive subpopulations are *groups* sharing distinctive characteristics. Individuals may belong to a sensitive subpopulation, but the designation usually excludes individuals considered alone, whose individual vulnerability to stressors depends upon his/her unique medical condition. Eventually each individual must die and, as the transition between life and death approaches, vulnerability to stressors may become arbitrarily great, and the presence or absence of the stressor arbitrarily insignificant in extending the dwindling life.

Examples of sensitive subpopulation commonly include the elderly, infants, and pregnant women. In the case of PFCs, individuals with specific pre-existing conditions may be unusually sensitive (ATSDR 2015, pages 313-4)[56]. These include people with elevated serum cholesterol, a risk factor for cardiovascular disease, and people with elevated serum uric acid, a risk factor for hypertension (high blood pressure). People with compromise liver function also may be unusually sensitive to PFCs, because the liver may be a target of PFC toxic activity.

Chemical Interactions

According to ATSDR (2015, page 311)[57]: *"No relevant studies were located regarding interactions of perfluoroalkyl compounds with other chemicals in children or adults."*

Serum Levels vs. Health Effects

Serum levels of PFOA associated with numerous human health conditions as reported in US EPA (2016)[58] are set forth in Table 6. Table 6 is divided into two parts. Table 6a reports serum PFOA levels associated with specific human health conditions. Table 6b ranks serum PFOA levels from lowest to highest, and for comparison shows the Town of Hoosick and Village of Hoosick Falls 50th-percentile serum level. As Table 6b illustrates, many health conditions have been reported associated with serum PFOA levels below those commonly occurring among Hoosick residents and former residents.

[56]**ATSDR.** *Draft Toxicological Profile for Perfluoroalkyls.* Atlanta, Georgia; U. S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 574 pages including appendices, http://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf, supersedes May 2009 draft profile and *"any previously released draft or final profile,"* August 2015;

[57]**Ibid.**;

[58]**US EPA.** *Health Effects Support Document for Perfluorooctanoic Acid (PFOA).* Washington, DC; U. S. Environmental Protection Agency, Office of Water, EPA 822-R-16-003, 322 pages, May 2016;

Table 6a. Human Health Effects and Associated PFOA in Blood Serum, By System Affected*

health effect	mean or median serum PFOA	source	EPA table
	(ug/mL = ppm)		
serum lipids, uric acid, from US EPA (2016)* Table B-4			
increased total cholesterol, triglycerides	1.03 to 1.90	Olsen *et al.* 2001b, 2003	B-4
increased total cholesterol, triglycerides	1.36 to 1.77	Olsen *et al.* 2001c, 2003	B-4
increased total cholesterol, VLDL, triglycerides, uric acid	0.428	Sakr *et al.* 2007a	B-4
increased total cholesterol	1.04 to 1.16	Sakr *et al.* 2007b	B-4
increased triglycerides, reduced HDL	2.21	Olsen and Zobel 2007	B-4
increased total cholesterol, uric acid	4.02	Costa *et al.* 2009	B-4
increased total cholesterol, LDL, non-HDL, triglycerides	0.08	Steenland *et al.* 2009	B-4
increased uric acid	0.086	Steenland *et al.* 2010	B-4
increased total cholesterol	0.0261	Winquist and Steenland 2014a	B-4
incr total chol., LDL, triglycerides in children, adolescents	0.0777 to 0.0618	Frisbee *et al.* 2010	B-4
increased total cholesterol, non-HDL lipoproteins	0.0046	Nelson *et al.* 2010	B-4
increased total cholesterol	0.0071	Eriksen, *et al.* 2013	B-4
endocrine disruption, from US EPA (2016)* Table B-5			
liver enzymes, elevation of GGT	0.428	Sakr, *et al.* 2007a	B-5
liver enzymes, elevation of AST	1.04 to 1.16	Sakr, *et al.* 2007b	B-5
liver enzymes, elevation of ALP, ALT, GGT	2.21	Olsen and Zobel 2007	B-5
liver enzymes, elevation of ALP, ALT, GGT	4.02	Costa, *et al.* 2009	B-5
liver enzymes, elevation in males: ALT, GGT	0.00505	Lin, *et al.* 2010	B-5
liver enzymes, elevation of ALT, GGT in females	0.00406	Lin, *et al.* 2010	B-5
chronic kidney disease, enzymes increase	0.0059	Shankar, *et al.* 2011	B-5
chronic kidney disease, eGFR decrease	0.0283	Watkins, *et al.* 2013	B-5
thyroid disease, hormone levels, from US EPA (2016)* Table B-6			
T3 thyroid hormone elevation	2.21	Olsen and Zobel 2007	B-6
free T4 thyroid hormone decline	2.21	Olsen and Zobel 2007	B-6
T3 thyroid hormone elevation	0.0104	Shrestha *et al.* 2015	B-6
T4 thyroid hormone elevation	0.0104	Shrestha *et al.* 2015	B-6
T4 thyroid hormone elevation in girls	0.000943 (cord)	de Cock *et al.* 2014	B-6
thyroid disease in women elevated	0.019 (women)	Melzer *et al.* 2010	B-6
thyroid disease in children elevated	0.0293	Lopez-Espinosa *et al.* 2012	B-6
immunotoxicity, from US EPA (2016)* Table B-7			
ulcerative colitis	0.113	Steenland, *et al.* 2015	B-7
rheumatoid arthritis	0.113	Steenland, *et al.* 2015	B-7
vaccine response, reduced antibody titer	0.0032	Grandjean, *et al.* 2012	B-7
vaccine response, reduced antibody titer	0.00406	Grandjean, *et al.* 2012	B-7
asthma, increased prevalence in asthmatics	0.0015	Dong, *et al.* 2013	B-7
asthma, increased prevalence in non-asthmatics	0.0010	Dong, *et al.* 2013	B-7
asthma, increased prevalence	0.0043	Humblet, *et al.* 2014	B-7
vaccine response, reduced antibody titer	0.0337	Looker, *et al.* 2014	B-7

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Table 6a. Human Health Effects and Associated PFOA in Blood Serum, By System Affected*

health effect	mean or median serum PFOA	source	EPA table
	(ug/mL = ppm)		
reproductive and developmental outcomes, from US EPA (2016)* Table B-8			
breastfeeding duration reduced	0.0056	Fei *et al.* 2007, 2008a, 2009, 2010a	B-8
birth weight reduced	0.0056	Fei *et al.* 2007, 2008a, 2009, 2010a	B-8
birth size reduced	0.0056	Fei *et al.* 2007, 2008a, 2009, 2010a	B-8
fecundity/fertility: time to pregnancy increased	0.0056	Fei *et al.* 2007, 2008a, 2009, 2010a	B-8
fecundity/fertility: infertility	0.0056	Fei *et al.* 2007, 2008a, 2009, 2010a	B-8
fecundity/fertility: time to pregnancy increased	0.00166	Vélez *et al.* 2015	B-8
fecundity/fertility: infertility	0.00166	Vélez *et al.* 2015	B-8
pregnancy-induced hypertension (preeclampsia)	0.031 to 0.0337	Darrow *et al.* 2013, 2014	B-8
weight, head circumference, ponderal index reduced	0.0016 (cord)	Apelberg *et al.* 2007	B-8
birth weight reduced	0.0037	Maisonet *et al.* 2012	B-8
male fertility: reduced normal sperm count (PFOA + PFOS)	0.0049	Joensen *et al.* 2009	B-8
male fertility: altered sperm quality PFOA, 6 PFCs (perfluoroalkyl compounds)	0.00429 to 0.00509	Buck Louis *et al.* 2015	B-8
neurodevelopmental: increased cerebral palsy in boys	0.00456	Liew *et al.* 2014	B-8
neurodevelopmental: increased hyperactivity	0.0014	Høyer *et al.* 2015a	B-8
neurodevelopmental: executive function; ADHD	0.0351	Stein *et al.* 2013	B-8
neurodevelopmental: increased ADHD	0.0044	Hoffman *et al.* 2010	B-8
postnatal devel.: reduced wt., BMI in boys 5-12 mos.	0.0052	Andersen *et al.* 2010	B-8
postnatal development: obesity in females at age 20 y	0.0037	Halldorsson, *et al.* 2012	B-8
postnatal developent: increased waist/height ratio	0.001 to 0.0018	Høyer *et al.* 2015b	B-8
postnatal development: delayed puberty in girls	0.02 to 0.026	Lopez-Espinosa *et al.* 2011	B-8
postnatal development: delayed puberty	0.0036 (maternal)	Kristensen *et al.* 2013	B-8
postnatal development: lower sperm concentration and total count	0.0038 (maternal)	Vested *et al.* 2013	B-8
*Derived from Tables B-4 through B-8 in:			
US EPA. *Health Effects Support Document for Perfluorooctanoic Acid (PFOA).* Washington, DC; U. S. Environmental Protection Agency, Office of Water, EPA 822-R-16-003, 322 pages, May 2016.			

Table 6b. Human Health Effects and Associated PFOA in Blood Serum, By Serum Level*

health effect	mean or median serum PFOA (ug/mL = ppm)	source	EPA table
Hoosick Falls 50th percentile	**0.0283**	**NYS DOH 2016; data to April 2016**	**...**
T4 thyroid hormone elevation in girls	0.000943 (cord)	de Cock *et al.* 2014	B-6
asthma, increased prevalence in non-asthmatics	0.0010	Dong, *et al.* 2013	B-7
postnatal developent: increased waist/height ratio	0.001 to 0.0018	Høyer *et al.* 2015b	B-8
neurodevelopmental: increased hyperactivity	0.0014	Høyer *et al.* 2015a	B-8
asthma, increased prevalence in asthmatics	0.0015	Dong, *et al.* 2013	B-7
weight, head circumference, ponderal index reduced	0.0016 (cord)	Apelberg *et al.* 2007	B-8
fecundity/fertility: infertility	0.00166	Vélez *et al.* 2015	B-8
fecundity/fertility: time to pregnancy increased	0.00166	Vélez *et al.* 2015	B-8
vaccine response, reduced antibody titer	0.0032	Grandjean, *et al.* 2012	B-7
postnatal development: delayed puberty	0.0036 (maternal)	Kristensen *et al.* 2013	B-8
postnatal development: obesity in females at age 20 y	0.0037	Halldorsson, *et al.* 2012	B-8
birth weight reduced	0.0037	Maisonet *et al.* 2012	B-8
postnatal development: lower sperm concentration and total count	0.0038 (maternal)	Vested *et al.* 2013	B-8
vaccine response, reduced antibody titer	0.00406	Grandjean, *et al.* 2012	B-7
liver enzymes, elevation of ALT, GGT in females	0.00406	Lin, *et al.* 2010	B-5
male fertility: altered sperm quality PFOA, 6 PFCs (perfluoroalkyl compounds)	0.00429 to 0.00509	Buck Louis *et al.* 2015	B-8
asthma, increased prevalence	0.0043	Humblet, *et al.* 2014	B-7
neurodevelopmental: increased ADHD	0.0044	Hoffman *et al.* 2010	B-8
neurodevelopmental: increased cerebral palsy in boys	0.00456	Liew *et al.* 2014	B-8
increased total cholesterol, non-HDL lipoproteins	0.0046	Nelson *et al.* 2010	B-4
male fertility: reduced normal sperm count (PFOA + PFOS)	0.0049	Joensen *et al.* 2009	B-8
liver enzymes, elevation in males: ALT, GGT	0.00505	Lin, *et al.* 2010	B-5
postnatal devel.: reduced wt., BMI in boys 5-12 mos.	0.0052	Andersen *et al.* 2010	B-8
birth size reduced	0.0056	Fei *et al.* 2007, 2008a, 2009, 2010a	B-8
birth weight reduced	0.0056	Fei *et al.* 2007, 2008a, 2009, 2010a	B-8
breastfeeding duration reduced	0.0056	Fei *et al.* 2007, 2008a, 2009, 2010a	B-8
fecundity/fertility: infertility	0.0056	Fei *et al.* 2007, 2008a, 2009, 2010a	B-8
fecundity/fertility: time to pregnancy increased	0.0056	Fei *et al.* 2007, 2008a, 2009, 2010a	B-8
chronic kidney disease, enzymes increase	0.0059	Shankar, *et al.* 2011	B-5
increased total cholesterol	0.0071	Eriksen, *et al.* 2013	B-4

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Table 6b. Human Health Effects and Associated PFOA in Blood Serum, By Serum Level*

health effect	mean or median serum PFOA	source	EPA table
	(ug/mL = ppm)		
T3 thyroid hormone elevation	0.0104	Shrestha *et al.* 2015	B-6
T4 thyroid hormone elevation	0.0104	Shrestha *et al.* 2015	B-6
thyroid disease in women elevated	0.019 (women)	Melzer *et al.* 2010	B-6
postnatal development: delayed puberty in girls	0.02 to 0.026	Lopez-Espinosa *et al.* 2011	B-8
increased total cholesterol	0.0261	Winquist and Steenland 2014a	B-4
chronic kidney disease, eGFR decrease	0.0283	Watkins, *et al.* 2013	B-5
Hoosick Falls 50th percentile	**0.0283**	**NYS DOH 2016; data to April 2016**	**...**
thyroid disease in children elevated	0.0293	Lopez-Espinosa *et al.* 2012	B-6
pregnancy-induced hypertension (preeclampsia)	0.031 to 0.0337	Darrow *et al.* 2013, 2014	B-8
vaccine response, reduced antibody titer	0.0337	Looker, *et al.* 2014	B-7
neurodevelopmental: executive function; ADHD	0.0351	Stein *et al.* 2013	B-8
incr total chol., LDL, triglycerides in children, adolescents	0.0618 to 0.0777	Frisbee *et al.* 2010	B-4
increased total cholesterol, LDL, non-HDL, triglycerides	0.08	Steenland *et al.* 2009	B-4
increased uric acid	0.086	Steenland *et al.* 2010	B-4
rheumatoid arthritis	0.113	Steenland, *et al.* 2015	B-7
ulcerative colitis	0.113	Steenland, *et al.* 2015	B-7
increased total cholesterol, VLDL, triglycerides, uric acid	0.428	Sakr *et al.* 2007a	B-4
liver enzymes, elevation of GGT	0.428	Sakr, *et al.* 2007a	B-5
increased total cholesterol, triglycerides	1.03 to 1.90	Olsen *et al.* 2001b, 2003	B-4
increased total cholesterol	1.04 to 1.16	Sakr *et al.* 2007b	B-4
liver enzymes, elevation of AST	1.04 to 1.16	Sakr, *et al.* 2007b	B-5
increased total cholesterol, triglycerides	1.36 to 1.77	Olsen *et al.* 2001c, 2003	B-4
free T4 thyroid hormone decline	2.21	Olsen and Zobel 2007	B-6
increased triglycerides, reduced HDL	2.21	Olsen and Zobel 2007	B-4
liver enzymes, elevation of ALP, ALT, GGT	2.21	Olsen and Zobel 2007	B-5
T3 thyroid hormone elevation	2.21	Olsen and Zobel 2007	B-6
increased total cholesterol, uric acid	4.02	Costa *et al.* 2009	B-4
liver enzymes, elevation of ALP, ALT, GGT	4.02	Costa, *et al.* 2009	B-5

*Derived from Tables B-4 through B-8 in:

US EPA. *Health Effects Support Document for Perfluorooctanoic Acid (PFOA).* Washington, DC; U. S. Environmental Protection Agency, Office of Water, EPA 822-R-16-003, 322 pages, May 2016.

Regulation-Based Risk Management

Much information is available about the unusually low concentrations of PFCs, especially PFOA, that have been shown to be toxic to people. This information has been used to form the basis for promulgating health advisories (Table 7), but not legally enforceable regulations such as Maximum Contaminant Levels (MCLs) under the 1974 Safe Drinking Water Act (Public Law 93-523). Data on PFCs are less detailed for cancer than non-cancer effects. Accordingly, health advisories primarily have been based upon extrapolating to drinking water the PFC concentrations in blood serum at which non-cancer effects have been observed to occur.

Cancer. PFOA has been associated causally with testicular and renal (kidney) cancer based upon limited evidence in people (US EPA 2014)[59]. The United Nations International Agency for Research on Cancer (UN IARC) Working Group classified PFOA in Group 2B, *"possibly carcinogenic to humans."* Evidently, limited quantitative data on human exposure and on subsequent cancer incidence together have precluded elucidation of the dose-response curve in the low-dose range in sufficient detail for use in quantitative health risk assessment. Accordingly, regulation based upon carcinogenicity may be forthcoming with more detailed quantification of needed dose-response parameters.

Non-Cancer effects. ATSDR (2015)[60] *"has derived an intermediate-duration oral MRL* [Minimal Risk Level] *of* $2x10^{-5}$ *mg/kg/day* [mg/kg d] *for PFOA based on a BMDL* [benchmark dose level] *of* $1.54x10^{-3}$ *mg/kg/day* [mg/kg d] *for increased absolute liver weight in monkeys administered PFOA via a capsule for 26 weeks (Butenhoff et al. 2002). The BMDL was estimated using serum PFOA levels as a dose metric; a HED* [human equivalent dose] *was estimated using an empirical clearance model. The* $BMDL_{HED}$ *was divided by an uncertainty factor of 90 (3 for animal to human extrapolation with dosimetric adjustment, 10 for human variability, and 3 for database deficiencies, particularly the lack of developmental and immunological studies in monkeys."*

[59] **US EPA.** *Health Effects Document for Perfluorooctanoic Acid (PFOA).* Washington, DC; U. S. Environmental Protection Agency, EPA 822R14001, 268 pages, February 2014;

[60] **ATSDR.** *Draft Toxicological Profile for Perfluoroalkyls.* Atlanta, Georgia; U. S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 574 pages including appendices, http://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf, supersedes May 2009 draft profile and *"any previously released draft or final profile,"* August 2015;

Table 7. Health Advisories and Related Benchmarks for Perfluoroalkyl Compounds*

New Jersey**	40 ppt	PFOA	"chronic (lifetime)"
New Jersey**	10 ppt	PFNA	interim specific groundwater criterion
Vermont***	20 ppt	PFOA	chronic
US EPA, national	400 ppt	PFOA	short-term
US EPA, Region 2	100 ppt	PFOA	chronic
US EPA, national	70 ppt	PFOA + PFOS	lifetime
US EPA, national	20 ppt	PFOA	Minimum Reporting Level (MRL)

*__PFNA__: perfluorononanoic acid; __PFOA__: perfluorooctanoic acid; __PFOS__: perfluorooctane sulfonate;

**__NJ DOH.__ *Drinking Water Facts: Perfluorinated Chemicals (PFCs) in Public Water Systems.* Trenton, New Jersey Department of Health, Environmental and Occupational Health Surveillance Program, http://www.nj.gov/health/eohs/pfc_in_drinkingwater.shtml;

***__VT DOH.__ *PFOA (Perfluorooctanoic Acid).* Burlington, Vermont Department of Health http://healthvermont.gov/enviro/pfoa.aspx, 7 June 2016.

ATSDR (2015, page 435) also reported: *"EPA has not derived reference dose (RfD) or reference concentration (RfC) values of perfluoroalkyl compounds."* The RfD and RfC are limits placed upon exposure via ingestion and inhalation, respectively. They differ significantly, in that the RfD is expressed in units of daily intake per unit of body weight [for example, mg/(kg d)], whereas the RfC is expressed as an airborne concentration (for example, mg/M^3). Both units are derived based upon many assumptions, critically including absorption efficiency (via the digestive or respiratory tract) and the relative source contribution of each exposure route.

In 2009 the U. S. EPA established a Provisional Health Advisory of 0.4 ppb (400 ng/L = 400 ppt) for short-term exposure (up to about two weeks) to PFOA in drinking water. As a concentration rather than an intake dose, the health advisory value is analogous to an RfC. As with RfC derivations, a critical parameter for derivation of the health advisory value was the relative source contribution, which is the share of total PFOA exposure assumed to be attributable to drinking water. EPA, in accordance with policy, assumed that 80 percent of total exposure to PFOA originates from non-drinking water pathways, and that 20 percent of total exposure is attributable to drinking water. In the Village of Hoosick Falls, other sources have been reported, including PFOA containers disseminated to the community and airborne sources of PFOA emitted from manufacturing processes. Such widespread dissemination, combined with the stability of PFOA in the environment, gives rise to the likelihood of biomagnification in the food chain, affecting garden vegetables, fish, and (hunted) birds consumed by residents. Children playing in soil contaminated with PFOA might consume it via hand-to-mouth contact, which tends to be exacerbated among people (children and adults) who habitually mouth non-food items, in a condition known as 'pica'. Other exposure pathways of potential significance in the Village and elsewhere include cooking, bathing, and showering.

Inasmuch as most residential exposure to substances via drinking water occurs for years rather than weeks, EPA Region 2 in January 2016 augmented EPA's 400-ppt short-term exposure advisory for PFOA by issuing an interim chronic health advisory value of 0.1 ug/L (100 ng/L = 100 ppt)[63]. Chronic exposure refers to an exposure period from a year, more or less, to a period of years, up to exposure for a lifetime, in health risk assessment typically assumed to be 70 years. This interim value was effective during deliberations over a 'final' health advisory value for chronic exposure to PFOA. In April 2016 EPA promulgated its final "lifetime" health advisory value, 70 ppt as the sum of the concentrations of PFOA and PFOS.

[63] **US EPA.** *Statement on Private Wells in the Town of Hoosick and Village of Hoosick Falls, NY.* U. S. Environmental Protections Agency, 1 page, 28 January 2016: *"The EPA is developing a lifetime health advisory level for PFOA. While this work continues, the EPA recommends that people in the Town of Hoosick and the Village of Hoosick Falls who have private wells at which PFOA has been found to be present at a level greater than 100 parts per trillion not use that water for drinking or cooking…"*

Superfund designation. The SGPP McCaffrey Street site acquired New York State Superfund status in 2016 and, via letter of 11 February[64], potentially responsible parties (SGPP and Honeywell) were ordered to enter into a consent agreement for site remediation. As of this writing, U. S. EPA classification of PFOA as a hazardous substance has not occurred, but would qualify the site for inclusion on the Federal Superfund's National Priority List (NPL).

Technology-Based Risk Management

Technology-based risk management includes mitigation and remediation technologies. Remediation of groundwater contamination emanating from a particular source is likely to include pumping to create a 'cone of depression', thereby reversing outward flow of groundwater from the source. Instead, groundwater flow in the vicinity would converge toward the source, at which continued pumping gradually would abate the contamination, eventually all the way to the cleanup goal. Treatment of pumped groundwater could include use of granular activated carbon (GAC) filtration for removal of PFCs and other substances.

When drinking water is contaminated with PFCs, the main mitigation technology used to remove them has been GAC filtration. Filtration units marketed for homes that are supplied by individual private wells, however, may include both GAC and reverse osmosis modules connected in series. GAC treatment has been used for municipal water treatment systems such as the system serving the Village of Hoosick Falls.

The GAC system for the Village consists of two carbon beds operating in series. A performance standard of 20 ng/L (20 ppt) initially was proposed for the Village, on the premise that a more stringent performance standard would be unnecessary and/or infeasible. This claim is false based upon abundant experience in the operation of GAC filters for removal of PFOA, both in the U. S. and abroad. For example, PFOA routinely is removed from water supplied by the Little Hocking Water Association, a rural user-owned water system in Washington County, Ohio. This facility's GAC system is especially notable because, like the Village's, the Little Hocking system is configured with two carbon bed units operating in series.

Dual units of two in-series carbon beds operate in the Little Hocking system. PFOA generally is undetected in finished water produced by each of the two units. The method detection limit (MDL) for PFOA is indicated with each reported sample value, and most commonly it is the nominal MDL of 1.7 ppt for U. S. EPA analytical Method 537, which is used widely, including in the Village of Hoosick Falls.

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[64] **NYS DEC.** *Demand related to Hoosick Falls Perfluorooctanoic Acid (PFOA) Contamination.* Albany, New York State Department of Environmental Conservation; Deputy Commissioner Thomas Berkman to Edward Canning (Global Environmental Health and Safety Manager, Saint-Gobain Performance Plastics) and D. Evan Van Hook (Corporate Vice President, Honeywell International, Inc.), 4 pages plus Exhibits (6 pages), 11 February 2016;

EPA Method 537 invites procedural alterations to reduce its MDL if desired. That is, a lower MDL than 1.7 ppt may be applicable to routine PFOA analysis in finished drinking water. The Little Hocking database, for example, includes multiple samples in which PFOA was undetected at an MDL of 1.0 ppt. If performance at that more sensitive level can be achieved in the Little Hocking system, it unquestionably can be achieved in the Village of Hoosick Falls.

GAC technology is highly effective. Even so it requires close monitoring to quantify the rate at which PFC removal efficiency declines as the adsorptive surface area of the constituent carbon particles gradually but inevitably is exhausted. This raises the inter-related issues of performance standards to which treatment systems must be designed, drinking water sampling frequency, and PFC detection and Minimum Reporting Levels (MRLs). U. S. EPA MRLs for unregulated substances in drinking water are set forth in a document known as UCMR 3[65] and MRLs for six PFCs are listed in Table 3. EPA's MRL for PFOA, for example, is ≤20 ppt.

[65] **US EPA.** *The Third Unregulated Contaminant Monitoring Rule (UCMR 3) - Fact Sheet for Assessment Monitoring of List 1 Contaminants.* Washington, DC; U. S. Environmental Protection Agency, Office of Water, 4 pages, EPA 815-F-12-003, https://www.epa.gov/ground-water-and-drinking-water, May 2012;

Discussion, Conclusions, and Recommendations

PFC Levels in Drinking Water and Blood Serum

PFCs, most notably PFOA and PFOS found in drinking water in the ppt range at which they are toxic, reveal the need for routine monitoring, aggressive cleanup, and promulgation of enforceable regulation to control human exposure, prevent disease, and help to clarify accountability, thereby preventing similar incidents elsewhere. PFOA was introduced into commerce in the 1940s when stringent environmental regulation was non-existent and routine monitoring of ppt-range residues in environmental media infeasible. Historical data on PFC concentrations typically are unavailable. In view of its long industrial history, however, the Village of Hoosick Falls appears to have experienced unabated exposure to PFOA over a period of years at least, and more likely decades to a century. The time profile of exposure might be inferred from sampling for PFCs emitted to the atmosphere and deposited to the ground, from hydrogeological investigations to quantify PFC entry into groundwater, from data on groundwater direction and flow by depth, and from studies of PFC concentrations at increasing distance downstream (and downwind) of the Saint-Gobain Performance Plastics facility.

By comparison with the Village's apparently long exposure history, the time required to reach a steady-state level of PFOA in the blood plasma was ≤17 days in the Lau, *et al.* (2006) high-exposure mouse study used to derive EPA's initial (400-ppt) Provisional Health Advisory. The time to achieve steady-state serum concentrations in people exposed to environmental PFOA levels prevailing in the Village is unknown, but likely to be a small fraction of exposure duration. Once a steady state is attained, however, concentrations in serum will not decline unless and until exposure ceases or substantially abates. In the absence of exposure, the half-time for human elimination of PFOA, which is not metabolized appreciably, is approximately four years (as documented earlier). That means that exposure via drinking water and other sources is subject to a multiplier effect, in which mechanisms of substance toxicity may continue acting for multiples of the exposure duration, for much or all of a lifetime, even after exposure is terminated completely.

In short, PFOA exhibits a 'perfect storm' of troubling properties: essentially infinite lifetime in the environment, resistance to human metabolism, bioconcentration in the food chain, transmissibility to infants via breastfeeding, years-long excretion half-time in the human body, and causation of human cancer and non-cancer effects. These properties, along with widespread use in manufacturing Teflon and other widely used products of modern society, have resulted in PFCs becoming ubiquitous contaminants in the global environment. As a result they also have been detected ubiquitously in blood serum in the U. S. sampled around 2000,[66]

[66]**Calafat, A. M., Z. Kuklenyik, J. A. Reidy, *et al.*** *Serum concentrations of 11 polyfluoroalkyl compounds*

with median concentrations of 5 ng/mL (ppb) for PFOA and 30 ppb for PFOS. Concentrations in the serum of children have been reported generally to be higher than in adults.[67]

Table 6 lists PFOA concentrations in blood serum that EPA reports as *"associated"* with specific adverse health effects in people. The concept of 'association' encompasses relationships running the full gamut of the degree of certainty of causality, from causal to non-causal ('casual'), for example: 'proven cause', 'known cause', 'presumptive cause', 'probable cause', 'likely cause', and 'possible cause'. Many if not most of the studies included in Table 6 are supported by animal bioassays or other data and, accordingly, were included based upon credible public comments or peer review recommendations[68].

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in the U.S. population: data from the national health and nutrition examination survey (NHANES). Environmental Science and Technology, 41: 2237–42, 2007;

[67]**Grandjean, Philippe; and Richard Clapp.** *Perfluorinated alkyl substances: emerging insights into health risks.* New Solutions: A Journal of Environmental and Occupational Health Policy, 25(2) 147–63, 2015;

Kato K; A. M. Calafat, L. Y. Wong, *et al.* *Polyfluoroalkyl compounds in pooled sera from children participating in the National Health and Nutrition Examination Survey 2001–2002.* Environmental Science and Technology, 43: 2641–47, 2009;

[68]**Appendix B: Studies Evaluated Since August 2014**

The tables that follow [including Tables B-4 through B-8] *identify the papers that were retrieved and reviewed for inclusion following the August 2014 peer review for the draft PFOS Health Effects Support Document. The papers listed include those recommended by the peer reviewers or public commenters, as well as those identified from the literature searches between the completion of the peer review draft and December 2015…*

The criteria utilized in determining the papers that were included in the HESD after the peer review and presented in the Background were the following:

1. *The study examines a toxicity endpoint or population that had not been examined by studies already present in the draft assessment.*
2. *Aspects of the study design, such as the size of the population exposed or quantification approach, make it superior to key studies already included in the draft document.*
3. ***The data contribute substantially to the weight of evidence for any of the toxicity endpoints covered by the draft document.***
4. *There are elements of the study design that merit its inclusion in the draft assessment based on its contribution to the mode of action or the quantification approach.*
5. *The study elucidates the mode of action for any toxicity endpoint or toxicokinetic property associated with PFOA exposure.*
6. *The effects observed differ from those in other studies with comparable protocols.*

All of the studies included in Table 6 report on health effects that fall into one or more of five well-documented *categories* of PFOA adverse health effects. These health effect categories were explicated earlier (in the *Results* section):

--serum lipids, uric acid;
--immunotoxicity,
--thyroid disease,
--endocrine disruption, and
--reproductive and developmental outcomes.

The health effects are grouped within their relevant health effect categories in Table 6a, and form a strong basis for using Table 6b as a basis for comparisons of individuals' PFOA serum levels with the (presumptive) causative serum levels reported in the table.

A concept in science generally, and in epidemiology specifically[69], is that of the default assumption which, in experiments, also may be termed the 'null hypothesis'. The weight of evidence subtly shifts the default assumption, which is the assumption that is most likely to be true based upon available evidence. Progress in science occurs when a null hypothesis is tested, whether or not it is refuted, but usually more so if it is refuted. In short, with respect to the studies included in Table 6, PFOA must be regarded as *at least* the presumptive cause of the reported 'associated' adverse health effects.

In public health policy, substances differ from people in our vaunted legal system: as a precaution, substances must be shown, not presumed, to be innocent. A corollary is that health effects cannot scientifically, and should not be dismissed as mere associations with high PFOA levels, without ominous implications for the affected individuals, notwithstanding a recent fact sheet issued by NYS DOH (2016)[70] regarding its biomonitoring (serum PFOA) program.

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[69] **Hill, A. B.** *The environment and disease: association or causation?* Proceedings of the Royal Society of Medicine, 58:295-300, 1965;

[70]**NYS DOH.** *PFOA Biomonitoring (Blood Sampling) Program.* Albany, New York State Department of Health, 5 pages, http://www.health.ny.gov/environmental/investigations/hoosick/docs/pfoa_blood_sampling_q_and_a_8-1-16.pdf, 1 August 2016:

> ***4. What do the studies show about health effects, cancer, and PFOA exposure?*** *Some human health studies have found associations between PFOA exposure and health effects. Others have not. The studies that found associations were not able to determine with certainty if the health effects were caused by PFOA or some other factors. These studies did not show that PFOA caused diseases…*
>
> *An association does not mean that one thing caused the other. For example, people with blue eyes tend to be taller than people with other eye colors. This is an association. However, eye color does not cause people to be taller and height does not cause people to have blue eyes. Northern European*

The NYS DOH (2016) fact sheet regarding its biomonitoring program in the Village of Hoosick Falls fails to acknowledge the high probability that individuals with elevated serum PFOA probably have elevated risk of experiencing adverse health effects with which PFOA is associated, such as those reported in Table 6[71]. The fact sheet diligently explicates the meaning of 'association', most notably distinguishing it from 'causation'. Regarding future risk, however, the fact sheet includes excessively disarming statements, such as:

> *"Individual results only provide exposure information and are not cannot* [sic] *be used to determine of* [sic] *whether a person's current illness is due to PFOA or if a future illness is likely to result from PFOA…*
>
> *Future studies of PFOA exposure by scientists, public health experts, and government agencies may provide more definitive information on health effects. Knowledge of an individual's exposure may be helpful in applying this information in the future."*

The NYS DOH fact sheet likewise is excessively disarming in presenting a comparison of *"Average PFOA Levels in Blood"* in eight populations, where the lowest is the U. S. population: 2 ug/L (ppb). The highest average PFOA level is reported in 3M workers in Decatur, Alabama: 1125 ug/L (ppb). By misleading comparison, *"Hoosick Falls area, NY (all participants)"* are reported to have an average PFOA level of 23.5 ug/L. Although this is still nearly 12 times the U. S. average, it understates the magnitude of the serum PFOA elevation caused by PFOA contamination of groundwater emanating from the Saint-Gobain facility. To capture the magnitude of the resulting serum PFOA elevation, NYS DOH should report the

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ancestry is known to be associated with blue eyes, and Northern European ancestry is associated with being relatively tall. But genetics alone do not cause increased height. Other factors, such as nutrition, are important as well" [emphasis added].

[71] **Ibid**:

> ***What do the studies show about health effects, cancer, and PFOA exposure?*** *Some human health studies have found associations between PFOA exposure and health effects. Others have not. The studies that found associations were not able to determine with certainty if the health effects were caused by PFOA or some other factors. These studies did not show that PFOA caused diseases…*
>
> *An association does not mean that one thing caused the other. For example, people with blue eyes tend to be taller than people with other eye colors. This is an association. However, eye color does not cause people to be taller and height does not cause people to have blue eyes. Northern European ancestry is known to be associated with blue eyes, and Northern European ancestry is associated with being relatively tall. But genetics alone do not cause increased height. Other factors, such as nutrition, are important as well"* [emphasis added].

average serum PFOA level in current residents until recently consuming the PFOA-contaminated public water supply, which is drawn from groundwater adjacent to the Saint-Gobain facility. Instead, the reported average is diluted via inclusion of the relatively low serum PFOA levels of biomonitoring program participants who are former residents, and people who have private wells[72], most of which are located at relatively great distance from the Saint-Gobain facility.

Though PFCs persist in the environment, their concentrations in human blood serum declined significantly in the years since 2000,[73] possibly reflecting their gradual phase-out from U. S. commerce, completed in 2015. Thus, the public health benefit of phasing out PFCs appears to be evident based upon blood serum as an exposure marker, but this benefit clearly is unavailable to communities such as the Village of Hoosick Falls that are situated near a continuing source of PFC contamination. Yet, having been phased out of commerce, PFCs are regulated only by unenforceable health 'advisories', whereas persistent environmental contamination with PFCs would suggest the need for enforceable limits, especially in surface water and groundwater used for direct human consumption, gardening, and agriculture.

As a further concern, NYS DOH's blood sampling program for Hoosick residents and former residents has resulted in disclosure to participants of their personal PFOA serum levels, and in public disclosure of the range of PFOA serum concentrations found. NYS DOH, however, has failed to disclose to individuals or to the public the range of serum concentrations of other PFCs. Although PFOA has been the predominant PFC detected in water in the Village of Hoosick Falls, only empirical data can reveal whether PFOA likewise is the predominant PFC in blood serum. Residents and former residents may have been exposed to PFCs environmentally, possibly via airborne sources emanating from manufacturing processes at the Saint-Gobain Performance Plastics facility. PFOA levels in serum therefore should be viewed in the context of related compounds that are likely also to be present. Moreover, distribution of PFCs in serum is a valuable marker of overall PFC exposure. Finally, SGPP employees might have occupational exposure to other PFCs, not just more exposure to PFOA than non-occupational residents. NYS DOH therefore should expand the scope of its disclosures to individuals and to the public regarding PFCs other than PFOA.

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[72] *"The level shown for PFOA in blood for the Hoosick Falls area is the geometric mean and is based on test results for 2,081 participants including people using Village water, people using private wells, people who work in the area, and former residents."*

[73] **Kato, K; L. Y. Wong, L. T. Jia, *et al.*** *Trends in exposure to polyfluoroalkyl chemicals in the U.S. population: 1999–2008.* Environmental Science and Technology, 45: 8037–45, 2011;

Olsen, G. W.; C. C. Lange, M. E. Ellefson, *et al.* *Temporal trends of perfluoroalkyl concentrations in American Red Cross adult blood donors, 2000–2010.* Environmental Science and Technology, 46: 6330–38, 2012;

PFC Regulation via Advisories

The 2009 EPA health advisory value of 400 ppt for PFOA in drinking water, though legally unenforceable, nonetheless was influential in guiding the advice provided by some officials on the issue of whether or not residents of the Village of Hoosick Falls should consume their PFC-tainted drinking water. Indeed, the unenforceability of the health advisory seems to have precipitated official reversion to a far less stringent, but enforceable, standard of 50,000 ppt. Specifically, in 2015 the Village Newsletter[74] reported on advice sought by the Village from the New York State Department of Health. The response, received from the Rensselaer County Department of Health on 12 January 2015, read in part: *"Samples taken from the water supply wells on October 2 and November 4, 2014 were found to contain PFOA at levels ranging from 0.17 micrograms per liter (ug/L) to 0.54 ug/L… These levels are below the New York State unspecified organic contaminant public drinking water standard of 50 ug/L"* (50,000 ng/L = 50,000 ppt; emphasis added).

The EPA health advisory in fact was essentially irrelevant because it was intended to apply only to short-term exposure durations of up to about two weeks, commensurate with the 17-day exposure duration used in the Lau, *et al.* (2006) study on which the advisory was based.[75] This exposure duration might be commensurate with a typical vacation, but not with residential exposure, which typically is chronic (a year or, more often, multiple years). Accordingly, by the end of January 2016, EPA Region 2 promulgated a health advisory of 100 ppt for chronic exposure to PFOA in drinking water in Region 2.

The 2009 Health Advisory also was challenged by Grandjean and Budtz-Jørgensen (2013) based upon concentrations of PFCs in blood serum vs. immunological effects in children of the Faroe Islands (near Denmark) as the critical toxicological end point.[76] Their conclusion suggests that an appropriate PFOA limit in drinking water would be in the range of just 1 ppt: *"when the results are converted to approximate exposure limits for drinking water, current limits appear to be several hundred fold too high. Current drinking water limits therefore need to be reconsidered."*

Similarly, Grandjean and Clapp (2015) found that *"carcinogenicity and immunotoxicity*

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[74] **Village of Hoosick Falls.** *Village Water Quality Update,* page 3 of 14 pages*;* 14 September 2015;

[75] **Lau, C; J. R. Thibodeaux, R. G. Hanson, *et al*.** *Effects of perfluorooctanoic acid exposure during pregnancy in the mouse.* Toxicological Science, 90(2): 510-8, 2006;

On 14 January 2016 a public meeting was held in the Village of Hoosick Falls, at which I alerted attending EPA Region 2 officials of the irrelevance of the EPA Provisional Health Advisory.

[76] **Grandjean, Philippe; and Esben Budtz-Jørgensen.** *Immunotoxicity of perfluorinated alkylates: calculation of benchmark doses based on serum concentrations in children.* Environmental Health, 12(35):1-7, http://www.ehjournal.net/content/12/1/35, 2013;

now appear to be relevant risks at prevalent exposure levels. Existing drinking water limits are based on less complete evidence than was available before 2008 and may be more than 100-fold too high[77]*."* A confirmatory study also was published, following up previous work in the Faroe Islands, involving children age 13 years[78]. At least one publication has suggested the possible need for a PFOA drinking water acceptability concentration that is even below 1 ppt[79].

Recently the U. S. EPA replaced the Region 2 advisory value of 100 ppt by promulgating a new advisory of 70 ppt for "lifetime" exposure to the sum of PFOA and PFOS concentrations in drinking water nationally. Substitution of the term "lifetime," which usually refers to 70 years in health risk assessment parlance, for the previously used "chronic," referring to one year or more, is troubling because it suggests that EPA might regard a (70-times) higher value acceptable for chronic exposure for, say, just one year. Thus, the new 70-ppt 'lifetime' advisory for PFOA + PFOS may be interpreted as being less stringent than the Region 2 'chronic' 100-ppt advisory for PFOA alone.

The latest (PFOA + PFOS) EPA national advisory is supported by description of, at best, a lengthy and uncertain pathway toward enforceable regulation[80]. EPA also has failed to show that its new advisory, even if enforced, is sufficiently stringent to protect public and environmental health. Several support documents[81] were found on EPA's website, but none

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[77] **Grandjean, Philippe; and Richard Clapp.** *Perfluorinated alkyl substances: emerging insights into health risks.* New Solutions: A Journal of Environmental and Occupational Health Policy, 25(2) 147–63, 2015;

[78] **Grandjean, Philippe; Carsten Heilmann, Pal Weihe, Flemming Nielsen, Ulla B. Mogensen, and Esben Budtz-Jørgensen.** *Serum vaccine antibody concentrations in adolescents exposed to perfluorinated compounds.* Environmental Health Perspectives, Advance Publication, http://dx.doi.org/10.1289/EHP275, 24 pages, 9 August 2016;

[79] **EWG; Bill Walker and David Andrews.** *Teflon chemical unsafe at smallest doses – EPA's "safe" level is hundreds or thousands of times too weak.* Washington, DC; Environmental Working Group, www.ewg.org, 8 pages, August 2015;

[80] **US EPA.** *Fact Sheet: PFOA and PFOS Drinking Water Health Advisories.* Washington, DC; U. S. Environmental Protection Agency, 4 pages, May 2016:

"EPA is evaluating PFOA and PFOS as drinking water contaminants in accordance with the process required by the Safe Drinking Water Act (SDWA)… [and] *"In accordance with SDWA, EPA will consider the occurrence data from UCMR 3, along with the peer reviewed health effects assessments supporting the PFOA and PFOS Health Advisories, to make a regulatory determination on whether to initiate the process to develop a national primary drinking water regulation."*

[81] **US EPA.** *Health Effects Support Document for Perfluorooctanoic Acid (PFOA).* Washington, DC; U. S. Environmental Protection Agency, Office of Water, EPA 822-R-16-003, 322 pages, May 2016;

US EPA. *Drinking Water Health Advisory for Perfluorooctanoic Acid (PFOA).* Washington, DC; U. S. Environmental Protection Agency, Office of Water, EPA 822-R-16-005, 103 pages, May 2016;

US EPA. *Health Effects Support Document for Perfluorooctane Sulfonate (PFOS).* Washington, DC; U. S.

was linked to the advisory. Failure to link the support documents to the health advisory document has the effect of obscuring EPA's technical justification, and critical comments by peer reviewers and members of the public.

EPA's support document[82] for the 2016 PFOA (and PFOS) drinking water advisory indicates that it is based upon *"a reference dose (RfD) derived from a developmental toxicity study in mice; the critical effects included reduced ossification in proximal phalanges and accelerated puberty in male pups following exposure during gestation and lactation"* (page 9). The mathematics of the derivation are set forth in EPA's support document, including adjustment of animal dosing to equivalent human dosing. Setting aside the issue of the technical merit of the derivation, the choice of the animal study over available human studies, most notably Grandjean, *et al.* (2013),[83] to derive the advisory is questionable and, indeed, was criticized in peer review[84].

The essential issue is that the Grandjean, *et al.* (2013) study would produce a lower health advisory value, which is undisputed by EPA. EPA's basis for the decision to reject the study deserves scrutiny. The study showed that routinely administered childhood vaccinations produced a weaker antibody response among children whose PFC levels in serum were elevated compared with children with lower serum PFC levels. EPA rejected the study because it (and related studies) were confounded by multiple PFCs, and because the incidence of disease among children with weaker antibody response to vaccination was not observed to be elevated[85].

Environmental Protection Agency, Office of Water, EPA 822-R-16-002, 245 pages, May 2016;

US EPA. *Drinking Water Health Advisory for Perfluorooctane Sulfonate (PFOS).* Washington, DC; U. S. Environmental Protection Agency, Office of Water, EPA 822-R-16-004, 88 pages, May 2016;

US EPA. *EPA Response to External Peer Review Comments on EPA Draft Documents: Health Effects Support Document for Perfluorooctanoic Acid (PFOA) and Health Effects Support Document for Perfluorooctane Sulfonate (PFOS).* Washington, DC; U. S. Environmental Protection Agency, Office of Science and Technology, Health and Ecological Criteria Division, 99 pages, May 2016;

US EPA. *Science Guides Public Health Protection For Drinking Water.* Washington, DC; U. S. Environmental Protection Agency, 1 page, May 2016;

[82] **US EPA.** *Drinking Water Health Advisory for Perfluorooctanoic Acid (PFOA).* Washington, DC; U. S. Environmental Protection Agency, Office of Water, EPA 822-R-16-005, 103 pages, May 2016;

[83] **Grandjean, Philippe; and Esben Budtz-Jørgensen.** *Immunotoxicity of perfluorinated alkylates: calculation of benchmark doses based on serum concentrations in children.* Environmental Health, 12(35):1-7, http://www.ehjournal.net/content/12/1/35, 2013;

[84] **US EPA.** *EPA Response to External Peer Review Comments on EPA Draft Documents: Health Effects Support Document for Perfluorooctanoic Acid (PFOA) and Health Effects Support Document for Perfluorooctane Sulfonate (PFOS).* Washington, DC; U. S. Environmental Protection Agency, Office of Science and Technology, Health and Ecological Criteria Division, 99 pages, May 2016;

[85] **DeWITT COMMENT AND EPA RESPONSE:**

EPA often addresses multiple substances together. Examples include chlorinated dioxins, PAHs, and PCBs, even though nearly all studies of the toxicological effects of each of these groups may be confounded by the presence of multiple members of the group in a particular study. Indeed, EPA's latest health advisory combines PFOA and PFOS. Clearly, an advisory could focus on the sum of all PFCs in addition to the sum of just the two specific PFCs.

EPA interpreted the Grandjean (and related) studies as if they primarily raised the narrow issue of childhood vaccine effectiveness. EPA ignored the broader significance of the Grandjean, *et al.* (and related) studies: that immunosuppression is a serious clinical outcome for anyone, and especially for children. Immunosuppression signifies that the effectiveness of immunosurveillance is reduced. Immunosurveillance is the essential bodily function of maintaining vigilance to detect invading foreign pathogens, and of mounting an antibody attack against foreign cells or against cancer cells, which a healthy immune system would interpret as 'foreign'. Most essentially, immunosurveillance protects children against childhood cancers and against pathogens, whether or not vaccines against them were administered.

EPA did not cite evidence that PFOA (or PFOS, or any PFC) reduces the titer of only a particular vaccination disease target. The reasonable default assumption must be made, therefore, that PFOA-induced (and PFC-induced) immunosuppression is general, not disease-

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Granum, B.; L. S. Haug, E. Namork, *et al.* *Pre-natal exposure to perfluoroalkyl substances may be associated with altered vaccine antibody levels and immune-related health outcomes in early childhood.* Journal of Immunotoxicology, 10:373–9, 2013;

Looker, C.; M. I. Luster, A. M. Calafat, *et al.* *Influenza vaccine response in adults exposed to perfluorooctanoate and perfluorooctane sulfonate.* Toxicological Science, 138:76–88, 2014;

"Any time the Grandjean et al. (2012) findings related to PFCS and vaccine responses are discussed, these references could/should be discussed as well as they report related findings in human populations. Although they also are confounded by multiple PFCs (as was the Grandjean et al. study), they lend additional support to immunotoxicity as an endpoint worthy of consideration. However, it is noted that these references were published after the cutoff date for consideration for inclusion in the document."

EPA Response. *"Both the Granum et al. 2013 and Looker et al. 2014 studies were added to both HESDs [Health Effect Support Documents]. A summary and conclusions write-up was added to the epidemiology section, which discusses the immune function-related findings together."*

Statement in EPA Health Effects Assessment Support Document for PFOA. *"None of the studies demonstrated a clinically recognizable increased risk of infectious diseases as a consequence of a diminished vaccine response. Overall, although these results are not sufficient to establish a causal effect of PFOA exposure on an impaired serological vaccine response, some of the positive associations are striking in magnitude and require replication in independent studies."*

specific. That is, the assumption must be made that failure to observe elevated incidence of the single vaccine disease target among low-antibody titer children is not probative, and therefore not reassuring, regarding PFOA (or PFC) risk of adverse effects on children.

EPA's decision to construe Grandjean, *et al.* (and related studies) narrowly, at the expense of stringency in protecting children's health, must be viewed in the context of EPA's longstanding special mandate regarding children's health, embodied by EPA's Children's Health Risk Initiative.[86] In 1997 the Office of Children's Health Protection was instituted within EPA. Its mission was and remains *"to make children's health protection a fundamental goal of public health and environmental protection… [by] ensuring strong standards that protect children's health…"*

PFC Performance Standards for Water Treatment Facilities

The performance standard of 20 ppt that initially was proposed for the GAC system serving the Village of Hoosick Falls water treatment facility was excessive. Given evidence of a long history of PFOA release in the Village, public health protection requires that the GAC filter performance standard be set at a value that reflects the lowest feasible exposure going forward, with the tandem goals of reducing serum PFOA levels as quickly as possible and preventing disease. These goals are best met by specifically establishing the most stringent feasible performance standard for PFOA in the water supply.

Four primary conclusions are drawn below regarding the performance standard that is appropriate for the GAC filter for the Village of Hoosick Falls:

--1. All routine analysis for PFOA should be conducted via EPA Method 537 and adhere to its nominal method detection level of 1.7 ppt or better; likewise for other PFCs;

--2. All data produced by such analysis should be placed in the public domain,

--3. The initially proposed performance standard of 20 ppt for PFOA in finished water is unacceptably high, as is the MRL published in UCMR 3; and

--4. The GAC unit should be designed to reduce PFOA in finished water to the minimum concentration found to be feasible for routine sampling, which

[86] **US EPA.** *Region 2's Management of Children's Health Risk Initiative and Related Projects.* Office of Inspector General Audit Report, Grant Management, Report No. 2001-P-00002, 129 pages, https://www.epa.gov/sites/production/ files/2015-12/documents/kidshealth.pdf, 30 January 2001;

evidently is in the range of 1.0 to 1.7 ppt based upon experience of the Little Hocking water system in Ohio.

NYS DOH Cancer Cluster Analysis in the Village of Hoosick Falls

Reports of rare cancers and clusters of more common cancers in the Village of Hoosick Falls roughly coincided with discovery of PFOA in drinking water. The New York State Department of Health (NYS DOH) therefore is undertaking a health study to investigate possible cancer clustering, termed *"unusual elevations".*[87] The scope of the NYS DOH community health study should be expanded to include non-cancer effects. The cancer study also should include the following features:

--Adopt a health-protective criterion of statistical significance to trigger further investigation of cancer clusters, rather than 95-percent confidence, to assure that real clusters will not be interpreted as statistical flukes;

--Consider rare cancers, whose incidence is expected to be zero in the small population of Hoosick Falls (about 5,000), not just more common cancers in the Cancer Registry. Reports of multiple types of rare cancers are even more unlikely statistically, unless caused by stressors, and should be considered probabilistically together, not just individually, in isolation;

--Conduct a prospective health risk assessment to supplement retrospective assessment of cancer cases. Elevations of cancer incidence might be statistically insignificant, even in the presence of real cancer causes;

--Incorporate the time dimension into cancer incidence analysis. The time period of the NYS DOH study, 1995 through 2012, should be expanded

[87]**NYS DOH**. *PFOA in Drinking Water in the Village of Hoosick Falls and Town of Hoosick.* Albany, NYS Department of Health, https://www.health.ny.gov/environmental/investigations/hoosick/, access date 16 February 2016:

"The State Health Department will conduct an investigation to see if there are unusual elevations of cancer among Village residents. The investigation will include total cancers and specific types of cancer diagnosed from 1995 through 2012. To accomplish this, the State Health Department will use data from the New York State Department of Health Cancer Registry, which receives reports on all cases of cancer occurring in New York State. The planned start date is 1995 because street address at the date of diagnosis is available in computerized form for all cases starting with that year. The planned end date is 2012 because 2012 is currently the most recent year for which data are available. The State Health Department will produce a report on the findings of the investigation."

using ancillary data. The longer period should be subdivided into time windows to examine possible trends in the appearance of cancer cases, such as individual years as illustrated in Kulldorff, *et al.* 1998)[88];

--Conduct detailed investigations aimed at attributing cancers to specific causes. NYS DOH fails to state the objective of elucidating the cause(s) of *"unusual elevations"* that might be found; and

--Consider anecdotal and other ancillary data, such as documented cancers among coworkers or among pets living in the same household. Animals may be more intimately associated than people with the water, soil, and biota in their outdoor environment. NYS DOH fails to explicate that such potentially probative data will be sought and used.

The standard of 95-percent confidence typically adopted in academic scientific publications, including for cancer cluster identification (Kulldorff, *et al.* 1998), may be inappropriate where human health and human lives are at stake, because it might result in rejection of real cancer clusters that might be, say, only 90 percent certain not to have occurred by chance alone. Classifying a cancer cluster as real may be required to justify measures, such as health monitoring, to protect life and health. Such protective measures should be taken if a cluster probably is real (a common legal standard: *more probable than not),* not just when it is 95-percent certain to be real.

The small size of the population of the Village of Hoosick Falls limits sample sizes, and thereby increases the degree of cancer incidence elevation needed to attain statistical significance and recognize cancer clusters. The small size of the study population, however, can be and should be used to advantage statistically with respect to rare cancers, whose incidence in a small population would be expected to be zero. The occurrence of unusual or rare cancers among Village residents should be accorded due weight. NYS DOH plans to study "*total cancers and specific types of cancer,"* but fails to assure that the specific types will include rare cancers, even if absent from the Cancer Registry, or to describe how rare cancers might be evaluated, specifically, the statistical significance that they might be accorded if found in a small population in which they might be unexpected. Finally, NYS DOH fails to describe how the Agency might interpret multiple types of rare cancers occurring in the Village, where each individually might be unexpected in such a small population, but all of which considered

[88] **Kulldorff, Martin; William F. Athas, Eric J. Feuer, Barry A. Miller, and Charles R. Key.** *Evaluating cluster alarms: a space-time scan statistic and brain cancer in Los Alamos, New Mexico.* American Journal of Public Health, 88(9):1377-80, September 1998;

together might be expected to co-occur so rarely as to demand explanation as a real cancer cluster rather than an inevitable statistical deviation from randomness.

All effects have causes and, specifically, all cancer cases have causes. Investigation of particular populations, such as Village residents and Saint-Gobain Performance Plastics Corporation employees, might reveal active cancer causes, and possibly might rule out inactive causes, even in the absence of any statistical elevation of cancer incidence at all. For example, the occurrence of related cancers among all members of a work team might be attributable to occupational exposure to PFOA, even in the absence of a statistical signal when cases among these coworkers are diluted into the larger population of Saint-Gobain employees, or into the even larger population of Village residents.

Public health professionals, like scientists generally, are accustomed to applying the 95-percent confidence criterion of statistical significance ($P \leq 0.05$). The goal is to be conservative, that is, to protect the body of scientific knowledge from corruption by errors introduced by inadequate stringency. Public health professionals, however, simultaneously are responsible for being conservative in protecting human health and human life. Indeed, the American Statistical Association recently issued a statement to combat pervasive misunderstanding in the scientific, business, and public policy communities of the 95-percent confidence limit and its routine, often inappropriate application.[89]

Being conservative requires giving serious consideration to observed associations that probably are causal rather than casual, or even to associations that only might be causal rather

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[89] **Goodman, Steven N.** *Aligning statistical and scientific reasoning.* Science, 352:1180-1, 3 June 2016;
Wasserstein, Ronald L.; and Nicole A. Lazar. *The ASA's Statement on p-Values: Context, Process, and Purpose.* The American Statistician, 70:2, 129-33, DOI: 10.1080/00031305.2016.1154108, 25 June 2016:

"***Scientific conclusions and business or policy decisions should not be based only on whether a p-value passes a specific threshold.***

Practices that reduce data analysis or scientific inference to mechanical "bright-line" rules (such as "p < 0.05") for justifying scientific claims or conclusions can lead to erroneous beliefs and poor decision making. A conclusion does not immediately become "true" on one side of the divide and "false" on the other. Researchers should bring many contextual factors into play to derive scientific inferences, including the design of a study, the quality of the measurements, the external evidence for the phenomenon under study, and the validity of assumptions that underlie the data analysis. Pragmatic considerations often require binary, "yes-no" decisions, but this does not mean that p-values alone can ensure that a decision is correct or incorrect. The widespread use of "statistical significance" (generally interpreted as "p ≤ 0.05") as a license for making a claim of a scientific finding (or implied truth) leads to considerable distortion of the scientific process."

than casual. Public health professionals cannot overlook a cancer cluster, for example, because it is only 90 percent likely to be real rather than a statistical fluke. In statistics terms, the conflict is between Type 1 vs. Type 2 errors: rejecting a true null hypothesis (for example, a real cancer cluster is not recognized) vs. accepting a false null hypothesis (for example, a statistical fluke is interpreted as a real cancer cluster).

The conflict between conservatism in the interest of academic science vs. public health protection has not always been resolved in favor of the latter. Investigating brain cancers in Los Alamos, New Mexico, Kuldorff, *et al.* (1998),[90] using a widely accepted statistical program called SaTScan, found that perceived clusters actually were statistical flukes: *"The community was informed that such a finding could easily have resulted from random fluctuation in the incidence of a rare disease within a small population… With adjustment for age, sex, and race, the most likely cluster is in the Albuquerque-Santa Fe area during 1985 through 1989… With a P value of 0.074* [92.6 percent confidence limit]*, the cluster is not statistically significant"* (pages 1378-9). Even so, it might have been real; it might have been caused by an environmental stressor, such as radioactivity of recent vintage, or radioactive residues dating back to the era of the Manhattan Project at Los Alamos.

In the case of the Village of Hoosick Falls, a strictly statistical approach narrowly focusing on incidence data seems fraught with the peril of overlooking possible clusters that are worthy of further, detailed investigation. The challenge after recognizing a cluster is attributing a cause or probable cause to it, if possible. This is another function of further, detailed investigation. In short, suggestive data should be investigated further, in detail, to avoid overlooking cancer clusters and cancer cluster causes.

Setting Enforceable PFC Regulations for the Nation

Revise Reporting Limits for PFCs. Reporting limits for unregulated substances are set forth in a U. S. EPA publication nicknamed UCMR-3[91]. Determination of safe levels of PFCs in water, however, is underway, not completed. Until completion, a conservative approach to PFC reporting is appropriate. UCMR-3 therefore should be updated to specify reporting limits for PFCs that are identical to EPA Method 537 detection limits for PFCs. Higher reporting limits eventually might be justified but, until then, they are unjustified and potentially harmful

[90] **Kulldorff, Martin; William F. Athas, Eric J. Feuer, Barry A. Miller, and Charles R. Key.** *Evaluating cluster alarms: a space-time scan statistic and brain cancer in Los Alamos, New Mexico.* American Journal of Public Health, 88(9):1377-80, September 1998;

[91] **US EPA.** *The Third Unregulated Contaminant Monitoring Rule (UCMR 3) - Fact Sheet for Assessment Monitoring of List 1 Contaminants.* Washington, DC; U. S. Environmental Protection Agency, Office of Water, 4 pages, EPA 815-F-12-003, https://www.epa.gov/ground-water-and-drinking-water, May 2012;

because they can hide PFCs detected in water at concentrations below the current reporting limit that still might be found to be unsafe as a result of deliberations that are underway.

Revise basis for PFOA drinking water health advisory. The PFOA component of the most recent U. S. EPA advisory is based upon animal bioassay data rather than human immunosuppression studies as previously described, most notably in children. EPA's justification fails, as also described earlier. If more persuasive reasoning were available, presumably EPA would have applied it. Accordingly, EPA should derive its drinking water advisory based upon the human immunosuppression studies, unless the Agency indeed can justify its contrary approach using more persuasive reasoning.

Issue drinking water health advisories for more PFCs. EPA's most recent advisory addresses PFOA and PFOS, but not the suite of four additional PFCs that are measured routinely via Method 537, and not the numerous additional PFCs to which people might be exposed in their drinking water and/or environmentally. Accordingly, EPA should expand the scope of advisories for PFCs to include at least those that are routinely measured via Method 537, and possibly additional PFCs as well. Toward this goal, EPA should consider structure-activity relationships (SARs) to the maximum extent justifiable given the available data.

SARs may be discerned qualitatively and possibly also quantified, producing either qualitative or quantitative SARs for PFCs, as exemplified by Hagenaars, *et al.* (2011) [92]. In either case SARs are derived based upon the premise that substances exhibiting similar chemical structure (structural analogs) often also exhibit similarities in other properties. This may make them useful commercially, resulting in substitutions of structural analogs when regulations preclude use of an analog that is in use, but then is banned for use. Structural analogs, however, also may exert similar toxic effects, which makes them dangerous to introduce into commerce without prior safety testing. Accordingly, EPA's approach to expanding the scope of its PFC health advisories should be pro-active, with maximum justifiable use of SARs.

Promulgate enforceable regulations for PFCs. PFOA and other PFC risks may be managed, retrospectively, via PFC classification as hazardous substances, and PFC site inclusion among State and Federal Superfund sites. Available data also support creation of enforceable regulations for PFOA and other PFCs to manage risks prospectively. EPA's most recent health advisory for "lifetime" exposure to the sum of PFOA and PFOS in drinking water, however, is supported by description of, at best, an uncertain and lengthy pathway toward enforceable

[92] **Hagenaars A.; L. Vergauwen, W. De Coen, and D. Knapen.** *Structure-activity relationship assessment of four perfluorinated chemicals using a prolonged zebrafish early life stage test.* Chemosphere, 82(5):764-72; doi:10.1016/j.chemosphere.2010.10.076; Epub 15 December 2010; January 2011;

regulation. Such regulations potentially should include promulgating primary drinking water standards for PFCs under the Safe Drinking Water Act, and establishing cleanup targets under Superfund and other laws.

Summary. The present investigation reveals that EPA has issued three successive health advisories for PFOA in drinking water, moving from a 'sub-chronic' exposure value of 400 ng/L to a 'chronic' value of 100 ng/L and, most recently, to a (PFOA + PFOS) 'lifetime' value of 70 ng/L. The present investigation also concludes that EPA has failed to show that its latest advisory, even if enforced, is sufficiently stringent to protect public and environmental health. The process of successive approximation toward an enforceable national standard must be concluded, and a more appropriate, enforceable value identified and promulgated forthwith. Available data explicated in *Findings* support the following U. S. EPA actions:

--Update UCMR-3 to incorporate Method 537 MDLs for PFCs,

--Revise the PFOA drinking water health advisory by basing it on immunosuppression, most notably as documented in children,

--Issue drinking water health advisories for more PFCs,

--Designate PFCs as hazardous substances and PFC-contaminated sites as eligible for inclusion in the Federal Superfund's NPL; and

--Promulgate enforceable national regulations/standards for PFOA and other PFCs in environmental media such as water and soil.

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