FluoroCouncil
Global Industry Council
for FluoroTechnology

October 18, 2013

Dr. Ruth Lunn
Director
Office of the Report on Carcinogens
NTP, NIEHS
P.O. Box 12233, MD K2-14
Research Triangle Park, NC 27709

Re: Nominations to the Report on Carcinogens; Request for Information (78 Fed. Reg. 183, 57868 (September 20, 2013))

Dear Dr. Lunn:

The FluoroCouncil is providing this response to the U.S. National Toxicology Program's (NTP's) request for information on perfluorooctanoic acid (PFOA) (CAS No. 335–67–1) as it considers substances nominated for possible review in future editions of the NTP's Report on Carcinogens. The FluoroCouncil offers the attached comments to inform and enhance the NTP's assessment of PFOA.

The FluoroCouncil is a global membership organization representing the world's leading manufacturers of fluoropolymers, fluorotelomers, and other fluorinated surfactants and surface property modification agents.[1] All members of the FluoroCouncil were early adopters of the 2010/2015 PFOA Stewardship Program, the global partnership between the U.S. Environmental Protection Agency (EPA) and industry based on voluntary corporate goals to reduce human and environmental exposure to PFOA and higher homologues by eliminating those chemicals from facility emissions and product content by 2015.

If you have any questions or if we can provide any additional information, please contact me at 202-249-6737 or jessica_steinhilber@fluorocouncil.com.

Sincerely,

[Redacted]

Jessica S. Steinhilber
Executive Director

[1] The FluoroCouncil's members are Arkema France, Asahi Glass Co., Ltd., Clariant International, Ltd., Daikin Industries, Ltd., DuPont Company, and Solvay Specialty Polymers.

Information on the Production, Use and Human Exposure of PFOA

I. Production: FluoroCouncil members have committed to phase out the production and use of PFOA by the end of 2015.

In 2006, eight U.S. and non-U.S. companies[2] (including all FluoroCouncil member companies) committed to the U.S. EPA 2010/2015 PFOA Stewardship Program, a global partnership between the EPA and manufacturers based on voluntary commitments to reduce human and environmental exposure to PFOA, precursor chemicals that can break down to PFOA, and related higher homologue chemicals by working toward eliminating those chemicals from facility emissions to all media and product content by the end of 2015.

As agreed to under the Program, participating companies submitted baseline year data (2000-2004) on facility emissions and product content by 31 October 2006. Through 2015, companies report annual progress toward goals versus baseline in terms of both U.S. and global operations each October, with final reports due in October 2016. Company commitment letters, annual progress reports, and other information about the Program are available on EPA's website at http://www.epa.gov/oppt/pfoa/pubs/stewardship/index.html. Program participants no longer make PFOA in the U.S.

Strategies are being implemented to replace PFOA and higher homologues with alternatives with improved environmental and biological profiles. These alternatives are effective and have received approvals by various regulatory agencies. EPA is reviewing substitutes for Long Chain PFCAs under their New Chemicals Program, and over 150 alternatives of various types have been received and reviewed by EPA.

Based on the latest data reported pursuant to the Stewardship Program, total direct emissions from Program participants have declined by over 95%. (see: "EPA Summary Tables" at http://www.epa.gov/oppt/pfoa/pubs/stewardship/). Notably, companies will report 2012 data to EPA by October 31, 2013.

In 2009, EPA published its Long-Chain Perfluorinated Chemicals (LCPFCs) Action Plan. The Action Plan includes both perfluoroalkyl sulfonates (PFAS) and perfluoroalkyl carboxylates (PFAC). The PFAS sub-category includes perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), other higher homologues, and their salts and precursors. The PFAC sub-category includes perfluorooctanoic acid (PFOA), other higher homologues, and their salts and precursors.

The Action Plan indicated EPA's intent to propose regulations under the Toxic Substances Control Act (TSCA) to further implement the objectives of the Stewardship Program, by making its endpoints mandatory for all companies in the industry.

Pursuant to the Action Plan, EPA recently finalized Significant New Use Rules (SNUR) for certain long-chain PFAS and PFAC chemicals used in carpets to provide stain, soil, and grease repellant properties. EPA is also working on "additional regulatory actions to prevent resumption of [other ongoing uses of LCPFAC chemical substances] without prior notice to EPA."

[2] Companies participating in the Stewardship Program are Arkema Inc.; Asahi Glass Co. Ltd.; BASF Corporation (successor to CIBA); Clariant International Ltd.; Daikin America, Inc.; 3M/Dyneon; E.I. DuPont de Nemours and Company; and Solvay Solexis, Inc.

The FluoroCouncil has been generally supportive of the Action Plan and the associated efforts to take regulatory action to further reduce LCPFCs as part of an overall effort to facilitate the successful global transition from LCPFCs to alternative chemistries such as short chain fluoroproducts that are generally equally efficacious and have improved environmental and biological profiles.

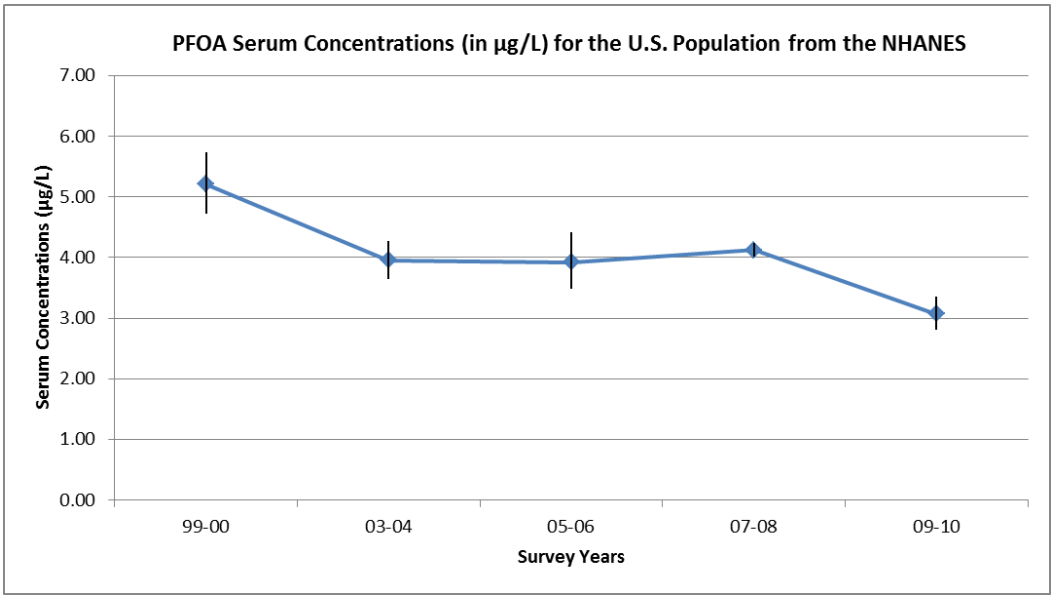
II. Use: Use of PFOA is declining and there is a commitment from major global producers to phase out the production and use of PFOA by the end of 2015.

As noted above, production and use of PFOA is declining and major U.S., European and Japanese producers are on track to phase out the manufacture and use of PFOA precursors by the end of 2015. Individual company reports to the EPA providing the current status of each company's transition program are available at: http://www.epa.gov/opptintr/pfoa/pubs/stewardship/index.html.

Based on the latest information from the US EPA Stewardship Program, total product content of PFOA from Program participants has declined by over 90%. (see: "EPA Summary Tables" at http://www.epa.gov/oppt/pfoa/pubs/stewardship/)

III. Human Exposure: Human exposure to PFOA is low and will continue to decline.

Human exposure to PFOA is low and will continue to decline. This is evident from ongoing data and monitoring information as presented below. For example, biomonitoring data indicate that PFOA serum concentrations for the U.S. population have declined by approximately 40% since 2000.



US Department of Health and Human Services, Centers for Disease Control and Prevention "Fourth National Report on Human Exposure to Environmental Chemicals"; Updated March 2013; p. 191-192 http://www.cdc.gov/exposurereport/pdf/FourthReport_UpdatedTables_Mar2013.pdf

Recommended Scientific Experts on PFOA

NTP requested information on scientists with expertise or knowledge of the substances listed. The following experts are recommended for consultation on PFOA:

1. Bruce Alexander Ph.D.

Professor
School of Public Health
Division of Environmental Health Sciences
University of Minnesota
420 Delaware St. SE, MMC 807
Minneapolis, MN 55455
Work Phone: 612-625-7934
Work Email: balex@umn.edu

Biography

Bruce Alexander earned an M.S. in environmental health from Colorado State University and a Ph.D. in epidemiology from the University of Washington. Dr. Alexander's expertise and scholarly interests are in the epidemiology of health effects due to chemical and physical hazards encountered in the environment, and the longer-term consequences of occupational and environmental disease and injury that are relevant to local, national, and global populations.

Expertise:

Cancer: Risk Factors / Incidence, Environmental Health, Epidemiology, Global Health, Injuries / Injury Prevention, Mining Health, Occupational Health & Safety, Pulmonary Disease, Research Methods

Professional Experience:

1987-1989 Epidemiologist, American Refugee Committee, Aranyaprathet, Thailand, Site 2 Camp for Displaced Cambodians. 1989-1990 Research Assistant, Harborview Injury Prevention and Research Center, University of Washington, Seattle, Washington. 1990-1994 Pre-Doctoral Trainee, NIEHS Training Grant, Department of Epidemiology, University of Washington, Seattle, Washington, School of Public Health and Community Medicine. 1994-1996 Post-doctoral Fellow in Epidemiology, NIEHS Training Grant, Department of Epidemiology, University of Washington, Seattle, Washington, School of Public Health and Community Medicine. 1996-1998 Research Scientist, Department of Environmental Health, School of Public Health and Community Medicine, University of Washington, Seattle, Washington. 1998-2005 Assistant Professor, Division of Environmental Health Sciences, School of Public Health, University of Minnesota, Minneapolis, Minnesota. 2005-present Associate Professor, Division of Environmental Health Sciences, School of Public Health, University of Minnesota, Minneapolis, Minnesota.

Research Interests:

Occupational and environmental epidemiology with emphasis on determinants of cancer, respiratory disease traumatic injury, biological markers and global health**.**

Selected Publications:

- Baker BA, Alexander BH, Mandel JS, Acquavella JF, Honeycutt R, Chapman P. Farm Family Exposure Study: methods and recruitment practices for a biomonitoring study of pesticide exposure. Journal of Exposure Analysis and Environmental Epidemiology 2005; 15:491-499.
- Zabel EW, Alexander BH, Mongin SJ, Doody, MM, Sigurdson AJ, Linet MS, Freedman DM, Hauptmann M, Mabuchi K, Ron E. Thyroid Cancer Incidence and Employment as a Radiologic Technologist International Journal of Cancer 2006;119:1940-1945.
- Alexander BH, Burns CJ, Bartels MJ, Acquavella JF, Mandel JS, Gustin C, Baker B. Chlorpyrifos Exposure in Farm Families: Results from the Farm Family Exposure Study. Journal of Exposure Science and Environmental Epidemiology 2006 16, 447-456.
- Carlson KF, Langner DM, Alexander BH, Gurney J, Gerberich SG, Ryan AD, Renier CM, Mongin SJ. Do parents' agriculture-related injuries influence their children's risk of injury? Analyses from the Regional Rural Injury Study-II, Archives of Pediatrics and Adolescent Medicine, 2006; 160:1137-1142.
- Alexander BH, Burns CJ, Bartels MJ, Acquavella JF, Mandel JS, Gustin C, Baker B. 2,4-D Exposure in Farm Families: Results from the Farm Family Exposure Study. Environmental Health Perspectives 2007;115:370-376.
- Alexander BH, Olsen GW. Bladder cancer in perfluorooctanesulfonyl fluoride manufacturing workers. Annals of Epidemiology. 2007;17(6):471-8.
- Grice MM, Alexander BH, Hoffbeck R, Kampa DM. Self-reported medical conditions in perfluorooctanesulfonyl fluoride manufacturing workers. Journal of Occupational and Environmental Medicine. 2007 49(7):722-729.
- Scher DP, Alexander BH, Adgate JL, Eberly LE, Mandel JS, Acquavella JF, Bartels MJ, Brzak KA. Agreement of pesticide biomarkers between morning void and 24-h urine samples from farmers and their children. Journal of Exposure Science & Environmental Epidemiology 2007;17(4):350-7.
- Lonn S, Bhatti P, Alexander BH, Pineda MA, Doody MM, Struewing JP, Sigurdson AJ. Papillary thyroid cancer and polymorphic variants in TSHR- and RET-related genes: a nested case-control study within a cohort of U.S. radiologic technologists. Cancer Epidemiology, Biomarkers & Prevention 2007;16(1):174-7.
- Grice MM, Feda D, McGovern P, Alexander BH, McCaffery D, Ukestad, L. Giving birth and returning to work: The impact of work-family conflict on women's health after childbirth. Annals of Epidemiology 2007;17(10):791-8.
- Sigurdson AJ, Bhatti P, Doody MM, Hauptmann M, Bowen L, Simon SL, Weinstock RW, Linet MS, Rosenstein, M, Stovall M, Alexander BH, Preston DL, Struewing JP, P Rajaraman. Polymorphisms in apoptosis- and proliferation-related genes, ionizing radiation exposure, and risk of breast cancer among U.S. Radiologic Technologists. Cancer Epidemiology Biomarkers and Prevention. 2007 16(10) 2000-2007.
- Larson-Bright M, Gerberich SGG, Alexander BH, Gurney JG,. Masten AS, Church TR, Ryan AD, Renier CM. Work practices and childhood agricultural injury. Injury Prevention 2007 2007;13(6):409-15
- Scher DP, Sawchuk RJ, Alexander BH, Adgate JL. Estimating absorbed dose of pesticides in a field setting using biomonitoring data and pharmacokinetic models. Journal of Toxicology and Environmental Health Part A 2008;71(6):373-83.
- Chodick G, Bekiroglu N, Hauptmann M, Alexander BH, Freedman DM, Doody MM, Cheung LC, Simon SL, Weinstock RM, Bouville A, Sigurdson, AJ. Risk of cataract after exposure to low doses of ionizing radiation: A 20-year prospective cohort study among US radiologic technologists. American Journal of Epidemiology 2008 ;168(6):620-31.

- Erkal S, Gerberich SG, Ryan A, Renier CM, Alexander BH. Animal-related injuries: a population-based study of a five-state region in the upper Midwest: Regional Rural Injury Study II. Journal of Safety Research (2008. 39(4): p. 351-63.
- Grice MM, McGovern P, Alexander BH. Flexible work arrangements and their association with job and home spillover in women after childbirth. Occupational Medicine 2008. 58(7): p. 468-74
- Johnson K, Alexander BH, Doody MM, Sigurdson AS, Linet MS, Spector LG, Hoffbeck RW, Simon SL, Weinstock RM, Preston DL, Ross JA. Childhood Cancer in the Offspring of U.S. Radiologic Technologists Born from 1921-1984. British Journal of Cancer 2008;99(3):545-50.
- Bhatti P, Doody MM, Alexander BH, Yuenger J, Simon SL, Weinstock RM, Rosenstein M, Stovall M, Abend M, Preston DL, Pharoah P, Struewing JP, and Sigurdson AJ, Breast cancer risk polymorphisms and interaction with ionizing radiation among U.S. radiologic technologists. Cancer Epidemiology, Biomarkers & Prevention, 2008. 17(8): p. 2007-11.
- Rajaraman P, Bhatti P, Doody MM, Simon SL, Weinstock RM, Linet MS, Rosenstein M, Stovall M, Alexander BH, Preston DL, and Sigurdson AJ, Nucleotide excision repair polymorphisms may modify ionizing radiation-related breast cancer risk in US radiologic technologists. International Journal of Cancer, 2008. 123(11): p. 2713-6.
- Sigurdson AJ, Bhatti P, Preston DL, Doody MM, Kampa D, Alexander BH, Petibone D, Yong LC, Edwards AA, Ron E, and Tucker JD, Routine diagnostic X-ray examinations and increased frequency of chromosome translocations among U.S. radiologic technologists. Cancer Research, 2008. 68(21): p. 8825-31.
- Carlson KF, Gerberich SG, Alexander BH, Masten AS, Church TR, Shutske JM, Ryan AD, and Renier CM, Children's behavioral traits and risk of injury: analyses from a case-control study of agricultural households. Journal of Safety Research, 2009. 40(2): p. 97-103.
- Lundin, JL, Alexander BH, Olsen GW, Church TR. Mortality of employees of an ammonium perfluorooctanoate production facility. Epidemiology 2008 (In Press).
  Hatfield LA, Hoffbeck RW, Alexander BH, Carlin BP. Spatiotemporal and Spatial Threshold Models for Relating UV Exposures and Skin Cancer in the Central United States. Computational Statistics and Data Analysis 2008 (In Press)

2. Jeffrey M. Peters PhD

Distinguished Professor of Molecular Toxicology & Carcinogenesis
The Pennsylvania State University
312 Life Sciences Building
University Park, PA 16802
Email: jmp21@psu.edu
Work Phone: 814-863-1387

Website

http://www.cmtc.psu.edu/peters_group/peters_home.asp

Education

1. Postdoctoral work, National Cancer Institute, 1995-99
2. Postdoctoral work, Institute of Toxicology and Environmental Health, University of California, Davis, 1992-95
3. Ph.D., Nutrition Science, University of California, Davis, 1992
4. B.S. Dietetics, University of California, Davis, 1985

Research:

Our laboratory studies the role of the peroxisome proliferator-activated receptors (PPARs) in the regulation of homeostasis, toxicology and carcinogenesis. PPARs are members of the nuclear receptor superfamily and are critical modulators of environmental and dietary stimulii. For example fatty acids and metabolic derivatives of fatty acids derived primarily from dietary sources are known ligands that can activate PPARs. Moreover, environmental chemicals can also activate PPARs, such as perfluorinated chemicals and phthalate monesters that are currently a major health concern. Acting as regulatory transcription factors, the PPARs modulate gene expression of target genes containing peroxisome proliferator responsive elements in response to ligand activation. Numerous genes that modulate lipid metabolism are regulated by PPARα, PPARβ/δ and PPARγ ligands/activators, and are clinically relevant for a number of diseases including diabetes, obesity, atherosclerosis and cancer. In addition to transcriptional regulation, PPARs can also epigenetically regulate transcription by interacting with other proteins including NF-κB. Our laboratory uses "knockout", transgenic mouse models, and high affinity agonists and antagonists to delineate the roles of PPARs, with a particular interest in epithelial and liver cancer. Through our studies, we are elucidating the molecular mechanisms by which exogenous (dietary) and endogenous (metabolic sources) lipids specifically modulate human health. We are particularly interested in delineating how natural compounds found in dietary constituents can activate PPARs with the goal of identifying new molecules/proteins that can be targeted with existing approaches to improve the efficacy of chemoprevention and chemotherapy. Our studies will likely lead to the identification of specific macronutrients that will effectively activate PPARs so that dietary formulations of agricultural products can be developed that will improve human and animal health and prevent serious diseases.

Research Interests

Molecular Toxicology & Carcinogenesis Research Faculty
Roles of peroxisome proliferator-activated receptors (PPARs) in the regulation of homeostasis, toxicology, and carcinogenesis.

3. James E. Klaunig

Environmental Health
School of Public Health
Indiana University Bloomington
jklauni@indiana.edu
(812) 856-2448
Keywords: toxicology, carcinogenesis, human health
Departmental faculty page

Research/Teaching/Professional Interests:

Dr. Klaunig's research interests are dedicated to understanding the mechanisms of chemically induced toxicology and carcinogenesis with emphasis on human health and genetic and environmental factors affecting human risk. He is board-certified as a hazardous materials manager, an Academy of Toxicological Sciences fellow, and American Board of Forensic Medicine diplomat. Dr. Klaunig has served as chair of various U.S. Environmental Protection Agency committees, programs, and reviews. He is also a scientific advisor for the International Life Sciences Insitute.

Selected Publications/Creative Activities:

- Klaunig, J.E., B.A. Hocevar, and L.M. Kamendulis. 2012. Mode of action analysis of perfluorooctanoic acid (PFOA) tumorigenicity and human relevance. *Reproductive Toxicology*, 33:410-418. doi: http://dx.doi.org/10.1016/j.reprotox.2011.10.014

- Klaunig, J.E., Z. Wang, X. Pu, S. Zhou. 2011. Oxidative stress and oxidative damage in chemical carcinogenesis. *Toxicology and Applied Pharmacology*, 254:86-99. doi: http://dx.doi.org/10.1016/j.taap.2009.11.028
- Meek, M.E. and J.E. Klaunig. 2010. Proposed mode of action of benzene-induced leukemia: Interpreting available data and identifying critical data gaps for risk assessment. *Chemico-Biological Interactions*, 184:279-285. doi: http://dx.doi.org/10.1016/j.cbi.2010.02.006
- Klaunig, J.E. and R. Snyder. 2009. Implication of recent data on benzene risk assessment: Weight of evidence for mode of action/human relevance and dose-response: Critical data gaps. Benzene 2009: Health Effects and Mechanisms of Bone Marrow Toxicity Implications for t-AML and the Mode of Action Framework, Munich, Germany.