MINNESOTA MDH DEPARTMENT OF HEALTH

Protecting, maintaining and improving the health of all Minnesotans

October 30, 2009

Agency for Toxic Substances and Disease Registry
Division of Toxicology and Environmental Medicine
1600 Clifton Road NE
Mail Stop F-62
Atlanta, Georgia 30333

RE: Comments on Draft Toxicological Profile for Perfluoroalkyls

Dear Sir/Madam:

The Minnesota Department of Health (MDH) is pleased to provide the attached comments on the Agency for Toxic Substances and Disease Registry's (ATSDR) Draft Toxicological Profile for Perfluoroalkyls, dated May 2009. MDH has had extensive experience with perfluoroalkyls (a.k.a. perfluorochemicals, or PFCs) due to 3M's long history of PFC manufacture and waste disposal in Minnesota. These activities have resulted in contamination of groundwater, drinking water, biota, and other environmental media. In response, MDH has developed health-based exposure limits, conducted health assessments documented in ATSDR-approved Health Consultations and Public Health Assessments, and conducted other relevant studies.

If you have any questions regarding these comments, please contact Helen Goeden (651-201-4904; helen.goeden@state.mn.us) or myself at 651-201-4910 or james.kelly@state.mn.us.

Sincerely,

James Kelly, M.S.
Research Scientist
Site Assessment and Consultation Unit
Environmental Health Division

Encl.

General Comments:

1) The draft document represents a good attempt at compiling a large amount of information. However, interpretation of the data (i.e., what does this potentially mean for human health) is limited and needs to be expanded.

2) Since multiple chemicals are contained within this review it can be rather confusing. Authors should consider including a subheading for each PFC, as appropriate, under each health effect section.

3) The draft document needs to be updated to include numerous papers that have been published since the literature review for this draft was conducted. In particular, the recently published results from the human C8 Study regarding cholesterol, uric acid and immunological effects need to be included. In addition, an updated study of mortality in PFC workers was recently published (Lundin et al 2009).

   It is also not clear why some papers, while contained within the reference list, were not cited within the document. For example, in the Mechanism of Toxicity section reviews from 1998 - 2003 are cited as the major source of information but the more recent review by Lau et al 2007 is not. Studies examining humanized PPARα receptors *in vitro* and *in vivo* should be included (e.g., Wolf et al 2008 and Foreman et al 2009). More recently publications regarding mechanism(s) of action and other sensitive health effects (e.g., alterations in serum thyroid hormone levels, immunotoxicity) have expanded the discussion well beyond liver and PPARα.

4) There is a general consensus that serum levels are a better dose metric for dose-response and for comparison across species than administered dose. Wherever possible serum levels should be provided, including tables and figures 3-1 through 3-5. In addition, a discussion of human equivalent doses should be presented to allow a more accurate comparison of effect levels.

5) The draft document includes statements that the lack of reported significant exposure-related adverse effects in humans precludes the derivation of MRLs. We are not aware of another chemical in which the absence of clear exposure-related adverse effects in humans was utilized as the major rationale for not deriving guidance. Guidance values, such as MRLs, are rarely based on human evidence but on evidence gathered in laboratory animals. Evidence of adverse effects has been clearly demonstrated in a wide range of laboratory species, including nonhuman primates. While there is limited evidence that some of the endpoints observed in rodents (enlarged livers) may not directly relevant to humans there currently is no evidence that the other health effects in rodents or the health effects in nonhuman primates are not relevant to humans.

   A secondary rationale, the uncertainty regarding animal-to-human extrapolation, is also given. Typically across species toxicokinetic information for chemicals is not available and therefore the differences are unknown. For several of the PFCs we have this information - it is not an unknown but a known quantitative difference. These differences can be addressed by utilizing serum levels as the dose metric or by adjusting the administered dose to account for differences in elimination half-life.

6) The summary of Regulations, Advisories and Guidelines is incomplete. Several other countries (e.g., Germany, Canada) as well as states have derived health-based guidance. Some of these values are listed below:
    a. North Carolina's Public Health Goal for PFOA (June 2007) is 0.63 ug/L;
    b. German Ministry of Health, Drinking Water Commission (July 2006) has several values. The Precautionary Action Values for composite PFOA and PFOS are: 5.0 ug/L immediate action to reduce adult intake; > 1.5 – 5.0 ug/L (1 yr tolerable max.); > 0.6 – 1.5 ug/L (3 yr tolerable max.); and > 0.1 – 0.6 ug/L (10 yr tolerable max.). The Provisional toxicological assessment lifelong health based guide value is 0.3 ug/L (applies to composite of PFOA & PFOS).
    c. Health Canada has developed a draft Drinking Water Guidance Value of 0.7 ug/L for PFOA and 0.3 ug/L for PFOS.
    d. United Kingdom, Drinking Water Inspectorate 2007 has a Tier 2 value of 10 ug/l for PFOA and of 1 ug/L for PFOS.
    e. In addition to the values for PFOA and PFOS the Minnesota Department of Health has health-based guidance for PFBA (see http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfba.pdf) and PFBS (see http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfbs.pdf).

Specific Comments:

1) Comparisons of administered dose and dose duration do not provide an accurate picture of species sensitivity. On page 119 the comparison of monkeys, rats and mice regarding sensitivity to the hepatic effects of PFOA would appear quite different if BMDL serum levels for hepatic effects are compared. The BMDL in Cynomolgus monkeys in the 26 week study (Butenhoff et al 2002) was ~23 ug/mL, in rats exposed for 70 - 90 days (Butenhoff et al 2004) it was ~ 25 ug/mL, in mice exposed throughout gestation it was ~ 29 ug/mL.
2) Half-life of PFBA in humans. The correct units (hours) is listed in Table 3-8, however, throughout the text the units are reported as days.
3) Maternal-infant transfer. It is incorrectly stated that no data regarding concentrations of PFCs in human milk in the US population are available. At least two studies have been conducted: Perfluorinated compounds in human milk from Massachusetts, U.S.A. Tao L et al. Environ Sci Technol. 2008, Apr 15; 42(8):3096-101 and Polyfluoroalkyl chemicals in the serum and milk of breastfeeding women. von Ehrenstein OS et al. Reprod Toxicol. 2009, Jun; 27(3-4):239-45. In fact, Tao et al 2008 is cited in Section 6 of the draft document.
4) Discussion contained in Section 3.10 Populations that are unusually susceptible and Section 6.7 Populations with potentially high exposures should also include issues such as conditions that could impact the ability to eliminate PFCs and health effects beyond liver effects (immunological and thyroid hormone effects).
5) 3M has reported that information on the import and export of PFCs from the United States is available from the U.S. Customs Service databases.
6) Section 6.2 – PFOS is still in use in specific applications exempted by EPA. For example, some chrome platers use surfactants containing PFOS to limit hexavalent chromium emissions. MDH summarized Minnesota's experience with this use in a Health Consultation (http://www.health.state.mn.us/divs/eh/hazardous/topics/pfcs/pfosdetectbrainerd.pdf). The U.S.

EPA also recently completed a study of PFOS levels in wastewater from chrome platers in Region 5 (see http://www.epa.gov/region5/water/npdestek/notices.htm).

7) Section 6.4.2 – The statement attributed to Chang et al (2008) regarding PFBA levels is misleading and inappropriate. PFBA has been detected at a levels as high as 21 micrograms per liter (ug/L) in a single private well, and at levels of 1-3 ug/L in literally hundreds of other private wells in Washington County, Minnesota as documented in a Health Consultation (http://www.health.state.mn.us/divs/eh/hazardous/topics/pfcs/prwelldata.pdf) and Public Health Assessment (http://www.health.state.mn.us/divs/eh/hazardous/topics/pfcs/pha/lakeelmooakdale/index.html) reviewed and approved by ATSDR.
8) Section 6.4.4 – a recent study published by Guo et al (2009) describes PFC levels in articles of commerce, and should be included here.
9) Section 6.5. MDH recently published the results of a pilot biomonitoring study of Washington County residents exposed to PFOA and PFOS in drinking water (http://www.health.state.mn.us/divs/eh/tracking/biomonitoringpilot.htm). The results of this study should be included in this section.
10) A discussion of drinking water treatment may also be relevant. MDH has conducted a study of water treatment devices for removing PFCs from drinking water. The study can be found at http://www.health.state.mn.us/divs/eh/hazardous/topics/pfcs/water.html.