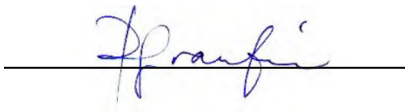
**STATE OF MINNESOTA DISTRICT COURT FOR THE COUNTY OF HENNEPIN FOURTH JUDICIAL DISTRICT**

**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**

Filed in Fourth Judicial District Court
11/17/2017 7:31 PM
Hennepin County, MN

Based on the available evidence, PFCs are convincingly associated with endocrine disrupting effects that may have substantial impacts on vulnerable population groups. While endocrine disruption is often thought to be related to reproductive toxicity, a wide variety of hormones play a role for various physiological functions, and their disruption can cause a variety of dysfunctions and diseases. Hormones addressed by PFC research include sex hormones, thyroxin, and insulin. The serum concentrations of some hormones vary during the day or with food intake, and variability of sampling times and lack of statistical control for such factors may hide or attenuate PFC-associated changes in hormone concentrations.

**1. Epidemiological evidence**

***Serum-hormone concentrations***

a. Early evidence on endocrine disruption associated with PFC exposure originates from a doctoral thesis project, where Frank Gilliland, MD, studied clinical pathology parameters in 111 male workers in 3M's Chemolite plant in Cottage Grove, MN. There was a positive correlation between PFOA exposure measured as serum total organic fluorine and estradiol (an adverse effect), and a negative correlation with free testosterone (also an adverse effect) with this association being stronger in older men. Dr. Gilliland therefore concluded that PFOA may affect male reproductive hormones.[hhhh] This study was not reported on its own in a scientific journal, but was referenced in a subsequent article led by 3M authors [88].

b. This subsequent follow-up study further explored serum hormone abnormalities in exposed workers and likewise showed a positive correlation between PFOA exposure and serum-estradiol (an adverse effect) [88] in 111 and 80 production workers studied in 1993 and 1995. The 10% increase in mean estradiol levels observed among those employees with the highest serum-PFOA concentration was argued to be potentially confounded by body mass index (although the risk of obesity may be increased at higher PFC exposures, see section VII.E). Despite the fact that two sets of data were available, and 68 participated in both (and some likely were also examined by Dr. Gilliland), the authors chose not to conduct comparisons over time, allegedly due to variability of the hormone analyses. The 3M authors concluded that the results provided reasonable assurance that, in this production setting, and contrary to the directionality of Dr. Gilliland's findings, there were no significant hormonal changes associated with PFOA at the serum levels measured. A memo from Dr. G. Olsen in 1998 proposes that the hormone concentrations were affected by misclassified body mass index as a confounder.[iiii] Interestingly, an anonymous reviewer who assessed the manuscript for a major occupational health journal questioned why the authors would present scatterplots for PFOA and some endpoints that were all non-significant, but not for the estradiol/testosterone results, which were statistically significant.[jjjj]

c. The C8 Health Project examined 25,957 women aged 18–65 years regarding serum estradiol concentrations [169]. There was a significant inverse association between PFOS and estradiol, though not between PFOA and estradiol, thereby suggesting that

[hhhh] AR226-0473. Frank Davis Gilliland, Fluorocarbons and Human health: Studies in an Occupational Cohort (October 1992) (unpublished Ph.D. thesis, University of Minnesota), with Summary. Page 003246.
[iiii] 3MA00652081.Memo to file. Geary Olsen. 1/15/98.
[jjjj] 3MA00630994. Reviewer 1, Occupational And Environmental Medicine 1997/187, page 3MA00630995.

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