C-8

Perfluorooctanoic acid

Perfluorooctanoic acid, commonly known as C-8, is also called PFOA and/or APFO

A 2006 C-8 Physician Reference

Ohio Department of Health

2013 UPDATE: The C-8 Physician Reference document was created in 2006 for physicians and other healthcare providers. Since the creation of this document, several activities have taken place as a result of the C8 Health Project class action lawsuit settlement. For more information on the new developments, visit: http://www.odh.ohio.gov/odhprograms/eh/hlth_as/FactSheets.aspx and click on the C8 Fact Sheet and C8 Science Panel Probable Links documents.

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C-8 Quick Facts
Questions & Answers

Q: I have seen C-8's ammonium salt, ammonium perfluorooctanoic acid (APFO) addressed in the literature. Are PFOA/C-8 and APFO the same thing?
A: ***Actually, APFO = C-8 and PFOA = C-8 acid. The term "C-8" is often used interchangeably between the two compounds. APFO is used in the manufacturing process for polytetrafluoroethylene, including some Teflon® brand products. APFO readily disassociates into PFOA in the human body and environment. To simplify, we use C-8 throughout our documents.***

Q: What is known and not known about the toxicology of the chemical perfluorooctanoic acid (C-8)?
A: ***Currently there are significant uncertainties regarding the toxicology and human health effects of C-8. Several concurrent activities are underway, as described in the 2006 C-8 Physician Reference document, to help address some of these uncertainties and data gaps.****

Q: Are there any human health conditions related to C-8 levels in the blood?
A: ***Federal and state public health officials do not know what human health conditions, if any, are related to C-8 blood levels and perhaps will not know for some time. There are major unresolved human health concerns including potential carcinogenicity of C-8 and the association of the chemical with developmental issues.****

Q: Are there any recommended changes in patient care due to the presence of C-8 in their blood?
A: ***In the interim, there are no recommended changes in patient care due to the presence of C-8 in their blood.****

Q: Are there any preventative care measures I can recommend for my patients?
A: ***A particular precautionary risk mitigation measure would be to avoid consuming a C-8 contaminated public water supply or private well water in known areas of contamination.****

Q: How should I manage a patient with a "high" C-8 blood level in the long-term?
A: ***Because there are no human health data currently available that link specific C-8 levels in blood with human health problems and/or the likelihood of the development of disease in the future, no specific patient management protocols for those with high C-8 blood level results are recommended at this time.****

Q: Are there specific diagnostic tests I should order annually/semiannually to be more alert to certain medical issues that might arise?
A: ***No specific diagnostic tests are recommended at this time for patients with C-8 exposures. DuPont's studies, which are ongoing, have found elevated levels of total cholesterol and triglycerides among workers exposed to high levels of C-8, but no indication that C-8 was the cause of these increased serum cholesterol and triglycerides.****

Q. Do exposures to C-8 cause cancer?
A. ***We do not know if exposures to C-8 cause cancer in humans. The majority of the U.S. EPA Science Advisory Board recommended that C-8 be designated as "likely to be carcinogenic in humans." This is based on the EPA classification of carcinogenic chemicals that are carcinogenic in more than one species, sex, strain, or exposure route, with or without evidence of carcinogenicity in humans. The Board recommended that the Agency conduct risk assessments on all of the C-8-related tumor types found in mice and rats.****

Q: Should caregivers use water contaminated with C-8 to prepare infant formula or food?
A: ***The Agency for Toxic Substances and Disease Registry (ATSDR) is currently writing a public health consultation to address the above contaminated water and infant formula/food question in further detail. Until the ATSDR's public health consultation is finalized, the Ohio Department of Health proposes a preventative approach, suggesting caregivers try to reduce their infant's exposure to C-8 contaminated water when preparing infant formula and food. To reduce exposure, both infant formula and food should be made with an alternative water source such as bottled water or the public-supplied water once treatment systems are installed and operating. Note: Public water supplies are fluorinated -- if bottled water is used for making baby formula, caregivers should consult their pediatrician about supplemental dietary fluoride.***

Q: Should mothers that live in the areas of C-8 groundwater contamination breastfeed their infants?
A: ***Preliminary research indicates that PFCs (*perfluorochemicals*) may not be as prevalent in human milk as they are in serum. More than two decades of research have established that breast milk is perfectly suited to nourish infants and protect them from illness. In the presence of the uncertainty about the PFCs and breastmilk, and the very well established benefits of breastfeeding, the Ohio Department of Health recommends that potentially C-8 exposed mothers continue to breastfeed their children. ATSDR is currently writing a public health consultation that considers the above breast milk and nursing question.****

Q: How should I advise patients who express concern about using Teflon® and other non-stick cookware?
A: ***Teflon® and other trademarked products are not C-8. C-8 is used during the application of non-stick coatings to cookware and other non-stick, non-stain coated products. At the present time, EPA does not believe there is any reason for consumers to stop using any consumer or industrial related products that contain C-8.***

Q: Where can I get more information?
A: ***To view the complete 2006 C-8 Physician Reference document, visit*** **http://www.odh.ohio.gov/odhprograms/eh/hlth_as/FactSheets.aspx** ***and select C-8.***
A: ***ATSDR: For general questions about ATSDR's C-8 related activities, contact ATSDR at*** **800-CDC-INFO (800-232-4636).**
A: ***ODH: For Ohio-specific public health questions, contact the Ohio Department if Health (ODH), Bureau of Environmental Health and Radiation Protection at (614) 466-1390 or e-mail at*** **BEH@odh.ohio.gov**
A: ***WV DHHR: For West Virginia public health or drinking water questions, contact the WV Department of Health & Human Resources, Bureau for Public Health, Office of Environmental Health Services at (304) 558-2981***
A: ***University of Pennsylvania: For questions about the University of Pennsylvania C-8 health study, contact Dr. Edward Emmett at (215) 349-5708*** **or e-mail: emmetted@mail.med.upenn.edu**

Ohio Department of Health

**** The information contained in the C-8 Quick Fact Q & A and the 2006 C-8 Physician Reference document will be updated as uncertainties and data gaps are addressed.***

Introduction

What is Perfluorooctanoic acid (C-8)?

Perfluorooctanoic acid, otherwise known as C-8 and/or PFOA, is a manmade chemical with unique properties that resists heat, water, oil, grease and stains. C-8 is used during the manufacturing process of making common household and industrial items such as nonstick pots and pans (e.g. Teflon®), flame-resistant and waterproof, breathable clothing (Gore-Tex®), wire coatings and chemical-resistant tubing. C-8 can also be formed by the breakdown of certain other highly fluorinated chemicals used in stain-resistant carpets and fabrics (e.g., Stainmaster®), stain-resistant paints, fire fighting foam, and oil and grease-resistant coatings on fast-food cartons/containers and wrappers.

C-8 is member of a family of manmade chemicals known as perfluorochemicals (PFCs). Perfluorochemicals are a class of organic chemicals in which fluorine atoms completely replace the hydrogen atoms that are typically attached to organic hydrocarbon molecules. Because of the very high strength of the carbon-fluorine bond, PFCs are inherently stable, nonreactive and resistant to degradation.

In 1999, the United States Environmental Protection Agency (U.S. EPA) began an investigation of PFCs after receiving data indicating another perfluorochemical, perfluorooctane sulfonate (PFOS), a widely used PFC, was persistent, bioaccumulative, caused reproductive toxicity in laboratory animals, and was found in both human and wildlife populations around the world. In May 2000, 3M, the sole manufacturer of PFOS in the United States and the principal manufacturer worldwide, announced it was discontinuing its perfluorooctanyl chemistries, including both PFOS and C-8.

Note: C-8, not PFOS, is the contaminant of concern in West Virginia and Ohio.

Chemical Abstracts Service Registry Number (CAS No.) PFOA (Octanoic acid, pentadecafluoro-; CAS No. 335-67-1) and its salts, predominantly ammonium perfluorooctanoate (APFO) (Octanoic acid, pentadecafluoro-, ammonium salt (CAS No. 3825-26-1)).

Note: Perfluorooctanoic acid, commonly known as C-8, is also called PFOA and/or APFO. To simplify, we use C-8 throughout this document.

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Human Exposure – C-8 Groundwater Contamination in Ohio & West Virginia

Since the 1950's, the DuPont Washington Works facility in Lubeck, Wood County, West Virginia used C-8 (as APFO) in its fluoropolymer manufacturing processes.[1] Production wastewaters and air emissions to the environment in the vicinity of the DuPont Washington Works facility led to the widespread contamination of the Ohio River surface waters and the contamination of six public water district groundwater supplies and private wells in Washington, Athens and Meigs Counties, Ohio and in Wood and Mason Counties, West Virginia. The six public water districts include Lubeck and Mason County in West Virginia and Belpre, Little Hocking, Tuppers Plains-Chester and Pomeroy in Ohio.

There are several concurrent C-8 health study activities presently being conducted in Ohio and West Virginia (as of August, 2006). Participants whose water is contaminated with C-8 were recruited to participate in the studies and their blood will be analyzed for various hormonal and organ system functions in addition to quantitative C-8 measurement/analysis (see "Current Research Activities" section).

Individuals who opt to have their blood tested will be instructed to have their results interpreted by their own family physicians. Due to the data gaps that exist, this can be quite a dilemma for the family physician tasked with explaining the results and potential risk(s).

Currently there is no consensus with regard to the toxicology of C-8 and the likely human health impacts that might result from exposure. There are no human health data currently available that associate specific C-8 levels in blood with any acute health threat and/or the likelihood of the development of disease in the future. On-going investigation may produce some answers to the many questions and data gaps present.

Results of past research

Toxicological Data

PFCs are an active area of ongoing toxicological research. Currently, we do not have any human toxicological data that link established levels of C-8 exposure to known human health effects. An extensive array of animal toxicity studies have been conducted with rodents and to a lesser extent monkeys.

Animal studies have shown that APFO is easily absorbed through ingestion, inhalation, and dermal contact. Once absorbed, APFO disassociates to the C-8 anion. C-8 is primarily distributed and found in the blood serum, liver and kidney. C-8 is not metabolized, and is excreted in the urine and feces at different rates in various test animal species and humans.

In rats, there are marked gender differences in the elimination of C-8, but these differences have generally not been observed in higher order animals and humans.[2] In addition, substantial differences in the half life of C-8 have been observed across species, as documented in rats, monkeys and humans. The gender and species differences are not completely understood and therefore the extent of potential risks to humans is uncertain.[3]

Exposure to high levels of C-8 is acutely toxic to test animals. Chronic or sub-chronic exposure to lower doses of PFOA in rats resulted in both reductions in body weight and weight gain, and in liver effects, such as increase in liver weight and alterations in lipid metabolism. The liver appears to be the primary target organ of C-8 toxicity in rats, although effects on the kidneys, pancreas, testes, and ovaries have been observed. The effects on the liver may be more pronounced in aged rats. Exposure to C-8 in rats results in a phenomenon in the liver known as peroxisome proliferation. Some of the adverse liver effects observed in rats that are in part attributed to peroxisome proliferation may not be seen in humans.

Adverse liver effects in higher animals are likely the result of a different mode of action.[4] For example, in a six month/26-week study of male cynomolgus monkeys administered APFO by oral capsule at doses of 0, 3, 10, or 30 (later adjusted to 20 due to toxicity) mg/kg-day, statistically significant increases in mean absolute liver weights and mean liver-to-body weight percentages were observed in all dose groups. The increased liver weights were considered to be treatment-related. The increased liver weight was thought to be due, in part, to hepatocellular hypertrophy (as demonstrated by decreased hepatic DNA content), which may in turn be due to mitrochodrial proliferation (as demonstrated by increased succinate dehydrogenase activity).[5] The six-month study of oral C-8 exposure in male cynomolgus monkeys exposed to different doses of APFO mentioned in the previous paragraph showed toxicity (primarily to the liver) at

even the lowest doses studied (3 mg/kg/day).[6] Acute toxicity was observed at the highest exposure level, prompting a modification of the dosage to prevent the death of the test animals. Even with the dosage adjustment, one test animal at the highest dose became extremely ill and had to be euthanized/removed from the study group, and a similar condition developed in one of the lowest dose animals. The toxicological mechanism for the apparent extreme adverse reaction in these two animals is unknown. A steady-state concentration of C-8 in the serum was reached within four to six weeks after dosing began; mean serum C-8 concentrations ranged from 77 ppm in the low dose group to 158 ppm in the high dose group.[7] This study demonstrates that the dose-response characteristics of APFO in male cynomolgus monkeys are very steep, indicating that a small increase in dose can be associated with a significant increase in the number or severity of adverse effects.[8]

A 90-day study of C-8 exposure in rhesus monkeys resulted in adverse effects on the adrenal glands, bone marrow, spleen, lymphatic system, and death in some animals. The rhesus monkeys were dosed with APFO by gavage at 0, 3, 10, 30, or 100 mg/kg-day. All of the rhesus monkeys in the 100 mg/kg-day group died during the study.

Scientific research with regard to the toxicity of C-8 is ongoing. As new information is finalized, our C-8 documents will be revised to include the new data.

Carcinogenicity

In January 2005, the U.S. EPA stated that its draft risk assessment of perfluorooctanoic acid and its salts found "suggestive evidence" of potential human carcinogenicity. The majority of members on the Agency's Science Advisory Board review panel concluded in May 2006 that C-8 is "likely" to be carcinogenic to humans and recommended the EPA conduct cancer risk assessments for a variety of tumors found in mice and rats.

It has not been determined that C-8 is carcinogenic to humans. At this time, the EPA is evaluating the scientific rodent cancer data and has not reached any conclusions on the potential significance to humans. This "likely to be carcinogenic" EPA descriptor was used by the Science Advisory Board panel because C-8 has tested positive in animal experiments in more than one species, sex, strain, site, or exposure route, with or without evidence of carcinogenicity in humans (see occupational studies section referenced later in this document). It should be noted that the Science Advisory Board review considered only the information used in the draft risk assessment, which was current as of June 2004, and that additional data developed since the draft assessment was submitted for review could impact the review panel's conclusions.

Exposure to high concentrations of C-8 (e.g., diets containing 0, 30, or 300 ppm APFO) over long durations (e.g., two or more years) has been causally linked to

cancer in rats, although the oncogenic and tumorigenic mechanisms are not fully understood. Rodent bioassays have shown that chronic APFO exposure is associated with a variety of tumor types (e.g., liver, pancreas, and testes). Evidence suggests that the cancers are a result of tumor promotion (via oxidative stress, cell death, or hormone-mediated mechanisms) and not from direct damage to the genetic material within cells (genotoxicity). The tumors observed in rats may be the result of peroxisome proliferation, and may not be seen in higher animals or be of relevance to humans.

Developmental Concerns

Various reproductive studies of rats followed for two generations showed postnatal deaths and various developmental effects in offspring of female rats exposed to relatively low doses of APFO. These studies demonstrate that exposure to APFO/C-8 can result in adverse effects on the offspring of rats exposed while pregnant. [9]

A study is now available from EPA that finds maternal and developmental toxicity of C-8 in the mouse, leading to early pregnancy loss, compromised postnatal survival, delays in general growth and development, and sex-specific alterations in pubertal maturation. [10]

The National Center for Environmental Health (NCEH) has measured PFCs in rodent breastmilk from rodents dosed with PFCs. NCEH analyzed 10 archived milk and serum samples collected on lactation day 14 from two case and eight control Sprague-Dawley rats from a 3M study where the rats were administered PFOS by gavage. PFOS was found in ppm levels in the rat serum (and milk) of the two treated animals. PFOS was not detected in the milk samples from the untreated animals. The presence of PFOS in the milk of the treated animals suggests that even though PFOA and presumably all PFCs are tightly bound to proteins in the plasma, PFCs may be incorporated into breastmilk. Most PFCs were not detected in two human breastmilk samples analyzed by NCEH. No information on the human exposure of the milk donors or the collection procedures was available, indicating caution in interpreting these results. These findings suggest, however, that PFCs may not be as prevalent in human milk as they are in serum, and that additional studies are needed to determine whether environmental exposure to PFCs can result in PFCs partitioning into milk.[11]

Note: Preliminary research indicates that PFCs (perfluorochemicals) may not be as prevalent in human milk as they are in serum. More than two decades of research have established that breast milk is perfectly suited to nourish infants and protect them from illness. In the presence of the uncertainty about the PFCs and breastmilk, and the very well established benefits of breastfeeding, the Ohio Department of Health recommends that potentially C-8 exposed mothers continue to breastfeed their children. ATSDR is currently writing a public health consultation that considers the above breast milk and nursing question.

Based on certain animal studies, there could be a potential risk of developmental and other adverse effects associated with C-8 exposures in humans. However, this assessment also reflects substantial uncertainty about the interpretation of the risk. EPA's preliminary risk assessment on potential developmental toxicity was based on a comparison of serum levels in the 2-generation rat reproductive study with those found in the human population. However, there are considerable species differences in the kinetics of C-8, particularly in rats.

In March 2001, the U.S. EPA received from an attorney representing class action plaintiffs in a case against DuPont, a number of DuPont documents with information about C-8. EPA had not previously received this information. Among these documents was a one-page document on C-8, dated May, 1981, indicating the presence of C-8 in the blood of newborns.

This one-page birth outcome report was generated by DuPont, after DuPont and U.S. EPA received preliminary notice from 3M in 1981 of a study conducted on C-8 in which the fetal offspring of dosed rats apparently displayed eye lens abnormalities. Subsequent reviewers attributed the lens effects in the rat study to an artifact of the freehand tissue sectioning technique rather than to the C-8 dosing. However, DuPont found similar birth defects in two of eight children born to women who worked at the Parkersburg, WV plant. The DuPont report stated that one child was born with an "unconfirmed eye and tear duct defect" and the other was born with "one nostril and eye defect." However, only one of these mothers had elevated levels C-8 in her blood (2.5 ppm) and the other mother had much lower levels (0.048 ppm).

In a deposition in the class action litigation, Dr. Bruce Karrh, DuPont's former medical director, reported that a DuPont Epidemiologist, Bill Fayerweather, had proposed in April, 1981 to conduct a detailed study of a potential link between C-8 exposure and facial birth defects. Fayerweather estimated that the rate of such birth defects in the general population was about two in every 1,000 people. If DuPont found two such problems in 10 children of plant workers, the rate would be "significantly higher" than that of the general population, Fayerweather stated. However, this proposed DuPont study was never conducted

Epidemiological Data

In 2001, a Michigan State University study found PFCs in the blood of 400 different mammals, fish and birds on all seven continents. Some of the highest concentrations have been found in bald eagles and mink in the Midwestern United States.[12]

The exposure routes leading to the presence of C-8 in human blood are not known. The nationwide presence of C-8 in human blood, contrasted with the limited geographic locations of fluorochemical plants making or using the chemical, suggests that there must be additional sources of C-8 in the environment and exposures beyond those attributable to direct releases from

industrial facilities. Whether these exposures are due to the presence of C-8 in the air, the water, in dusts or sediments, in dietary sources, use of consumer products, or through some combination of all these routes is currently unknown.

The mean C-8 sera levels in the 2001 results from a subset of U.S. blood banks were as follows: Los Angeles (4.6 ppb); Portland (4.3 ppb); Minneapolis-St. Paul (4.5 ppb); Charlotte (5.0 ppb); Hagerstown (4.5 ppb); and Boston (5.3 ppb). The PFOA sera concentrations in the blood donors of this study ranged from <1.92 to 52.3 ppb.[13]

C-8 is retained in the body for a long period of time (half-life of 3.8 years). Previous estimates of longer C-8 half-lives in workers may have been influenced by concurrent lower level environmental exposures that continued even after occupational exposures ceased. Preliminary data also appear to suggest that gender plays a role in the half-life of these chemicals in humans. Kinetics and half-life in humans remain current subjects of study.

Occupational Studies

DuPont has not found any human health effects that appear to be caused by C-8 exposures, even in workers who have significantly higher exposure levels than the general population.

The company also said that data from its employee health studies and those conducted by 3M, which stopped manufacturing PFOS in 2000, "deserve greater consideration in the EPA's final risk assessment rather than relying solely on animal testing models."

DuPont's studies, which are ongoing, have found elevated levels of total cholesterol and triglycerides among workers exposed to PFOA, but no indication that C-8 was the cause of increased serum cholesterol and triglycerides.

The DuPont study revealed a 10 percent increase in total cholesterol (most of which was in the LDL fraction) and a spike in triglycerides among some workers with C-8 levels higher than 1,000 ppb -- levels 200 times higher than those found in the general population. The study data did not indicate whether C-8 was the cause for the increases in serum cholesterol or triglycerides, according to DuPont. Additionally, the DuPont study found no associations between C-8 exposure and "good cholesterol" (HDL) and C-Reactive Protein (CRP). Furthermore, the study observed "slight" increases in uric acid and iron among employees with the highest C-8 blood levels.

Several epidemiological studies on the effects of C-8 in humans have been conducted on workers. An association with C-8 exposure and prostate cancer was reported in one study; however, this result was not observed in an update to the study in which the exposure categories were modified. A non-statistically significant increase in the levels of the hormone estradiol in workers with high

serum C-8 levels (>30 ppm) was also reported, but none of the other hormone levels analyzed indicated any adverse effects. 3M has monitored workers at its Cottage Grove facility for the presence of PFCs in their blood since the 1970s. Blood sera of these workers have shown C-8 concentrations up to 115 ppm. Epidemiological studies of these Cottage Grove workers do not appear to show an impact of PFC exposure on worker mortality.

Environmental Data

C-8 air emissions wash out of the air during rain events, readily move through soils and are very persistent once the chemical resides in groundwater or surface waters. As it does not hydrolyze, photolyze, or biodegrade, C-8 remains essentially unchanged for long periods of time in the environment.

In 2000, a West Virginia Department of Environmental Protection (WV DEP) investigation detected C-8 contamination in the surface water and in groundwater near the DuPont Washington Works plant, in the on-site landfill, in the Lubeck, WV well field, and at the Dry Run Landfill and Letart Landfill near the plant. Air modeling conducted by DuPont indicated that the bulk of air emissions of C-8 coming from the DuPont plant went to the NE, across the Ohio River and into Ohio.

Four public water systems have detected C-8 at 0.05 ppb or higher in Ohio (Little Hocking, Belpre, Pomeroy, and Tuppers Plains) and two public water systems in West Virginia (Lubeck and Mason Counties).[14]

The highest levels of C-8 detected in groundwater (up to 78 ppb) were found in found in a geoprobe sample from the Little Hocking Water Association wellfield, a privately-owned public water supply immediately NE of the DuPont facility, across the Ohio River, in Ohio. These contaminant detections, coupled with DuPont's air monitoring, strongly suggested that air releases from the DuPont facility were the source of groundwater contamination in downwind areas in adjacent portions of Ohio.

As of October 2005, DuPont began providing bottled water to Ohio residents who are customers of the Little Hocking Water Association or who own private wells in the Little Hocking Water Association service area.

Under the terms of a court settlement, DuPont is designing treatment systems for all affected public water supplies in Ohio and West Virginia. The treatment systems for Pomeroy and Belpre, Ohio were activated in February 2006.
In addition, DuPont is reporting filtration system is installed and functioning at Tuppers Plains. Treatment for the Little Hocking Water Association System in Ohio and for the West Virginia systems (Lubeck and Mason County) is still being negotiated, and it is not clear when these systems will be designed and implemented.

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Treatment systems in the form of carbon filtration systems were also installed recently on private wells and water systems in Ohio that had been previously sampled by ODH, the Washington County Health Department and DuPont's contractor and found to have measurable levels of C-8 in their water.

A summary of the community members still using contaminated water supplies in the combined West Virginia and Ohio affected area as of July, 2006 follow:

Private Water Supplies -- As of July, 2006, 59 of 80 private water supplies identified as a primary water source and with contamination in the West Virginia and Ohio area of concern have had treatment systems installed. The remaining 21 homes represent a population of approximately 100 or less community members.

Public Water Supplies -- Little Hocking, Ohio and the Lubeck and Mason County systems in West Virginia have not yet implemented treatment systems. Users in the Little Hocking service area are being provided the option of bottled water (the University of Pennsylvania reports that more than half of the affected residents are taking advantage of this offer). There is a population of 9,144 being supplied public water from the Lubeck system and a population of approximately 9,500 being supplied public water from the three Mason County water supplies. In all, about 19,000 community members in the area identified under the Wood County circuit court settlement continue to consume drinking water with C-8 concentrations exceeding 0.05 ppb.

Others -- In addition, there may be other affected public water systems not addressed by the Wood County circuit court settlement. For example, the Parkersburg, West Virginia public water system, which serves a community of 36,400, has had a sampling result of 0.057 ppb C-8. The Warren Community Water & Sewer Association public water system in Warren Township, Ohio, has not been tested, although nine residents tested from Fleming, Ohio show an average serum C-8 concentration of 48 ppb. There may also be other private water supplies that may exist with contamination but which were not identified during investigations to date.

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C-8/PFOA Data Gaps

Although federal and state public health officials have concerns with respect to the potential nationwide presence of C-8 in blood and with the potential for developmental and other health effects suggested by animal studies, there are significant uncertainties in the quantitative assessment of the health risks associated with exposure to C-8.

Some of the data gaps and uncertainties include:

- Research suggests that C-8 enters the human body through ingestion of contaminated water. Other routes of exposure, such as dermal or air, ingestion of contaminated foodstuffs such as fruits and vegetables, are less well studied.
- There are uncertainties with how C-8 gets into those pathways (including the products or processes that are responsible for the presence of C-8 in the environment).
- Although animal studies suggest specific toxicity and carcinogenicity of the chemical, it is difficult to translate this data to human exposure due to profound differences in metabolism and half-life of C-8 between the two species.
- There are uncertainties as to whether or not C-8 is a human carcinogen.
- If C-8 is a human carcinogen, what cancers does it cause?
- What, if any, non-carcinogenic heath effects are associated with C-8 exposure in humans?
- What, if any, organs/systems are targeted by C-8 exposure in humans?
- Research suggests that individuals who consume home-grown fruits and vegetables have elevated levels of serum C-8. It is uncertain, however, if the chemical is absorbed by the living plant or simply acquired in the cooking, cleaning or canning processes.
- Are some persons or groups of people more susceptible to the C-8 health impacts than others?
- How long does C-8 last in the human body and what is its half-life?
- How does the human body process C-8?
- What does C-8 do in the human body? Is it inert or reactive?
- Does C-8 bioaccumulate or bioconcentrate in the human body?
- Are there teratogenic or reproductive health effects in humans?
- Is there acute toxicity with human exposure?
- Is there a latency period prior to disease development?

Current Research Activities

Class Action Lawsuit *Leach, et al. v. E.I. DuPont de Nemours & Company.*

In August, 2001, attorneys filed a class action lawsuit in the Wood County Circuit Court against DuPont on behalf of West Virginia and Ohio residents exposed to C-8 through their drinking water supplies. The "class" in this suit included all persons having consumed drinking water for at least one year before December 3, 2004 supplied by: 1) the Little Hocking Water Association (OH); 2) the City of Belpre water supply (OH); 3) the Tuppers Plains-Chester Water District (OH); 4) the Village of Pomeroy (OH) water system; 5) Lubeck Public Service District (WV); 6) the Mason County Public Service District (WV); and 7) private water supplies within this area found to be contaminated with C-8. [15]

In February, 2005, DuPont agreed to an out-of-court settlement with the plaintiffs' attorneys. Under the terms of the settlement, DuPont agreed to:

- Provide new water treatment equipment to remove the C-8 from the water at six area public water systems (costs up to $10 million);
- Provide $5 million for the creation of an independent panel of experts to determine if there is an association between C-8 exposure and human disease; and
- If the panel concludes there is an association between C-8 exposure and disease in the impacted "class", Phase II will determine if there is a probable link between C-8 exposure and human disease;
- If the panel concludes there is a probable link between C-8 exposure and human disease, DuPont will pay up to $235 million on a medical monitoring program for impacted residents.

C-8 Health Project: Brookmar, Inc

As part of the settlement, the Wood County Circuit Court ordered the collection of health data to be used in a study to determine whether C-8 can be linked to human disease in the area impacted by the DuPont releases. Brookmar, Inc., a local Parkersburg, West Virginia company, was appointed by the Court to coordinate the health project.

The protocol for the C-8 Health Project, as developed by Brookmar, Inc., is to: 1) identify and verify members of the C-8 impacted "class", 2) have them complete a detailed health questionnaire (for which they would be paid $150), and have a blood sample drawn (for which the participant would receive $250).

Brookmar's staff would be responsible for developing the questionnaire, recruiting residents to participate in the study, verifying identities and eligibility of study participants, administering the questionnaire, collecting and preserving the

blood samples, delivering the samples to the laboratory for analysis and providing the results to study participants.

As a part of the Brookmar health questionnaire, each participant was required to submit a signature of consent. This consent allows Brookmar to receive individual patient notes/pathology reports from patient medical charts. Brookmar's Medical Records staff is contacting practitioners for 60,000+ patients' who reported a medical condition as part of the protocol for validating self-reported health conditions. Registered nurses are then used to validate diagnoses by detailed chart review and confirmatory pathology reports. The finalized participant information form that will be sent to the Science Panel will have a field that denotes validity of the self-reported medical condition(s).

Brookmar is testing for C-5 through C-12 and C-6 Sulfonate and C-8 Sulfonate. Exygen Laboratory in State College, Pennsylvania will be conducting the perfluorochemicals blood analysis and Axys in Vancouver, Canada will be conducting validation testing (QA protocol).

LabCorp is conducting the panel of 51 metabolic and serum blood chemistries. LabCorp was chosen for the contract due to the nationwide presence. Former residents that were exposed to the contaminated drinking water and are living in other areas of the state/nation can present to a local LabCorp site to be tested.

LabCorp receives specimens and run the blood panel the same day. When results come back, LabCorp reviews all metabolic and serum blood chemistries and will call Brookmar staff if there are any identified "critical lab" results. Brookmar staff will then contact the individual's primary care physician (as reported on his/her Brookmar questionnaire).

Note: It was noted there were several practitioners identified on the Brookmar health questionnaire who were no longer practicing medicine. If a provider was able to be reached, Brookmar would fax the labs to the provider and contact the patient to urge him/her to seek immediate medical care. If a participant does not have a primary care physician, he/she was instructed to visit an ER or Urgent Care type setting.

To date (August, 2006), over 70,000 participants have completed a health questionnaire and over 64,200 persons have had their blood drawn.

For more information on the C-8 Health Project, visit: www.c8healthproject.org

C-8 Science Panel: C-8 Community Study

The collected health histories and blood test results will be submitted to an independent Science Panel comprised of three internationally-recognized epidemiologists: Dr. Anthony Fletcher of London School of Hygiene and Tropical Medicine; Dr. David Savitz of the Mount Sinai School of Medicine, and Dr. Kyle Steenland of the Rollins School of Public Health at Emory University.

The collected health histories and results of the blood draws will be analyzed by the Science Panel, who will try to determine if there is any probable link between elevated C-8 levels in blood and specific incidence of disease in the exposed population as indicated by their (self-reported) respective health histories and blood tests. This analysis will be used to try to 1) determine the human health effects of exposure to C-8; 2) provide direction for additional toxicological and epidemiologic studies, and 3) identify those elements of the exposed population most impacted by the releases.

Note: There was a separate "opt-in" consent form made available to the C-8 Health Project participants which allows the Science Panel access to their personal identifying information and notes/pathology reports from their medical charts.

The Science Panel will conduct several studies to determine if any of the diseases suspected to be related to C-8 are in fact related. The different studies will require different time frames to address the health concerns. Some portions of the studies are estimated to take between 18 to 24 months to complete while others require up to four years.

C-8 Health Project: Medical Monitoring

Should the Science Panel finds a probable link between C-8 exposure and human disease among the class members, a medical monitoring fund will be established for the class members.

For more information on the C-8 Health Project and Science Panel, visit: www.c8healthproject.org and www.c8sciencepanel.org.

University of Pennsylvania

In February, 2004, Edward A. Emmett, MD, Professor of Occupational & Environmental Medicine at the University of Pennsylvania, School of Medicine started the initial phases of the nation's first government-sponsored epidemiological study of C-8. The University of Pennsylvania is conducting this study using an Environmental Justice Partnership grant from the National Institute of Environmental Health Studies (NIEHS).

The University of Pennsylvania study found that C-8 levels in the blood samples taken from 326 stratified randomly-sampled Ohio residents who get their water

from the Little Hocking Water Association (LHWA) were 60 to 80 times higher than those typically found in the general population. The median C-8 levels in blood of the LHWA participants were 340 ppb, while the median level of C-8 in the blood of the general U.S. population is ~5 ppb.

Increased levels were found in both sexes and all age groups, including children and the elderly. The highest levels in area residents (C-8 up to 2,000 ppb) were found in children less than six years of age and in elderly individuals above 60 years of age.

The University of Pennsylvania study, however, did not find any relationship between the blood levels of C-8 and medical testing for cholesterol, thyroid function test (TSH), thyroid stimulating hormone, kidney function (BUN, creatinine), liver function (serum protein, albumin, bilirubin, alkaline phosphatase, AST, ALT, GGT), red blood cells, white blood cells, platelets, being treated for or told by a doctor that you have any liver disease, or being treated for or told by a doctor that you have any thyroid condition.

The researchers detected no relationship between high C-8 levels in blood serum and alcohol consumption, cigarette smoking, eating fish caught locally, and eating meat or game harvested locally. They did detect a link, however, between the consumption of large quantities of homegrown fruits and vegetables and higher levels of C-8 in the blood.[15] It is not clear if this was due to C-8 in the fruits and vegetables themselves, in the water used for cooking, cleaning and canning, or if the people eating more homegrown fruits and vegetables had a different diet and/or drinking habits than those who consumed smaller quantities of homegrown fruits and vegetables.

The University of Pennsylvania's study found the C-8 level in people's blood depended on where they lived. Residents in Vincent had a higher median level of C-8 than residents in Belpre. However, differences in blood C-8 between Belpre and Vincent were not significant. The Vincent residents' median level was 369 parts per billion compared to 298 parts per billion in the blood of Belpre residents. Little Hocking residents had a median level of 327 parts per billion in their blood and Cutler residents had 316 parts per billion. Overall, all residents had a median level of 340 parts per billion in their blood. (Appendix A)

Dr. Emmett recently submitted a request for Ohio Cancer Incidence Surveillance System (OCISS) data for the Washington County, Belpre, Ohio population. Cancer incidence in Washington County, Ohio, as reported by OCISS, is no higher than any other county in the state.

Dr. Emmett also recently submitted two manuscripts on the PFOA study in Little Hocking, Ohio. "Community Exposure to Perfluorooctanoate: Relationships Between Serum Concentrations and Exposure Sources" and "Community Exposure to Perfluorooctanoate: Relationships Between Serum Levels and

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Certain Health Parameters" were accepted on June 6, 2006 and are scheduled for publication in the Journal of Occupational and Environmental Medicine in the August, 2006 issue.

For more information on the University of Pennsylvania study, visit the University of Pennsylvania at:
http://www.uphs.upenn.edu/news/News_Releases/aug05/C8study.htm

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2006 C-8 Physician Reference Summary

Studies have found PFCs in the blood of 400 different mammals, fish and birds on all seven continents. The nationwide presence of C-8 in human blood, contrasted with the limited geographic locations of fluorochemical plants making or using the chemical, suggests that there must be additional sources of C-8 in the environment and exposures beyond those attributable to direct releases from industrial facilities.

Data on the presence of C-8 in wildlife suggest that animals are not as likely as humans to have C-8 in their blood and that C-8 is not found as widely in animals as PFOS. Whether these differences may be due to different exposure pathways or to differences in how the chemicals are processed or retained by animals and humans is unknown.

In 2000, the West Virginia Department of Environmental Protection (WV DEP) detected C-8 in surface water and in groundwater in the Lubeck, WV well field. An investigation identified the widespread C-8 contamination of six public water district groundwater supplies and private wells in Washington County, Ohio and in Lubeck and Mason Counties, West Virginia. A random sample of residents in one contaminated water district in Ohio showed elevated levels of serum C-8 and these levels were associated with amount of tap water consumed. There were, however, no associated increases in serum health indicators associated with high C8 levels and there was no association between serum C-8 and self-reported history of thyroid or liver disease.[15]

Currently there is no consensus regarding the toxicology of C-8 and the likely human health impacts that might result from exposure. There are no human health data currently available that associate specific C-8 levels in blood with an acute health threat and/or the likelihood of the development of disease in the future.

An extensive array of animal toxicity studies has been conducted in rodents and monkeys. However, there are considerable species differences in the kinetics of C-8. Currently, we do not have any human toxicological data that link established levels of C-8 exposure to known human health effects.

DuPont states that their occupational studies have not found any human health effects that appear to be caused by C-8 exposures, even in workers who have significantly higher exposure levels than the general population.

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As described in this document, several health study activities are underway to help address some of these uncertainties and data gaps. In addition, the U.S. EPA submitted a nomination to the Centers for Disease Control and Prevention (CDC) to include PFOS, C-8 and certain related fluorochemicals, in the next National Health and Nutrition Examination Survey (NHANES). CDC accepted the nomination and is conducting this work. This will provide a national baseline of C-8 exposure, both to indicate whether current data are representative of the U.S. population and to offer a gauge with which to measure the effectiveness of actions to reduce exposures. The U.S. EPA also nominated a class study on perfluorinated sulfonic and carboxylic acids to the National Toxicology Program, in order to identify and fill data gaps on chemicals related to C-8 and PFOS, and that study is currently in its design phase.

Federal, state and local public health and regulatory agency partners will continue to develop and clarify issues relating to the hazard, exposure and human health risk of C-8, as the agencies continue to receive additional information that allows further resolution of the uncertainties identified in this document.

This 2006 C-8 physician reference was created by the Ohio Department of Health, Bureau of Environmental Health, Health Assessment Section and supported in whole by funds from the Cooperative Agreement Program grant from the ATSDR.

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2012 Update

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Contact Information

ATSDR	For questions about C8 and health effects, contact Lora Werner at (215) 814-3141 or by email: lkw9@cdc.gov
Brookmar, Inc. **C-8 Health Project**	For questions about Brookmar's role in the C-8 Health Project, contact Brookmar, Inc. visit: www.c8healthproject.org
C-8 Science Panel **C-8 Community Study**	For questions about the C-8 Science Panel (Dr. Tony Fletcher, Dr. David Savitz and Dr. Kyle Steenland) and the C-8 Science Panel Community Study, visit: www.c8sciencepanel.org
ODH:	For Ohio-specific public health questions, contact the Ohio Department if Health (ODH), Bureau of Environmental Health and Radiation Protection at (614) 466-1390 or e-mail at BEH@odh.ohio.gov
Ohio EPA	For information about C-8 in Ohio's drinking water, contact the Ohio EPA's Southeast District Office at (740) 385-8501
U.S. EPA	For information about U.S. EPA activities concerning PFOA, visit www.epa.gov/oppt/pfoa
WV DHHR	For West Virginia public health or drinking water questions, contact the WV Department of Health & Human Resources, Bureau for Public Health, Office of Environmental Health Services at (304) 558-2981

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Appendix A

Median C-8 levels in Little Hocking Water Area residents vs. other groups	
Group	**Median level in parts per billion (ppb)**
US. general population	5
Little Hocking water area	340
Washington works production workers	490
Other production workers	~5000
Belpre residents	298
Little Hocking residents	327
Cutler residents	316
Vincent residents	369

Emmett et. al. presentation: Community C8 Study Little Hocking Water Service Area, Warren High School August 15, 2005

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Appendix B *(PFC Fact Sheet)*

Electronic version found at:

http://www.odh.ohio.gov/odhprograms/eh/hlth_as/FactSheets.aspx

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Appendix B (cont.)

Electronic version found at:

http://www.odh.ohio.gov/odhprograms/eh/hlth_as/FactSheets.aspx

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Appendix C *(C-8 Community Fact Sheet)*

Electronic version found at:

http://www.odh.ohio.gov/odhprograms/eh/hlth_as/FactSheets.aspx

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Appendix C (cont.)

Electronic version found at:

http://www.odh.ohio.gov/odhprograms/eh/hlth_as/FactSheets.aspx

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Appendix C (cont.)

Electronic version found at:

http://www.odh.ohio.gov/odhprograms/eh/hlth_as/FactSheets.aspx

2006 C-8 Physician Reference

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2013 UPDATE: **The C-8 Quick Facts Questions & Answers document was created in 2012 for physicians and other healthcare providers. Since the creation of this document, several activities have taken place as a result of the C8 Health Project class action lawsuit settlement. For more information on the new developments, visit: http://www.odh.ohio.gov/odhprograms/eh/hlth_as/FactSheets.aspx and click on the C8 Fact Sheet and C8 Science Panel Probable Links documents.**

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