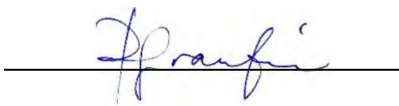


**STATE OF MINNESOTA DISTRICT COURT FOR THE
COUNTY OF HENNEPIN FOURTH JUDICIAL DISTRICT**

CIVIL ACTION NO. 27-CV-10-28862

STATE OF MINNESOTA, *et al.* v. 3M COMPANY

**EXPERT REPORT OF
PHILIPPE GRANDJEAN, MD, DMSc**



**PREPARED ON BEHALF OF
PLAINTIFF STATE OF MINNESOTA**

22 September, 2017

in elderly subjects from the Faroe Islands, where exposure levels are similar to background levels in the US (unpublished results).

h. Data from the C8 project showed that total cholesterol and LDL-cholesterol increased at higher PFOA exposures (and HDL increases in women) [235]. The variability in PFC-associated cholesterol changes is quite large [8], although a variety of factors, such as age, sex, and body mass index could affect the degrees of the relationship [284].

i. Indirect evidence suggests that PFC metabolism is not linked to changes in lipid metabolism (which would suggest a reverse causation), thereby rejecting a hypothesis that both PFCs and cholesterol could be affected by a common cause that would produce apparent positive associations between PFCs and cholesterol in serum. Thus, subjects who are taking statins to decrease their serum-cholesterol do not show any lower serum-PFC concentrations [282]. This report agrees with our findings in the Faroes (unpublished).

j. While early data from Cottage Grove suggested no risk, an increased risk of cerebrovascular disease was indicated by a mortality study that relied on comparisons with the general population [285]. The subsequent 3M-supported follow-up [76] again showed strongly elevated risk of cerebrovascular death in workers with high exposure, especially when compared to an internal control group. The draft report by Drs Lundin and Alexander from the University of Minnesotaⁱⁱⁱⁱ provides a balanced presentation, but the published article that was co-authored by 3M's Dr. Olsen calls the association "inconsistent" because the mortality was not clearly elevated when compared to the general Minnesota population.

k. Cross-sectional NHANES data suggest that serum-PFOA concentration is associated with systolic blood pressure and the risk of hypertension [286]. Hypertension may relate to an increased risk of cerebrovascular mortality.

l. NHANES data suggest that increased serum concentrations of PFOA and PFOS are associated with an increased risk of chronic kidney disease, as defined by a low glomerular filtration rate [287].ⁱⁱⁱⁱⁱ Here, reverse causation cannot be ruled out, i.e., that kidney disease prevents PFC excretion via the urine[59]. A major caveat, however, is that PFBA was not considered, as it may not have been detectable in the serum, while the major accumulation in the body is in the kidneys [52].

m. Regarding uric acid, the C8 Project examined its association with serum PFOA levels after adjustment for potential confounders. An increased risk of elevated uric acid was found in adults, including clinically defined hyperuricemia [288]. Again, this evidence is yet somewhat uncertain, as reverse causation may be present.

ⁱⁱⁱⁱ 3MA02557439.pdf. Final report, Mortality of Employees of an Ammonium Perfluorooctanoate Production Facility, August 22, 2007.

ⁱⁱⁱⁱⁱ I note that the first author of this article, and co-author of five other publications on cardiovascular outcomes in PFOS-exposed populations, has provided erroneous information to the West Virginia University regarding his educational background. The articles in question were co-authored by established colleagues, and none of them has been retracted.

270. Seacat AM, Thomford PJ, Hansen KJ, Olsen GW, Case MT, Butenhoff JL: Subchronic toxicity studies on perfluorooctanesulfonate potassium salt in cynomolgus monkeys. *Toxicol Sci* 2002, 68(1):249-264.
271. Bjork JA, Butenhoff JL, Wallace KB: Multiplicity of nuclear receptor activation by PFOA and PFOS in primary human and rodent hepatocytes. *Toxicology* 2011, 288(1-3):8-17.
272. Wan HT, Zhao YG, Wei X, Hui KY, Giesy JP, Wong CK: PFOS-induced hepatic steatosis, the mechanistic actions on beta-oxidation and lipid transport. *Biochim Biophys Acta* 2012, 1820(7):1092-1101.
273. Ikeda T, Aiba K, Fukuda K, Tanaka M: The induction of peroxisome proliferation in rat liver by perfluorinated fatty acids, metabolically inert derivatives of fatty acids. *J Biochem* 1985, 98(2):475-482.
274. Kennedy GL, Butenhoff JL, Olsen GW, O'Connor JC, Seacat AM, Perkins RG, Biegel LB, Murphy SR, Farrar DG: The toxicology of perfluorooctanoate. *Crit Rev Toxicol* 2004, 34(4):351-384.
275. Schwimmer JB, Deutsch R, Kahen T, Lavine JE, Stanley C, Behling C: Prevalence of fatty liver in children and adolescents. *Pediatrics* 2006, 118(4):1388-1393.
276. Pacifico L, Poggiogalle E, Cantisani V, Menichini G, Ricci P, Ferraro F, Chiesa C: Pediatric nonalcoholic fatty liver disease: A clinical and laboratory challenge. *World J Hepatol* 2010, 2(7):275-288.
277. Mukherjee D: Perfluorooctanoic Acid Exposure and Cardiovascular Disease: Potential Role and Preventive Measures Comment on "Perfluorooctanoic Acid and Cardiovascular Disease in US Adults". *Arch Intern Med* 2012:1-2.
278. Olsen GW, Zobel LR: Assessment of lipid, hepatic, and thyroid parameters with serum perfluorooctanoate (PFOA) concentrations in fluorochemical production workers. *Int Arch Occup Environ Health* 2007, 81(2):231-246.
279. Costa G, Sartori S, Consonni D: Thirty years of medical surveillance in perfluorooctanoic acid production workers. *J Occup Environ Med* 2009, 51(3):364-372.
280. Shankar A, Xiao J, Ducatman A: Perfluorooctanoic Acid and Cardiovascular Disease in US Adults. *Arch Intern Med* 2012:1-7.
281. Frisbee SJ, Shankar A, Knox SS, Steenland K, Savitz DA, Fletcher T, Ducatman AM: Perfluorooctanoic acid, perfluorooctanesulfonate, and serum lipids in children and adolescents: results from the C8 Health Project. *Arch Pediatr Adolesc Med* 2010, 164(9):860-869.
282. Steenland K, Tinker S, Frisbee S, Ducatman A, Vaccarino V: Association of perfluorooctanoic acid and perfluorooctane sulfonate with serum lipids among adults living near a chemical plant. *Am J Epidemiol* 2009, 170(10):1268-1278.
283. Nelson JW, Hatch EE, Webster TF: Exposure to polyfluoroalkyl chemicals and cholesterol, body weight, and insulin resistance in the general U.S. population. *Environ Health Perspect* 2010, 118(2):197-202.
284. Kerger BD, Copeland TL, DeCaprio AP: Tenuous dose-response correlations for common disease states: case study of cholesterol and perfluorooctanoate/sulfonate (PFOA/PFOS) in the C8 Health Project. *Drug Chem Toxicol* 2011, 34(4):396-404.
285. Alexander BH, Olsen GW, Burris JM, Mandel JH, Mandel JS: Mortality of employees of a perfluorooctanesulphonyl fluoride manufacturing facility. *Occup Environ Med* 2003, 60(10):722-729.