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Drinking Water Contaminant Candidate List 3--Draft (Federal Register:February 21, 2008, Volume 73, Number 35, p. 9627-9654, DOCID:fr21fe08-134)

To Whom It May Concern:

In response to Federal Register notice of the February 21, 2008, the New Jersey Department of Environmental Protection (NJDEP) is pleased to comment on the Draft Contaminant Candidate List 3 (CCL3). Our comments focus on four chemicals of concern to New Jersey: PFOA, 1,2,3-trichloropropane, MTBE, and perchlorate.

**General Comments**

Section 1412(b) (1) of the federal Safe Drinking Water Act (SDWA), as amended in 1996, requires USEPA to publish the Contaminant Candidate List every five years. The SDWA specifies that the list must include contaminants that are not subject to any proposed or promulgated National Primary Drinking Water Regulations, are known or anticipated to occur in public water systems (PWSs), and may require regulation under SDWA. The 1996 SDWA Amendments also specify three criteria to determine whether a contaminant may require regulation: 1) the contaminant may have an adverse effect on the health of persons; 2) the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and 3) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

Since the Contaminant Candidate List process began about 10 years ago, none of the contaminants included on the two prior Contaminant Candidate Lists have been adopted by the United States Environmental Protection Agency (USEPA) as National Primary Drinking Water Regulations. The NJDEP is very concerned about this practice since many of the contaminants on the past Contaminant Candidate Lists, as well as many of the contaminants on the present CCL3, both occur widely in drinking water and have health effects of potential concern. The health effects data for many of these chemicals are extensive and complicated. For such chemicals, the risk assessment involves a large amount of time and effort. Most states have limited resources as far as risk

assessment and cannot address all chemicals of concern in drinking water without assistance from USEPA. We urge USEPA to use its vast resources to address such chemicals by regulating when appropriate, rather than simply determining that every chemical evaluated does not need regulation.

## Specific Contaminants of Concern to New Jersey

### *Perfluorooctanoic acid (PFOA)*

PFOA is a chemical of concern in drinking water, which NJDEP strongly urges USEPA to address, as discussed below. It is well known that drinking water has been contaminated by PFOA from point sources, such as the Ohio and West Virginia area contaminated by the DuPont Washington Works facility in Parkersburg, West Virginia and the several sites contaminated by 3M in Minnesota. However, it is also important to recognize that the lower levels of PFOA found in drinking water not impacted by a known point source may also result in health effects of concern.

As discussed below, it appears that health-based drinking water concentrations developed using a very conservative approach involving application of standard uncertainty factors for Reference Dose development, as well as animal-to-human extrapolation based on blood levels instead of administered dose, do not protect against health effects in the human population.

New Jersey Occurrence Information

In 2006, NJDEP conducted a small statewide PFOA and perfluorooctane sulfonic acid (PFOS) occurrence study (NJDEP, 2007a). Twenty-nine samples from twenty-three ground and surface water systems were collected in various areas throughout the state. STL Denver, the only laboratory certified by NJDEP for PFOA, conducted the analysis. The detection limit was 0.001 ug/L and the quantitation limit was 0.004 ug/L. Samples consisted of raw groundwater and surface waters, as well as samples of finished water. PFOA was found in raw and treated surface water, and raw and treated ground water from unconfined wells.

The data from the occurrence study show levels of PFOA from 0.003 ug/L, a level that is detected but not quantified to 0.039 ug/L. PFOA was detected and quantified at 65% of the 23 systems sampled. If the samples where PFOA was detected but was not quantifiable are included, PFOA was found in 78% of the systems sampled.

NJDEP is continuing to sample at water systems where PFOA was detected. In this follow-up sampling, PFOA was detected at four water systems at or above 0.04 ug/L (the NJDEP health-based drinking water guidance level, discussed below). The highest concentration was measured at systems with no known point source of PFOA was 0.069 ug/L.

Significance of Drinking Water Exposure to Human Body Burden

Although these drinking water concentrations of PFOA are relatively low, they may contribute significantly to the body burden of PFOA in the general population (Post et al., 2007). The average blood concentration of PFOA in the general population is approximately 5 ug/L and the 90$^{th}$ percentile is 9.4 ug/L (USEPA, 2005a).

A study of a community whose drinking water was contaminated with PFOA showed that, on average, ingestion of water with a given PFOA concentration results in a blood concentration 100-fold higher (Emmett et al., 2006). Similar results are predicted by modeling done by Gray (2005) and Hinderliter and Jepson (2001). For example, ingestion of drinking water with 0.03 ug/L PFOA

would be expected to contribute about 3 ug/L to the blood concentration of PFOA. Therefore, the contribution to total human exposure of PFOA in drinking water at levels below 0.1 ug/L may be significant.

Toxicology and Risk Assessment

*New Jersey Health-based Drinking Water Guidance*

In 2007, NJDEP developed a health-based drinking water guidance for PFOA of 0.04 ug/L in response to a request from a New Jersey water supply with detections of up to 0.19 ug/L in its wells, located near a point source of PFOA (NJDEP, 2007b).

The NJDEP health-based drinking water guidance is based on the endpoints identified by USEPA (2005a) in its draft PFOA risk assessment. Since the half life of PFOA is much longer in humans than in the experimental animals used in the studies, the risk assessment was based on blood levels of PFOA rather than administered doses of PFOA. This approach was recommended by the USEPA Science Advisory Board (USEPA, 2006a). Appropriate uncertainty factors and a Relative Source Contribution factor were applied to the blood levels in the animal studies at the NOAELs and LOAELs identified by USEPA to determine target human blood levels. A similar approach was used for the cancer endpoint to determine the blood level at the $10^{-6}$ risk level. The 100:1 blood/drinking water concentration factor observed by Emmett et al. (2006) was used to determine drinking water concentrations anticipated to result in the target blood levels.

The most sensitive endpoints, resulting in a health-based drinking water concentration of 0.04 ug/L, were body weight and hematological changes in a chronic study of adult female rats. The drinking water concentrations based on endpoints from several other studies were very close to 0.04 ug/L (adult male rat – 0.08 ug/L, cynomolgus monkey – 0.05 ug/L, pregnant female rat – 0.07 ug/L, carcinogenicity in male rats at $10^{-6}$ risk level – 0.06 ug/L).

The USEPA (2005a) draft risk assessment did not consider more recent studies, which reveal additional effects of PFOA of serious concern, as discussed below.

*Recent mouse developmental data*

The developmental data considered by USEPA (2005a) were from rat studies. The rat is not a good model for developmental effects of PFOA because the half-life of PFOA in female rats is very short (2-4 hours), so that steady state is never reached with daily dosing, and the fetus receives minimal exposure. In contrast, PFOA has a longer half-life in female mice, resulting in a higher steady state blood level and greater exposure to the fetus. Recent mouse developmental studies, reviewed by Lau et al. (2007), have revealed effects resulting from prenatal exposure including post-natal mortality, decreased birth weight, delayed post-natal growth and development, obesity at 18 months of age, and inhibition of mammary gland development.

*Recent data on mechanism of liver carcinogenicity*

Very recent new data shed light on the relevance of the positive carcinogenicity studies in rats to PFOA's human carcinogenic potential, which has been a subject of ongoing controversy.

PFOA was found to induce liver adenomas, Leydig cell adenomas, and pancreatic acinar cell tumors in male Sprague-Dawley rats and mammary cell fibroadenomas in female rats, although USEPA (2005a) questioned the significance of the mammary tumors compared to historical background

incidences. USEPA (2005a) interpreted the liver, Leydig cell, and pancreatic acinar cell tumors as constituting a "tumor triad" known to be caused by a class of chemicals which are peroxisome proliferator-activated receptor-alpha (PPAR-α) agonists. USEPA (2005a) states that the relevance to humans of tumors caused by this group of chemicals is uncertain. Additionally, they state that there are no adequate human studies of PFOA's carcinogenic potential since the occupationally exposed cohorts are still quite young. Based upon this, USEPA (2005a) concluded that PFOA was best described as having "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential".

The USEPA Science Advisory Board (2006a) disagreed with USEPA (2005a) as to the most appropriate descriptor for the carcinogenicity of PFOA. They concluded that the PFOA cancer data are consistent with the USEPA cancer guidelines descriptor "likely to be carcinogenic to humans" which applies to chemicals which have been shown to cause tumors in more than one species, sex, strain, site, or exposure route, regardless of the existence of evidence in humans. Most Science Advisory Board panel members felt that the animal data are much stronger than the type of data which would warrant a "suggestive" descriptor. This conclusion was based on the following: 1) existence of two positive cancer studies in animals for PFOA, 2) data suggesting that PPAR-α activation may not be the sole mechanism of liver carcinogenesis (discussed above in regard to liver toxicity of PFOA), 3) disagreement about the appropriateness of comparison to historical controls rather than concurrent controls in evaluating the mammary tumor date, and 4) disagreement about the USEPA (2005a) assumptions about the mode of action for the Leydig cell and pancreatic acinar cell being related to PPAR-alpha agonist activity, and the USEPA comparison of mammary tumors to historical, rather than concurrent, controls.

A new study (Tilton et al., 2008) suggests that PFOA promotes liver tumors in rainbow trout by a mechanism independent of PPAR-alpha and peroxisome proliferation. The rainbow trout has been used as a model for chemically induced liver cancer in humans for over 40 years, and, like humans, is insensitive to liver toxicity through peroxisome proliferation. PFOA was shown to enhance liver carcinogenesis post-initiation through an estrogenic mechanism independent of peroxisome proliferation, which may be relevant to human carcinogenic potential.

*Recent human birth weight and clinical effects at very low exposures*

Recent human data suggest effects in humans at blood levels of PFOA typical of the general population, orders of magnitude below effect levels seen in animal studies.

Several studies associating PFOA blood levels in the general population with effects on birth weight and other fetal growth indicators (ponderal index, head circumference, and birth length) have been published (Apelberg et al., 2007; Fei et al. 2007; Fei et al., 2008). The effects observed within the general population are of a very large magnitude. For example, in a study of 1400 Danish mothers and their infants (Fei et al., 2007), the largest decrease in mean birth weight, 126 g, was seen between the lowest quartile for PFOA in maternal blood (3.91 ug/L or below) and the second quartile (3.91-5.20 ug/L). The decrease in mean birth weight between the lowest quartile (less than 3.91 ug/L and the highest quartile (6.97 ug/L and above) was 175 g. No association between birth weight and PFOS blood levels was observed.

Additionally, recent preliminary data from a study of approximately 70,000 Ohio and West Virginia residents exposed to PFOA in their drinking water at levels from 0.05 ug/L to 3 ug/L or higher suggest an association between several clinical parameters and exposure to PFOA. Apparent effects

are seen at blood levels orders of magnitude below the blood levels at which effects have been seen in animals (Frisbee, 2008). The effects involved include decreased C-reactive protein (an indicator of inflammation), decreased immunoglobulin G, increases in two liver enzymes (SGPT and SGOT), increased cholesterol in children, and effects on thyroxine levels. These effects are consistent with the known toxicity of PFOA from animal and/or human occupational studies, as reviewed by Lau et al. (2007), as PFOA is known to produce liver toxicity, suppress the immune system, and suppress inflammatory response in animal studies, and has been observed to increase thyroid hormone and cholesterol levels in occupational studies.

In this study, the study population was divided into deciles based on PFOA blood levels, with about 6700 people in each group. The mean blood levels for each decile is shown below (S. Frisbee, personal communication):

| Decile | Mean PFOA Blood Level (ug/L) |
|---|---|
| 1 | 5.65 |
| 2 | 9.80 |
| 3 | 13.47 |
| 4 | 18.06 |
| 5 | 24.28 |
| 6 | 33.26 |
| 7 | 47.44 |
| 8 | 71.33 |
| 9 | 124.11 |
| 10 | 482.33 |

The PFOA levels in the first decile and the second decile are almost identical to the mean and the 90$^{th}$ percentiles in the United States population. No threshold was apparent for a number of the observed effects in human populations, both for the birth weight study (Fei et al., 2007) and for clinical parameters (C-8 reactive protein, liver enzymes, and increased cholesterol in children), and effects appear to occur down to the lowest exposure groups, which are in the range of the mean concentration general population.

Effects are seen well below the blood levels derived by applying conservative uncertainty factors to animal data by NJDEP (2007b); the blood level for the most sensitive effect thus derived was 18 ug/L.

*Recommendation*

As discussed above, it appears that health-based drinking water concentration for PFOA developed using a very conservative approach involving application of standard uncertainty factors for Reference Dose development, as well as animal-to-human extrapolation based on blood levels instead of administered dose, is not protective against health effects in the human population. Because humans appear to be so sensitive to PFOA's effects and PFOA appears to occur ubiquitously in drinking water, based on New Jersey and other data, it is important that exposure to PFOA through drinking water be appropriately limited through MCL development.

***1,2,3-Trichloropropane***

1,2,3-Trichloropropane (1,2,3-TCP) is a chemical of concern in drinking water, which NJDEP strongly urges USEPA to address. 1,2,3-TCP is a potent genotoxic carcinogen which occurs in drinking water at levels resulting in significant cancer risk based on test results from New Jersey public and non-public water supplies. Currently, USEPA does not provide any information as to 1,2,3-TCP's carcinogenicity on its 2006 USEPA Office of Water Drinking Water Regulations and Health Advisory Table (USEPA, 2006b). Instead, it provides a Lifetime Health Advisory which results in a lifetime cancer risk of $4 \times 10^{-3}$ to $3 \times 10^{-2}$, based on available slope factors. This information, which is not protective of public health, has been used by several states to develop drinking water and groundwater guidance for 1,2,3-TCP, as the basis for evaluating situations of drinking water and groundwater contamination, etc. Therefore, NJDEP strongly urges USEPA to provide appropriate public health protective information in its Drinking Water Regulations and Health Advisory Table and to develop an MCL for 1,23-trichloropropane.

Uses

1,2,3-TCP is a known contaminant of nematocides and soil fumigants including D-D (NTP, 2005) (1,2-dichloropropane and 1,3-dichloropropene [mixed isomers] ) and Telone (1,3-dichloropropene). Telone has been reported to contain up to 0.17% 1,2,3-TCP by weight (WHO, 2003). This is thought to be the source of 1,2,3-TCP contamination of rural wells in New Jersey and other locations. When 1,2,3-TCP was detected in Galloway Township, Atlantic County, New Jersey, in 1999, three other chemicals were also found at the sampling sites: dibromochloropropane, 1,2-dichloropropane, and ethylene dibromide. The occurrence of 1,2,3-TCP is discussed in more detail.

1,2,3-TCP was extensively used in the past as a solvent, cleaning and degreasing agent, and paint and varnish remover. It is used as intermediate in the synthesis of several organic compounds including polysulfone liquid polymers, dichloropropene, hexafluorpropylene, and polysulfides (NTP, 2005).

1,2,3-TCP is a byproduct produced in significant quantities in the manufacture of other chlorinated compounds, including epichlorohydrin. It is listed as a component which is present at greater than 0.01% (a reporting threshold) on the Right to Know lists of New Jersey, Pennsylvania, and Massachusettes, as well as the California Proposition 65 list. According to the SPI Epichlorohydrin Task Force, the majority of 1,2,3-TCP produced as a byproduct of epichlorohydrin production today is incinerated on-site (WHO, 2003). 1,2,3-TCP is also a byproduct of dichloropropene, propylene dichlorohydrin, dichlorohydrin, and glycerol (NTP, 2005).

A polymer used as a coagulant in the treatment of potable water and wastewater is produced by reacting epichlorohydrin with dimethylamine. Epichlorohydrin is a known contaminant of these polymers, and is likely to be present in finished drinking water due to its use in the coatings of drinking water pipes (USEPA, 1985). Since 1,2,3-trichloropropane is a contaminant in epichlorohydrin, it might also be present in drinking water, especially since 1,2,3-trichloropropane is more stable in water than epichlorohydrin.

An NSF International (2000) report prepared for Health Canada on impurities in drinking water treatment, 1,2,3-TCP was identified as a contaminant in an unidentified well drilling aid. However, the Action Level (target drinking water level based on health effects) used by Health Canada was 5 ug/L, which is much higher than the health based drinking water level or practical quantitation limit (see below).

A health-based drinking water guidance of 0.005 ug/L was developed by NJDEP in 1999 based upon the $10^{-6}$ risk level and the slope factor of 7 $(mg/kg/day)^{-1}$ in the USEPA HEAST (1995) tables. This slope factor was based on the combined incidence of benign and malignant tumors at various sites in rats. Standard exposure factors for body weight (70 kg) and drinking water ingestion (2 L/day) were used. The New Jersey Drinking Water Quality Institute is currently in the process of recommending a Maximum Contaminant Level (MCL) to NJDEP for 1,2,3-TCP for possible standard setting. A more complete explanation of the risk assessment is presented below.

Occurrence

1,2,3-Trichloropropane has been found in both public water supplies (including in USEPA Unregulated Contaminant Monitoring) and private wells. As discussed above, it is known to be present in soil fumigants including D-D (mixed isomers of 1,2-dichloropropane and 1,3-dichloropropene) and Telone (1,3-dichloropropene), and there are also other potential sources of contamination. Because the health-based drinking water concentration (at the$10^{-6}$ risk level) for 1,2,3-trichloropropane is so low (see below), less sensitive analytical methods will miss occurrences at levels of concern, and reporting limits given by each state for the UCMR Round 1 monitoring ranged from 0.5 ug/L to 5 ug/L.

In 2005, NJDEP conducted a review of occurrence of 1,2,3-trichloropropane in New Jersey drinking waters. 1,2,3-Trichloropropane was detected at levels above the health-based drinking water guidance developed by NJDEP of 0.005 ug/L (see below) in 30 of the 2,640 private wells (1.1%) sampled during contaminated site investigations overseen by NJDEP's Site Remediation Program between 1999 and 2004. In addition, as part of NJDEP's Synthetic Organic Compound (SOC) Waiver Program sampling, 1,2,3-trichloropropane was detected at levels above the health-based drinking water guidance of 0.005 ug/L developed by NJDEP in 11 of approximately 260 community water systems (4%) sampled between 1999 and 2004.

In unregulated contaminant monitoring in California from 1989 through the 1990s, fewer than 20 sources reported detections, reflecting the less sensitive analytical methods available at that time, with a reporting limit of 0.5 µg/L. However, more recent monitoring in California with a more sensitive analytical method reported 1,2,3-trichloropropane detections in 303 sources, at levels up to 57 µg/L. Of the 303 detections, 2 were below 0.005 ug/L, 171 between 0.005 and 0.05 ug/L, 104 between 0.05 and 0.5 ug/L, 20 between 0.5 and 5 ug/L, 4 between 5 and 50 ug/L, and 1 above 50 ug/L. This dataset is not yet complete (CDPH, 2007).

California Department of Public Health (CDPH, 2007) states on its fact sheet that the primary possible contaminating activity for 1,2,3-TCP in drinking water appears to be hazardous waste sites. No further justification is given for this statement.

1,2,3-Trichloropropane is the main contaminant at a Superfund site, MacKenzie Chemical Works in Suffolk County, New York (ATSDR, 2004). ATSDR conducted an evaluation of this site in 2004, and used New York's MCL of 5 ug/L to evaluate the significance of the contamination. (5 ug/L is New York's MCL for Principal Organic Contaminants, a generic number for organic contaminants when there is no information indicating that a lower value is warranted.) The cancer risk level at 5 ug/L is about $10^{-3}$. Analytical methods used in this investigation were chosen with the belief that a detection limit below 5 ug/L was not needed.

According to the ATSDR report on this site, concentrations of 1,2,3-trichloropropane of up to 34,000 ug/L were detected in off-site groundwater, at 10,000 ug/L one block from the site, and above 100 ug/L more than 0.25 miles from the site. A well field is located about 0.5 miles downgradient from the site. No VOCs were detected in routine monitoring of a deep well in that well field that serves the local community. ATSDR concluded that "the site poses no public health hazard at the present because there are no known exposures to site-related contaminants." It is troubling that a drinking water benchmark of 5 ug/L, which is 1000 times above the public health protective concentration of 0.005 ug/L, was used by ATSDR and the state of New York to evaluate this highly contaminated site. This information was used to provide reassuring, but perhaps incorrect, conclusions to the local community that there is no exposure of concern to 1,2,3-trichloropropane.

Additional test results posted on web sites reveal many other cases of drinking water and ground water contamination by 1,2,3-trichloropropane at high levels, including a site in Dover Township, New Jersey where concentrations up to 210 ug/L in ground water were found (NJDHSS, 2001).

Toxicology and Risk Assessment

1,2,3-Trichloropropane is metabolically activated to a reactive intermediate and is a potent carcinogen. It is genotoxic in almost every system in which it was tested, and it caused a high incidence of tumors at multiple sites in male and female rats and mice in an NTP (1993) carcinogenicity bioassay. From the 1993 study, NTP concluded that there was clear evidence of carcinogenic activity in both sexes of both species. Additionally, it was reasonably anticipated to be a human carcinogen in the NTP Eleventh Report on Carcinogens (2005). Thus, the weight of evidence for carcinogenicity for 1,2,3-trichloropropane is much stronger than for many other chemicals which are treated as non-threshold carcinogens as a conservative default assumption. From this information, there is no doubt that the risk assessment for 1,2,3-trichloropropane should be based on a non-threshold low dose model, and that a risk assessment based on a Reference Dose is inappropriate for this chemical.

Three slope factors have been developed for 1,2,3-trichloropropane using the data from the 1993 NTP study: an older USEPA HEAST (1995) slope factor which was based on classification as a probable human carcinogen (B2) and the linearized multistage model, and slope factors in the draft risk assessments developed by USEPA IRIS (2007) and the California EPA Public Health Goal program (2007) which both use time-to-tumor low dose modeling, but differ in choice of species and modeling details. The range of drinking water concentrations at the $10^{-6}$ risk level, based on the three slope factors available, is 0.0015 ug/L to 0.009 ug/L, assuming water consumption of 2 liters per day.

A health-based drinking water guidance of 0.005 ug/L was developed by NJDEP in 1999 based upon the $10^{-6}$ risk level and the slope factor of 7 $(mg/kg/day)^{-1}$ in the USEPA HEAST (1995) tables. This slope factor was based on the combined incidence of benign and malignant tumors at various sites in rats. Standard exposure factors for body weight (70 kg) and drinking water ingestion (2 L/day) were used. The New Jersey Drinking Water Quality Institute is currently in the process of developing a Maximum Contaminant Level recommendation to NJDEP for 1,2,3-TCP.

Health Advisory information provided by USEPA Office of Water

The 2006 USEPA Office of Water Drinking Water Regulations and Health Advisory Table (HA Table) does not indicate that 1,2,3-trichloropropane is a carcinogen and provides a Lifetime Health Advisory for this contaminant. As you know, the users of this table do not necessarily have any

toxicology or risk assessment expertise, since it is a practical reference table intended to be used by persons directly addressing local public health issues, such as detection of drinking water contaminants without MCLs in public water supplies or private wells. Examples of users of the HA Table are county and local health officials or water purveyors.

As discussed above, there is no doubt that the cancer risk assessment for 1,2,3-trichloropropane should be based on a non-threshold linear low dose model, and that a risk assessment based on a Reference Dose is inappropriate for this chemical. In spite of this, the IRIS entry for 1,2,3-TCP, **fifteen years** after the 1993 NTP study was published in final form, provides a Reference Dose for non-cancer effects of 0.006 mg/kg/day which was developed in 1989, prior to completion of the 1993 NTP study. For carcinogenicity, the only entry is "no data, dated 11/1/1993."

USEPA Office of Water does not provide Lifetime Health Advisories for known or probable human carcinogens (Groups A or B, using the older weight of evidence terminology). However, the HA Table does not even indicate that 1,2,3-trichloropropane is a carcinogen, and gives a Lifetime Health Advisory of 40 ug/L, based on the IRIS Reference Dose of 0.006 mg/kg/day. The range of lifetime cancer risks at the Lifetime Health Advisory of 40 ug/L, using the slope factors currently being considered by USEPA and California EPA is $4 \times 10^{-3}$ to $3 \times 10^{-2}$ or **4 in 1000** to **3 in 100**. Thus, an unacceptably high level of cancer risk will result if the guidance provided in the table is used by local health officials to provide advice about 1,2,3-trichloropropane contamination of drinking water. Additionally, this guidance may be used as the basis to choose analytical methods which are not sensitive enough to detect levels of concern.

Current USEPA Office of Water procedures do not allow information from final NTP studies, HEAST, NCEA, IRIS drafts, or other such reliable sources, to be posted on the HA Table, even if this information clearly demonstrates that the information provided on the HA Table is not protective of public health. USEPA Office of Water procedures do not allow for inclusion of any carcinogenicity information until the IRIS cancer assessment for this chemical is finalized, which will likely take years due to the number of time consuming reviews required by the IRIS process.

Ironically, older versions of the Drinking Water Regulations and Health Advisory Table (e.g. 1996) listed 1,2,3-trichloropropane as a Group B2 (probable human) carcinogen and provided a drinking water concentrations based on cancer risk, based on the slope factor provided in the 1995 HEAST table. As discussed above, the HEAST slope factor was the basis for the drinking water guidance value of 0.005 ug/L developed by NJDEP in 1999.

The Lifetime Health Advisory of 40 ug/L provided in the HA Table is widely used by states and other parts of USEPA as a health-based drinking water concentrations for 1,2,3-trichloropropane. Some examples follow:

1) Situations where Lifetime Health Advisory from the HA Table has been routinely used by state and local environmental or public health officials in states with no listed guidance to assess the significance of detections in drinking water. It is obviously not possible to determine how many times that this has occurred, since this information is not normally posted on the Internet.

2) Several states, including Arizona (42 ug/L), Florida (42 ug/L), Minnesota (40 ug/L), New York (5 ug/L) Washington (21 ug/L), and Wisconsin (50 ug/L) have drinking water standards

or guidance concentrations at high risk levels, based on the USEPA's incorrect and outdated toxicity information (USEPA, 2000; HSDB, 2008).

3) Because the health-based drinking water concentration (at the $10^{-6}$ risk level) for 1,2,3-trichloropropane is so low, less sensitive analytical methods will miss occurrences at levels of concern, and reporting limits given by each state for the Unregulated Contaminant Monitoring Round 1 monitoring ranged from 0.5 ug/L to 5 ug/L.
Additionally, the 2001 USEPA Office of Water reports "Occurrence of Unregulated Contaminants in Public Water Systems-A National Summary" (Table V.A.1) (USEPA, 2001a) and "Occurrence of Unregulated Contaminants in Public Water Systems-An Initial Assessment" (Tables A58 a, c) (USEPA, 2001b) incorrectly give 40 ug/L as the "MCL" for 1,2,3-trichloropropane, although it is currently not a regulated contaminant.

Recommendations

NJDEP strongly urges USEPA Office of Water to update its HA Table to provide appropriate public health protective drinking water guidance based on the carcinogenic effects of 1,2,3-TCP. NJDEP strongly urges USEPA Office of Water to develop an MCL for 1,2,3-TCP based on its occurrence in drinking water and its carcinogenic effects.

***Methyl tertiary butyl ether (MTBE)***

MTBE is a chemical of concern in drinking water, which NJDEP strongly urges USEPA to address, as discussed below. MTBE was listed on CCL1 and CCL2, and both times a decision was made not to regulate this chemical. In addition, MTBE is included in the current CCL3. There is as much or more relevant toxicology data on MTBE than for many other regulated chemicals, and it is a contaminant which is commonly found in drinking water throughout the United States. At least 41 of 50 states have developed a drinking water or ground water standard or guidance for MTBE as shown on a map linked from the USEPA website ( http://www.epa.gov/swerust1/mtbe/mtbemap.pdf ). MTBE is the most frequently detected volatile organic contaminant in data collected through New Jersey's Private Well Testing Act. Of the 51,028 wells tested under the Private Well Testing Act, 38 (0.01%) exceeded the New Jersey MCL of 70 ug/L and the highest concentration detected was 1550 ug/L.

New Jersey was among the first states to develop an MCL for MTBE. The basis for New Jersey's MCL was published in 1994 (NJDWQI, 1994), and it was adopted in 1996.

There is controversy over the reporting and interpretation of the results of the only available chronic oral study for MTBE (Belpoggi et al.,1995; Belpoggi et al., 1998). In this study, rats were dosed with MTBE by gavage in olive oil. The New Jersey Drinking Water Quality Institute (1994) recognized the uncertainties regarding the carcinogenicity of MTBE, specifically by oral exposure, and classified MTBE as a possible human carcinogen (equivalent to USEPA Group C under the 1986 USEPA guidelines). This classification forms the basis for New Jersey's Drinking Water Health-based Maximum Contaminant Level (MCL) for MTBE. The Health-based MCL is based on a subchronic oral gavage study in rats (Robinson, 1990), and the endpoint of concern was increased relative kidney weight. An additional uncertainty factor of 10 was incorporated to account for possible carcinogenic effects, following USEPA's and New Jersey's approach for drinking water risk assessment of possible human carcinogens. Some states have followed New Jersey's approach, while other states have based their MTBE risk assessments on a cancer slope factor.

A subchronic drinking water study for MTBE in rats was recently conducted (Bermudez et al., 2008) in order to set the doses for a two year drinking water study. This two year study is currently in progress, with the in-life phase expected to end in April 2009. The target date for the final report for this study is January 2010 (E. Bermudez, personal communication). The results of this study may answer some of the unresolved issues regarding the oral carcinogenicity of MTBE.

Recommendation

MTBE is a contaminant for which the states have a strong need for guidance from USEPA. It is recommended that USEPA evaluate the results of the current chronic oral drinking water study when it is complete, along with other toxicology information, and develop an MCL for MTBE.

***Perchlorate***

Perchlorate is a chemical of concern in drinking water, which NJDEP strongly urges USEPA to address, as discussed below. Perchlorate is a chemical with diverse uses in flares, fireworks, rocket fuel, and explosives. It is also found in fertilizers from certain geographic regions. Its widespread occurrence in drinking water has been well documented by others. After perchlorate was found in New Jersey drinking water as part of monitoring required by USEPA's Unregulated Contaminant Monitoring Rule, the New Jersey Drinking Water Quality Institute was asked by NJDEP to recommend a drinking water standard for perchlorate. NJDEP anticipates proposing a perchlorate MCL of 5 ug/L in the near future, as discussed below.

The National Research Council (2004) recommended a Reference Dose for perchlorate based on a small, but detailed study by Greer et al. (2002), which measured the inhibition of iodine uptake by the thyroid and the levels of thyroid hormone in adults receiving doses of perchlorate. The No Observed Effect Level for inhibition of iodine uptake in this study was 0.007 mg/kg/day. Iodine uptake is a full biological step away from a reduction in thyroxine or an increase in TSH, neither of which was observed even at the highest dose of perchlorate in this study.

The Reference Dose of 0.0007 mg/kg/day incorporates an uncertainty factor of 10 to protect sensitive subpopulations including fetuses and infants. Additional uncertainty factors were not considered necessary since the observed effect was not in and of itself considered adverse. This conclusion was supported by other data indicating the absence of effects on thyroid hormone in newborns and pregnant women in areas with perchlorate in the drinking water. Additional data since then has confirmed this for both groups. This Reference Dose was adopted by USEPA IRIS in 2005.

After reviewing the scientific literature the New Jersey Drinking Water Quality Institute concurred with National Research Council's Reference Dose (NJDWQI, 2005). From this Reference Dose, the Institute established a drinking water equivalent level of 24.5 micrograms of perchlorate per liter of water based on a 70 kilogram adult.

The last step in developing a health-based drinking water concentration is to adjust the drinking water equivalent level to account for other sources of exposure, such as food. When little data is available on other exposures that may add to the exposure from water, the default assumption is that the drinking water contribution should be limited to 20% of the total. Application of a 20% Relative Source Contribution factor results in a health-based drinking water concentration of 5 ug/L, which was recommended as the basis for New Jersey's MCL (NJDWQI, 2005). Based on their relative intakes of water and formula or breast milk, infants were considered to be protected. This is

supported by the recent publication of Food and Drug Administration data on exposure to perchlorate in foods.

Recommendation
NJDEP strongly urges USEPA to develop an MCL for perchlorate based on its widespread occurrence, well characterized effects on thyroid function, and adequate information on the relative contributions of food and drinking water to perchlorate exposure.

***Other CCL3 Contaminants Addressed by NJDEP***
New Jersey has developed Health-based MCLs (equivalent to USEPA MCLGs) for formaldehyde, n-hexane, and ethylene glycol, and is currently in the process of developing analytical methods for these so that an MCL may be adopted. The basis for the formaldehyde and n-hexane Health-based MCLs is found on the New Jersey Drinking Water Quality Institute's website http://www.nj.gov/dep/watersupply/njdwqinstitute.htm. A recommendation has been made to revise the Health-based MCL for ethylene glycol from 290 ug/L to 10,000 ug/L, based on evaluation of more recent data on both renal toxicity and developmental effects.

New Jersey promulgated an MCL for 1,1-dichloroethane in 1996. The New Jersey carcinogenicity classification, Reference Dose, and Health-based MCL for 1,1-dichloroethane, which were developed in 1994 and are found on the website given above, were recently reevaluated by the New Jersey Drinking Water Quality Institute. Based on reevaluation of the data relevant to carcinogenic effects and the current cancer risk assessment guidelines, it is recommended to classify 1,1-dichloroethane in New Jersey Carcinogenicity Category II, equivalent to Group C, under the previous (1986) USEPA guidance, and analogous to Suggestive Evidence of Carcinogenic Potential under the current (2005) guidance. USEPA IRIS does not provide a slope factor for 1,1-dichloroethane. It was recommended that an additional uncertainty factor of 10 for potential carcinogenicity be incorporated into the Reference Dose.

The current basis of the Reference Dose, kidney effects in cats exposed by inhalation, is a more sensitive endpoint than a newer rat oral subchronic study, and it was recommended to continue to use the current endpoint. It is recommended that the uncertainty factor of 5 currently used for small number of animals in the cat study be removed. The basis for the Reference Dose is already very conservative and health protective and the total uncertainty factor would exceed the maximum uncertainty factor of 10,000 used in Reference Dose development.

Based on the above, the recommended Reference Dose is 0.0032 mg/kg/day, which is a two-fold decrease from current Reference Dose of 0.0065 mg/kg/day. The recommended Health-based MCL is 23 ug/L, also a two-fold decrease from the current value of 46 ug/L.

**Conclusion**
We appreciate the opportunity to comment on the Draft Contaminant Candidate List 3. If you have any questions or require additional information, please contact Dr.Gloria Post of the NJDEP Division of Science, Research and Technology at (609) 292-8497 or gloria.post@dep.state.nj.us.

Attachment

Sincerely,

Judith Louis, Ph.D., Chief
Bureau of Environmental Assessment
Division of Science Research and Technology

Barker Hamill, Assistant Director
Water Supply Operations
Division of Water Supply

C: Eileen Murphy, NJDEP
Michele Putnam, NJDEP
Sandra Krietzman, NJDEP

Attachment

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**Senate**
**State of Minnesota**

May 20, 2008

**Re: Drinking Water Contaminant Candidate List 3 - Draft (EPA-HQ-OW-2007-1189)**

To Whom It May Concern:

I am writing in support of the regulation of perfluorooctanoic acid (PFOA) under the Safe Drinking Water Act.

Minnesota is one of seven states with widespread contamination of Perfluorochemicals (PFC), including PFOA. In 2005, PFOA was first detected in the community of Oakdale, Minnesota. It has since been detected in seven additional metropolitan communities located near or on the Mississippi River and former industrial waste disposal sites used by the manufacturing company 3M.

PFOA is a very stable, man-made chemical that the human body is unable to break down, and if exposure is constant, the chemicals are likely to persist in humans' bodies. The long term potential health risks of PFOA have been documented by a growing body of scientific research that shows PFOA causes liver cancer, testicular cancer and may cause other types of cancer such as breast cancer, as well as, birth defects, weakened immune system and Altered Hormone System Function. In 2006, the EPA Science Advisory Board classified PFO as a likely human carcinogen. A recent industry funded study, showed that 3M employees exposed to PFOA died of stroke and prostate cancer at higher rates than other workers at the company's Chemolite plant in Cottage Grove, Minnesota.

As the state senator who represents many people who have been exposed to PFOA and other perflourochemicals, I urge federal regulation of PFOA. Without such regulation, it is incumbent on states to try to set guidelines for exposure. While Minnesota has such a guideline for exposure to PFOA, it is a higher rate than other states. This, in effect, leaves Minnesotans to question whether the Minnesota Department of Health has set appropriate levels of exposure.

For the safety of the thousands of people around the country whose drinking water has been contaminated with PFOA, I strongly urge the EPA to increase regulation of PFOA through the Safe Drinking Water Act.

Sincerely,

Katie Sieben

Katie Sieben
Minnesota State Senator

ENVIRONMENTAL WORKING GROUP

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May 21, 2008

Water Docket (2822T)
Environmental Protection Agency
1200 Pennsylvania Ave., NW.
Washington, DC 20460

Regarding: Drinking Water Contaminant Candidate List 3—Draft; Docket EPA–HQ–OW–2007–1189 FRL-08529--7

To Whom It May Concern:

The Environmental Working Group (EWG) is a non-profit public health and environmental research and advocacy organization based in Washington, DC. EWG research addresses toxic industrial chemicals that pollute the environment and may be present in everyday consumer products. With this letter, we provide detailed comments and recommendations to the EPA regarding its draft Drinking Water Contaminant Candidate List 3 (CCL3), especially highlighting the urgent need for the inclusion of pharmaceuticals and perfluorochemicals (PFCs) on the final CCL3, and the promulgation of drinking water standards for these wide-spread pollutants that pose health risks to millions of Americans.

EWG analysis of water utilities' tap water test results shows that nationwide, water contaminated with 260 chemicals, including 166 industrial pollutants, such as plasticizers, solvents, pharmaceutical production ingredients, and propellants, are served to 210,528,000 people in 42 states (EWG 2005b). Fifty six percent of those people drink water with one or more industrial contaminants present at levels above non-enforceable EPA guidelines. In fact, more than 140 of the chemical contaminants detected in tap water are unregulated, without an enforceable, health-based limit in tap water. Due to the lack of federal oversight and the absence of monitoring and health standards, vulnerable populations, especially pregnant women and children, are not protected from this multitude of toxic chemicals in drinking water.

As highlighted by the recent national investigation by the Associated Press (Mendoza 2008), in addition to industrial chemicals, a wide range of pharmaceuticals that include antibiotics, sex hormones, and drugs used to treat epilepsy and depression, contaminate drinking water supplies of at least 41 million Americans. With every refreshing glass of water, millions of Americans are also drinking low-level mixtures of highly potent pharmaceuticals. The health effect of this cocktail of chemicals and drugs has not been studied, but there are many reasons to be concerned about risks for infants and others who are vulnerable. Pharmaceuticals, hormones, pesticides, and

anti-microbial ingredients from personal care products contaminate many streams around the entire United States (Kolpin 2002). Chemical pollution of ambient waters contributes to the load of chemicals in tap water. EPA needs to show leadership and act with utmost dedication to protecting public health by mandating monitoring and setting enforceable health standards for these hazardous contaminants.

We especially urge the EPA to include perfluorinated compounds on the final CCL3 list. PFCs are persistent, long-lasting industrial chemicals that have been utilized in a variety of manufacturing applications such as production of non-stick Teflon cookware, stain-proof Scotchgard products, grease-resistant food packaging and other types of paper materials, as well as carpets, water-proof textiles, and fire-fighting foam. In addition to the major fluorochemical producers (DuPont and 3M in the United States), many secondary manufacturers have used PFCs for decades in their products. Industrial wastewater discharges and air emissions of PFCs from businesses that produce stain- and grease-resistant paper, carpets, textiles, and furniture likely contributed to the PFC pollution of drinking water supplies across the country. Due to their extraordinary stability, PFCs last in the environment for thousands of years. PFCs accumulate in bodies of both wildlife and humans, recirculating through groundwater, lakes, rivers, and oceans, and coming back to people with water, food, air and dust. As a result of decades of environmental discharges of PFCs, these toxic chemicals are now found in many areas of the country, in many bodies of water, and in bodies of more than 98% of all Americans (Calafat, Kuklenyik 2007; Calafat, Wong 2007). At least 11 different states have documented drinking or ambient water contamination with PFCs and a national survey is critically needed to reveal the full extent of PFC water contamination.

PFCs such as perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS) and related chemicals, bioaccumulate and remain in blood, liver, and other tissues for years. This persistence in the human body distinguishes PFCs from other contaminants and significantly elevates the level of health concern, making monitoring and the establishment of tap water standards critical for PFC compounds. Contamination of drinking water with PFCs creates a constant source of exposure and has been associated with some of the highest blood levels of these toxic compounds ever measured. Some residents of communities in Ohio and West Virginia drinking PFOA contaminated tap water had blood levels of PFOA 250 times the national average. These individuals experienced PFOA exposures equivalent to occupational levels and in amounts associated with serious adverse health effects, as demonstrated by initial data obtained in a major ongoing epidemiological study in the region (West Virginia University School of Medicine 2008). It is thus reasonable to feel concerned that other communities in other states drinking PFOA contaminated water would face similarly elevated exposures and health problems.

PFCs have a broad spectrum of adverse health effects. PFOA exposure has been associated with impaired fetal and neonatal development, changes in reproductive and thyroid hormones, compromised immune and liver function, increased blood cholesterol levels, and potential

predisposition to chronic diseases later in life. Gestational period, newborn babies and young children are the most sensitive developmental stages that should be especially protected from PFC contaminants in drinking water. During pregnancy, PFCs move to the body of the fetus through the placenta (Apelberg, Goldman 2007; Inoue 2004; Midasch 2007; Tittlemier 2004); a newborn child also gets a large dose of PFCs with breast milk (Arcaro 2008; Karrman 2007; Kuklenyik 2004; So 2006; Tao 2008; Volkel 2007). Tap water standards for PFOA and other PFC will go a long way in protecting the health of this vulnerable population from adverse effects both in early development and in later life.

The Safe Drinking Water Act (SDWA) requires EPA to publish an updated list every five years which details currently unregulated drinking water contaminants that may pose human health risks. From this list, EPA must make determinations on whether to establish tap water standards for at least five contaminants with a national primary drinking water regulation. EPA originally considered three candidate perfluorochemicals for inclusion into the Contaminant Candidate List 3: PFOA, a processing aid for manufacturing of Teflon non-stick and water-resistant chemicals, PFOS, the primary ingredient in the furniture stain-proofing coating Scotchgard that was phased out in 2000, and perfluorobutanoic acid (PFBA), a replacement chemical that manufacturers are increasingly using instead of longer-chain PFCs.

Of the three PFCs nominated for CCL3, only PFOA was included in the current draft of CCL3. While we support the EPA decision to place PFOA on the list, we urge the agency to add other perfluorochemicals including, but not limited to PFOS and PFBA, as potential water contaminants that ought to be regulated under the Safe Drinking Water Act. Given the widespread use of PFCs in industrial applications and consumer goods ranging from food packaging to carpets and textiles, as well as detection of multiple PFCs in bodies of 98% of Americans, PFC contamination of drinking water requires thorough scrutiny in order to meet current scientific and regulatory standards for safety.

Specifically, we urge EPA to:

- List a full range of perfluorochemicals on the CCL3, including, but not limited to, PFOA, PFOS, PFBA, and other PFCs that have been found in the environment and in people and that are likely to contaminate both finished and ambient water sources;
- Establish regulatory standards for PFOA in drinking water;
- Include in the final CCL3 a broader list of contaminants found by water utilities in tap water, especially focusing on antibiotics and other pharmaceuticals.

Details and our rationale for these recommendations are provided below.

**1. List a full range of perfluorochemicals on the CCL3, including PFOA, PFOS, PFBA, and other PFCs found in the environment and in people.**

We support the EPA decision to place PFOA on the Draft Drinking Water Contaminant Candidate List 3. However, we disagree with the Agency's decision to exclude PFOS and PFBA from consideration as hazardous water contaminants. The stability of PFCs in the environment makes these chemicals distinct from many other classes of chemical water pollutants that have been previously regulated by the EPA (Conder 2008). Biomonitoring studies carried out by the Center for Disease Control found PFOS, PFOA, perfluorohexane sulfonic acid (PFHxS) and perfluorononanoic acid (PFNA) in more than 98% of 2,094 people tested. For some of these chemicals, children younger than 12 years of age have higher levels than adults (Olsen, Church 2004). PFCs enter human bodies from different sources, such as food, chemical-laden dust and water (Emmett 2006; Frisbee 2008). Various PFCs have been detected in finished and/or ambient water sampled in various locations in 11 states (Table below). PFOA has been found in tested water samples from all of these 11 states, PFOS has been found in 7 states, and PFBA appears poised to become an emergent water contaminant (MDH 2008).

We urge the Agency to add PFOS and PFBA to the CCL3. Even though production of PFOS has been banned by the EPA (US EPA 2002), this persistent and bioaccumulative compound is still present in many water sources in the US (MDH 2008). PFOS negatively affects early development in animals and humans (Apelberg, Witter 2007; Lau 2004); it interferes with the function of the nervous system and causes neurobehavioural defects (Johansson 2008), kills immune cells and weakens body's capacity to resist infection (Keil 2008; Peden-Adams 2008), and affects thyroid hormones that are critical for normal growth and maturation in children (Lau 2003; Luebker 2005). Considering how common is PFOS contamination of water sources, we believe EPA needs to set a regulatory standard to protect the health of people, especially young children, from PFOS.

In the absence of EPA guidance, states need to carry out their own risk assessments and set water contamination levels for PFCs. For example, the Minnesota Department of Health issued advisory guidelines of 1.0 μg/L for PFBA and set the limits for other PFCs chemicals in drinking water as well (MDH 2008). The presence of PFBA and other PFCs in groundwater at the fluorochemical manufacturing sites points to the potential of these replacement PFC chemicals to become new, emergent water contaminants whose health consequences will be directly tested on people exposed through drinking water. Now that the human health effects of PFC contamination in drinking water are becoming widely known from the C8 (PFOA) Health Project (West Virginia University School of Medicine 2008), it is imperative to protect vulnerable populations from future exposures to PFCs.

EPA needs to assess cumulative risks associated with multiple PFCs in finished and ambient water sources for children and other vulnerable populations. New data are constantly coming to light that demonstrate the extent of water contamination with PFCs (Fuchs 2008; Fuquay 2008; Hawthorne 2008; Konwick 2008; United Steelworkers Union 2006). Already, drinking and ambient water in 11 states is contaminated with PFCs and the full scope of this problem might be

even larger since businesses using fluorochemical products are found all around the country. This gap in our knowledge should be filled with a national survey of PFCs in water and a full range of PFCs should be included in the Unregulated Contaminant Monitoring Program.

In summary, we urge the EPA to list perfluorochemicals on the final CCL3, including, but not limited to, PFOA, PFOS and PFBA, and other PFCs that are commonly detected in people and the environment, so that the agency can mitigate the human health risks posed by these chemicals.

**2. Establish regulatory standards for PFOA in drinking water.**

We support the EPA in including PFOA on the Contaminant Candidate List 3 and we urge the agency to take the next, urgently needed step for public health protection by issuing national regulatory standards for PFOA levels in drinking water. In order to help the individual states that look to EPA for guidance and protect the health of all Americans, the agency should proceed with this step immediately, even while the data on other PFC water contaminants are collected.

Unquestionably, PFOA meets all the criteria for a contaminant that requires regulation by the EPA. Together with other PFCs, PFOA is now found in bodies of 98% of Americans (Calafat, Wong 2007); often, children younger than 6 years of age have higher PFOA levels compared to adults (Emmett 2006; Olsen, Church 2004). PFOA can cross the placenta and transfer from the mother's body to the fetus (Apelberg, Goldman 2007; Inoue 2004; Midasch 2007; Tittlemier 2004). PFOA contaminates the milk of breast-feeding mothers (Karrman 2007; Kuklenyik 2004; So 2006; Tao 2008; Volkel 2007). Once ingested with food or water, PFOA accumulates in the human body to 100-fold greater levels and persists for many years (Emmett 2006; Olsen, Burris 2007). This means that trace levels of PFOA in tap water can produce much higher long term exposures in people. For example, drinking water from the Little Hocking water system in Ohio was contaminated with PFOA at about 3.5 parts per billion (ppb), but some individuals drinking this water, who had no other unique exposures to PFOA, had blood levels of PFOA as high as 1,000 ppb (Emmett 2006).

As demonstrated by numerous studies in people and in animals, PFOA has an adverse effect on many health parameters, such as fetal and neonatal development (Lau 2004), immune function (DeWitt 2008; Yang 2002), reproductive and thyroid hormones (Lau 2007), liver function (Frisbee 2008; Son 2007), and blood levels of cholesterol and other lipids (Frisbee 2008; Olsen and Zobel 2007; Sakr, Kreckmann 2007; Sakr, Leonard 2007). In two studies of newborn babies, higher PFOA levels correlated with smaller weight and size at birth (Apelberg, Witter 2007; Fei 2007, 2008). PFOA exposure increases predisposition to obesity, heart disease, diabetes, and stroke (European Congress on Obesity 2008; Leonard 2007; Lundin 2007). PFOA causes liver, pancreatic, testicular, and mammary cancer in animals (Sibinski 1987). In epidemiological studies, PFOA has been shown to increase the risk of various cancers, especially prostate cancer, as well as liver, kidney, and bladder cancers (Leonard 2007; Lundin 2007; Olsen, Burlew 2004).

Despite extensive denial of PFOA health effects by the chemical industry, toxic effects of this chemical have been revealed by the chilling initial results from the C8 Health Project (West Virginia University School of Medicine 2008), a major epidemiological survey of residents in Ohio and West Virginia whose drinking water supply has been contaminated by PFOA. Sixty nine thousand people have been enrolled in the project, making it by far the largest study ever of PFC health effects in people (Frisbee 2008). The health effects observed in the study population are strong indicators of health problems that might be caused by PFOA in average Americans. Toxic effects from PFOA were observed in study participants with blood levels of the chemical equal to those found in the more highly exposed individuals in the US population. It is reasonable to expect that people in other states with contaminated drinking water may reach the same levels of exposure associated with significant adverse health effects in this study. As reported by the scientific team from the West Virginia University:

- Higher levels of PFOA in people correlate with lower levels of liver-produced C-reactive protein that helps the body fight bacteria, viruses, and other pathogens.
- PFOA exposure is associated with higher serum levels of two enzymes that can indicate liver damage; the same findings as have been found in occupational studies (Olsen and Zobel 2007; Sakr, Kreckmann 2007). These two findings indicate powerful liver toxicity of PFOA.
- Elevated PFOA levels in children are associated with high cholesterol levels, predisposing children to future weight problems and accompanying risk of heart disease.
- PFOA-exposed people have abnormal levels of thyroid hormones.

The multitude of PFOA health effects is especially worrisome because both PFOA and other PFCs are known to occur in public water systems with a frequency and at levels of public health concern. PFOA has been detected in public water supplies in many localities in West Virginia and Ohio (Emmett 2006; WVDEP 2005), 78% of drinking water systems tested by the New Jersey Department of Environmental Protection (NJDEP 2007), and in multiple townships in Washington County, Minnesota (MDH 2008). Additionally, drinking water supplies in some localities in Georgia may potentially be contaminated with PFOA (United Steelworkers Union 2006), where surface waters have been shown to be polluted with high levels of various PFCs (Konwick 2008). Other affected states include North Carolina (NCDENP 2008a), where groundwater contamination with PFOA in the vicinity of DuPont's Fayetteville Works plant doubled between 2006 and 2007 (Fuquay 2008), Alabama, where the Tennessee River is contaminated with PFOA and PFOS emitted by the 3M fluorochemical plant (Decatur) (Hansen 2002), Illinois, where both PFOA and PFOS have been detected in Chicago drinking water supply (Hawthorne 2008) as well as New York and Virginia (Clean Water Action Alliance of Minnesota 2008). All of these data are presented in the Table below:

| State/affected water sources | PFCs detected | References |
|---|---|---|
| Ohio (drinking water serving city of Belpre, Little Hocking Water Association, Tuppers Plains, Village of Pomeroy) | PFOA | (Emmett 2006; Frisbee 2008) |
| West Virginia (drinking water serving Lubeck Public Service district, Mason county) | PFOA | (Frisbee 2008; WVDEP 2005) |
| New Jersey (78% of 23 drinking-water systems tested) | PFOA, PFOS | (NJDEP 2007) |
| Minnesota (cities of Oakdale, Lake Elmo, Woodbury, Cottage Grove) | PFOA, PFOS, PFBA | (MDH 2008) |
| Alabama: Decatur/Tennessee river;<br>Mobile River | PFOA, PFOS<br>PFOA | (Hansen 2002);<br>(3M 2001) |
| Georgia: Conasauga River; streams and ponds near Dalton, GA;<br><br>city of Dalton drinking water supply;<br><br>city of Columbus drinking water | PFOA, PFOS, PFNA, PFDA, PFUA, PFOSA*<br>PFOA, PFOS<br><br>PFOS | (Fuchs 2008; Konwick 2008);<br><br>(United Steelworkers Union 2006);<br>(3M 2001) |
| North Carolina (ground water in Bladen County) | PFOA | (Fuquay 2008) |
| Illinois (Chicago tap water) | PFOA, PFOS | (Hawthorne 2008) |
| Virginia (ground and surface water) | PFOA | (Clean Water Action Alliance of Minnesota 2008) |
| New York (rivers and lakes) | PFOA, PFOS | (Sinclair 2006) |
| Florida (Port St. Lucie, surface water) | PFOA, PFOS | (3M 2001) |
| Lakes Erie and Ontario | PFOA, PFOS | (Boulanger 2004) |

*perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUA), perfluorooctane sulfonamide (PFOSA).

All together, various PFCs have been detected in finished and/or ambient water sampled in various locations in 11 states. PFOA has been found in tested water samples from all of these 11 states; PFOS has been found in 7 states. Most worrisome, groundwater levels of PFBA, a replacement chemical for some of the older PFC applications, appear to be on the rise (MDH 2008).

Without federal health standards for PFOA, individual states are forced to set their own standards so as to protect their citizens. For example, PFOA standards or risk-based levels have been established by North Carolina (2 μg/L) (NCDENP 2008b), Minnesota (0.5 μg/L) (MDH

2007) and New Jersey (0.04 μg/L) (NJDEP 2007). The 2006 consent order between EPA and DuPont required the company to offer alternative drinking water source or treatment for both public and private water users living near the Washington Works plant in Parkersburg, West Virginia whenever PFOA levels in their drinking water exceed 0.5 μg/L (US EPA 2006).

When confronted with such regulatory patchwork and the lack of guidance from the EPA, many states do not know how best to proceed, leaving the health of Americans at jeopardy (Hawthorne 2008; Sohn 2008). Many other states do not have the resources or expertise to establish and enforce drinking water standards for PFCs. Most states and the people who live in them depend on the EPA to protect them from drinking water contaminants. A failure to act will leave the residents in those states drinking tap water contaminated with highly toxic and persistent PFC pollutants for many years to come.

EPA regulation of PFOA and other PFCs that are commonly detected in people and the environment presents a meaningful opportunity for reduction of health risk due to these industrial chemical pollutants in drinking water. We urge the EPA to take much-needed action on PFOA and set a health-protective standard for PFOA in drinking water that will rely on the best available science and safeguard the health of millions of people.

**3. Include in the final CCL3 a broader list of contaminants found by water utilities in tap water, especially focusing on antibiotics and other pharmaceuticals.**

Pharmaceutical residues contaminate drinking water supplies when people take various prescribed and over the counter medications. While their bodies absorb and metabolize some of the chemicals, the rest is flushed out of the body and down the drain. Drinking water treatment plants are not designed to remove these residues, and the Associated Press (AP) National Investigative Team uncovered data showing these same chemicals in treated tap water and water supplies in 24 major metropolitan areas around the US (Mendoza 2008). Together with earlier publications by the US Geological Survey that identified pharmaceuticals and personal care product chemicals in waters bodies and streams around the United States (Kolpin 2002), the results of the AP investigation point to the potential health dangers presented by pharmaceuticals in drinking water.

All of the pharmaceuticals reported in drinking water supplies are unregulated in treated tap water—any level is legal. So far, the federal agencies have failed to set standards for pharmaceuticals which are generally exempted by the FDA from any environmental assessment (FDA 2008). Moreover, the EPA has not even required water utilities to test for these chemicals. Drug residues in tap water join hundreds of other synthetic chemicals Americans are exposed to daily, as contaminants in food, water, and air, or in common consumer products. EWG found an average of 200 industrial chemicals, pesticides and other pollutants in umbilical cord blood from 10 babies born in the U.S., indicating that our exposures to toxic chemicals begin in the womb, when risks are greatest (EWG 2005a). EWG analysis shows that of the top 200 drugs commonly

prescribed in the U.S., 13 percent are known to have serious side effects at levels less than 100 parts-per-billion (ppb) in human blood, with some causing potential health risks in the parts-per-trillion range. These levels are dangerously close to the ones found in drinking and ambient water sources (Kolpin 2002; Mendoza 2008).

We now call on the EPA to take swift action by setting standards for antibiotics and pharmaceuticals in tap water that will protect the health of all Americans, especially children. By the very nature of their design, pharmaceuticals can have effects on human body even at low doses. We urge the EPA to include in the final CCL3 a broad range of pharmaceutical resides and other contaminants found in tap water. This action will serve as the first, much needed step for ensuring the long-term health of our tap water – and the people who drink it.

In conclusion, presence of pharmaceuticals and perfluorochemicals in all states where water samples have been tested for these compounds, and their effects on the environment and on human health makes these chemicals very important candidates for federal regulation under the Safe Drinking Water Act. Federal drinking water policies and regulations should be set to ensure that vulnerable populations, including pregnant women and children, are protected from chemical contaminants in drinking water. Ingestion of drugs and PFCs with drinking water presents a significant hazard for human health, especially during sensitive times in life, such as *in utero*. Most states do not have the resources to establish or enforce drinking water standards, and people in these states depend on strong protections from the EPA. Regulation of these pollutants will assure equitable and uniform protection for the health of all Americans. Thus, we urge the EPA to follow up on the draft CCL3 by setting regulatory standards for both pharmaceuticals and PFCs in drinking water.

Sincerely,

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NJ ENVIRONMENTAL FEDERATION *Working Everyday to Prevent Harm to the Environment, Public Health & Our Communities*

**Docket:** EPA-HQ-OW-2007-1189
Drinking Water Contaminant Candidate List 3

May 21, 2008

The NJ Environmental Federation (NJEF) thanks EPA for giving us the opportunity to comment on drinking water standards under the Safe Drinking Water Act. The NJ Environmental Federation has 100,000 members and 100 member groups, and is the NJ chapter of Clean Water Action.

NJEF is concerned with a particular chemical listed on the Contaminant Candidate List, PFOA (perfluorooctanoic acid), as well as another perfluorinated chemical, PFOS (perfluorooctane sulfonic acid). We are aware of EPA's decision to exclude PFOS from the draft CCL 3, and the agency's willingness to accept comments on that decision.

EPA has long known of human health concerns of PFOS, and its unique ability to bind to proteins, unlike most persistent organic compounds, which accumulate in fatty tissue. Eight years ago, EPA acknowledged that:

> *"PFOS accumulates to a high degree in humans and animals. It has an estimated half-life of 4 years in humans. It thus appears to combine Persistence, Bioaccumulation, and Toxicity properties to an extraordinary degree."*

In addition, citing a 3M rat study, EPA noted:

> "PFOS caused postnatal deaths (and other developmental effects) in offspring in a 2-generation reproductive effects rat study (NOAEL of 0.1 mg/kg/day and LOAEL of 0.4 mg/kg/day). At higher doses in this study, all progeny in the first generation died while at the LOAEL many of the progeny from the second generation died. It is very unusual to see such second generation effects."
>
> (Source:
> http://www.chemicalindustryarchives.org/search/pdfs/scotchgard/20000516_226-0629.pdf

Further, PFOS has been of great interest to the Organisation for Economic Co-operation and Development (OECD) who, in 2006, made strong recommendations for industry and government to monitor the impact of PFOS.
(Source: http://www.olis.oecd.org/olis/2007doc.nsf/LinkTo/NT00002AB6/$FILE/JT03229256.PDF)

While it is presently ubiquitous in the environment, the threat of exposure is likely to increase as consumers dispose of household products containing PFOS. In turn, it is reasonable to anticipate that PFOS will continue to accumulate in the environment, including in ground and surface water, aquatic biota and humans. Although PFOS is no longer being manufactured, its persistence, and bio-accumulative and toxic properties warrant careful monitoring and regulation.

The EPA is well aware of the numerous studies documenting the exposures and dangers of PFOA. Although DuPont, currently the only major U.S. producer of PFOA, continues to claim that there is no proof that PFOA causes harm to human health, evidence to the contrary continues to mount, such as:

The New Jersey Environmental Federation (NJEF) is a state chapter of Clean Water Action. NJEF has over 100 member groups & 100,000 individual members.

| STATE OFFICE | LEGISLATIVE OFFICE | SOUTH JERSEY OFFICE | NORTH JERSEY OFFICE | NATIONAL OFFICE |
|---|---|---|---|---|
| 1002 Ocean Avenue | 1 Lower Ferry Road | 223 Park Avenue | 559 Bloomfield Avenue | 4455 Conn. Ave NW Suite A300 |
| Belmar, NJ 07719 | Trenton, NJ 08628 | Marlton, NJ 08053 | Montclair, NJ 07042 | Washington DC 20008 |
| Ph: 732.280.8988 | Ph: 609.530.1515 | Ph: 856.767.1110 | Ph: 973.744.3005 | Ph: 202.895.0420 |
| Fax: 732.280.8988 | Fax: 609.530.1508 | Fax: 856.768.6662 | Fax: 973.744.3069 | Fax: 202.895.0438 |

• EPA's Science Advisory Board identifies PFOA as a "likely" human carcinogen. (Source: Washington Post; *Compound in Teflon a "likely carcinogen*;" Juliet Eilperin; June 29, 2005)

• Researchers found PFOA and PFOS in the umbilical cord blood of children indicating that these chemicals cross the placenta between mother and child. (Source: Environmental Working Group/Commonweal, *Body Burden Study- The Pollution in Newborns*, Executive Summary; July 14, 2005)

• The Centers for Disease Control and John Hopkins University have reported health impacts in newborn babies such as low birth weight and reduced head circumference. (Source: *Possible Etiologies of PFAA-Induced Developmental Effects: Reflections from a Pediatric Perspective*; Johns Hopkins University, Baltimore, MD; U.S. Centers for Disease Control and Prevention)

• PFOA has been found in the breast milk of nursing mothers, and has been found in children between the ages of 2 and 12 at blood levels similar to those found in adults. (Source: Study conducted by Kathleen Arcaro of the University of Massachusetts Amherst—results are scheduled for publication in Environmental Science and Technology (http://www.umass.edu/loop/talkingpoints/articles/74700.php); other breast milk studies reported in February and May 2007 Issue of Environmental Health Perspectives)

• A study by the National Institute for Occupational Safety and Health has shown that PFOA may prime the immune system to overreact to allergens in mice. (Source: *Toxicological Sciences*, DOI: 10.1093/toxsci/kfm053; From Issue 2609 of New Scientist magazine, page 14; June 25, 2007)

• Researchers at the University of Pennsylvania School of Medicine found PFOA to be present in about 96 percent of the U.S. population, tending to accumulate within the body. (Source: Today's Sunbeam; *DuPont reports PFOA testing*; Randall Clark; May 07, 2008)

• Exposure to PFOA may be associated with changes in liver and immune function, as well as higher cholesterol levels in children. In May 2008, the preliminary results of a study of PFOA's possible impacts on the health of nearly 70,000 residents in the mid-Ohio Valley were released. The study examined the potential health impacts of PFOA released from DuPont's Washington Works plant south of Parkersburg, West Virginia. Previous studies of workers exposed to PFOA revealed elevated levels of kidney cancer, heart disease and diabetes. (Source: AScribe Newswire; *Big Study of Teflon Chemical in People Suggests Harm to Immune System, Liver, Thyroid*; May 13, 2008; www.hsc.wvu.edu/som/cmed/ophp/grandRoundsWebcast.asp)

The NJ Environmental Federation first became active in PFOA issues over three years ago, when PFOA was detected in the public water supply wells in Penns Grove and Carneys Point in NJ, some of which exceeded the interim NJ DEP guidance for PFOA of .04 ppb. United Steel Workers has tested the blood of some of their DuPont members and retirees at the Chambers Works facility in Pennsville, New Jersey and discovered exposure levels in some individuals to be hundreds of times higher than those found in the general public.

Studies have shown that some workers exposed to perfluorinated chemicals (PFCs) are more prone to prostate and bladder cancer and experience higher than normal levels of cholesterol — a risk factor for heart attack and stroke. (Source: Minneapolis Star Tribune; *Death rate up for 3M workers exposed to PFOA;* Tom Meersman; March 5, 2008

Numerous samples of surface water and drinking water supplies taken by the USW and others have revealed the presence of PFOA, PFOS and other PFCs. The PFCs being found in drinking water supplies are also

found in the blood of the general population as reported by the Centers for Disease Control and Prevention. The agency found 11 polyfluoroalkyl compounds, including perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and perfluorohexane sulfonic acid (PFHxS) in 1562 serum samples collected from a representative U.S. population 12 years of age and older in the 1999-2000 National Health and Nutrition Examination Survey. (Source: Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Abstract Received for review November 9, 2006, Revised manuscript received January 31, 2007, Accepted February 2, 2007)

NJEF believes that the EPA must determine nation-wide regulations to protect the public from further exposure to PFOA and PFOS. States, such as Minnesota, North Carolina and New Jersey have instituted their own standards or guidelines for one or both PFCs. For example, after finding widespread contamination of drinking water supplies in the state, the NJDEP set a safe drinking water guidance value of .04 parts per billion for PFOA. (Source: http://www.state.nj.us/dep/watersupply/pfoa.htm)

PFOA makes its way into products and downstream industries further exacerbating the contamination of people and the environment. DuPont and other companies promised EPA they would reduce and eventually eliminate PFOA use and manufacture via the 2010/2015 PFOA Stewardship Program. Unfortunately, DuPont refuses to make public verifiable annual PFOA production amounts. Recent test results of wells conducted by DuPont near its Chambers Works, NJ facility show levels of PFOA that exceed the NJDEP guidance level. (Source: Today's Sunbeam; *DuPont reports PFOA testing*; Randall Clark; May 07, 2008)

The 2010/2015 PFOA Stewardship Program is voluntary. We have little faith this program will achieve its goals, nor will it assure the protection of public water supplies. NJEF believes voluntary promises are not a substitute for much needed regulation and accountability. Therefore, it is vital to regulate PFOA through the Clean Water Act.

Submitted by
Jane Nogaki, Vice Chair
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223 Park Avenue
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**UNITED STEELWORKERS**

**UNITY AND STRENGTH FOR WORKERS**

**Docket:** EPA-HQ-OW-2007-1189

Drinking Water Contaminant Candidate List 3

May 21, 2008

Please see the enclosed comments regarding the Drinking Water Contaminant Candidate list submitted by the United Steel, Paper and Forestry, Rubber, Manufacturing, Energy, Allied-Industrial and Service Workers International Union AFL-CIO/CLC (USW).

For further information regarding USW's comments please contact either Diane Heminway or Shawn Gilchrist at 412-562-2400.

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USW SC Global Bargaining Department

**UNITED STEELWORKERS**

**UNITY AND STRENGTH FOR WORKERS**

**Docket:** EPA-HQ-OW-2007-1189
Drinking Water Contaminant Candidate List 3

May 21, 2008

The United Steel, Paper and Forestry, Rubber, Manufacturing, Energy, Allied-Industrial and Service Workers International Union AFL-CIO/CLC (USW) thanks EPA for giving us the opportunity to comment on drinking water standards under the Safe Drinking Water Act. The USW is North America's largest manufacturing union. We represent over 850,000 workers in the U.S. and Canada.

The union is concerned with a particular chemical listed on the Contaminant Candidate List, PFOA (perfluorooctanoic acid), as well as another perfluorinated chemical, PFOS (perfluorooctane sulfonic acid). We are aware of EPA's decision to exclude PFOS from the draft CCL 3, and the agency's willingness to accept comments on that decision.

EPA has long known of human health concerns of PFOS, and its unique ability to bind to proteins, unlike most persistent organic compounds, which accumulate in fatty tissue. Eight years ago, EPA acknowledged that:

> *"PFOS accumulates to a high degree in humans and animals. It has an estimated half-life of 4 years in humans. It thus appears to combine Persistence, Bioaccumulation, and Toxicity properties to an extraordinary degree."*

In addition, citing a 3M rat study, EPA noted:

> *"PFOS caused postnatal deaths (and other developmental effects) in offspring in a 2-generation reproductive effects rat study (NOAEL of 0.1 mg/kg/day and LOAEL of 0.4 mg/kg/day). At higher doses in this study, all progeny in the first generation died while at the LOAEL many of the progeny from the second generation died. It is very unusual to see such second generation effects."*
> (Source:
http://www.chemicalindustryarchives.org/search/pdfs/scotchgard/20000516_226-0629.pdf

Further, PFOS has been of great interest to the Organisation for Economic Co-operation and Development (OECD) who, in 2006, made strong recommendations for industry and government to monitor the impact of PFOS.
(Source: http://www.olis.oecd.org/olis/2007doc.nsf/LinkTo/NT00002AB6/$FILE/JT03229256.PDF)

While it is presently ubiquitous in the environment, the threat of exposure is likely to increase as consumers dispose of household products containing PFOS. In turn, it is reasonable to anticipate that PFOS will continue to accumulate in the environment, including in ground and surface water, aquatic biota and humans. Although PFOS is no longer being manufactured, its persistence, and bio-accumulative and toxic properties warrant careful monitoring and regulation.

The EPA is well aware of the numerous studies documenting the exposures and dangers of PFOA. Although DuPont, currently the only major U.S. producer of PFOA, continues to claim that there is no proof that PFOA causes harm to human health, evidence to the contrary continues to mount, such as:

- EPA's Science Advisory Board identifies PFOA as a "likely" human carcinogen. (Source: Washington Post; *Compound in Teflon a "likely carcinogen*;" Juliet Eilperin; June 29, 2005)

- Researchers found PFOA and PFOS in the umbilical cord blood of children indicating that these chemicals cross the placenta between mother and child. (Source: Environmental Working Group/Commonweal, *Body Burden Study- The Pollution in Newborns*, Executive Summary; July 14, 2005)

- The Centers for Disease Control and John Hopkins University have reported health impacts in newborn babies such as low birth weight and reduced head circumference. (Source: *Possible Etiologies of PFAA-Induced Developmental Effects: Reflections from a Pediatric Perspective*; Johns Hopkins University, Baltimore, MD; U.S. Centers for Disease Control and Prevention)

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USW represents 1,600 members at six DuPont facilities. We first became active in PFOA issues over three years ago. USW has tested the blood of some of our DuPont members and retirees at the Chambers Works facility in Pennsville, New Jersey and discovered exposure levels in some individuals to be hundreds of times higher than those found in the general public.

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PFOA that exceed the NJDEP guidance level. (Source: Today's Sunbeam; *DuPont reports PFOA testing*; Randall Clark; May 07, 2008)

The 2010/2015 PFOA Stewardship Program is voluntary. We have little faith this program will achieve its goals, nor will it assure the protection of public water supplies. USW believes voluntary promises are not a substitute for much needed regulation and accountability. Therefore, it is vital to regulate PFOA through the Safe Drinking Water Act.


# NRDC Comments on the Draft Drinking Water Contaminant Candidate List 3

## Docket Number: EPA-HQ-OW-2007-1189
## May 21, 2008

Pursuant to the Safe Drinking Water Act Amendments of 1996 (SDWA), the U.S. Environmental Protection Agency (EPA) is required to publish, every five years, a list of unregulated contaminants that are known or anticipated to occur in public water systems and may require regulation under the SDWA. The Agency then must make a decision about whether or not to regulate at least five of the contaminants on the list.

EPA is on the third round of this process and has published a list of candidate contaminants, called the CCL3. The draft list contains 104 contaminants: 11 microbiological contaminants and 93 chemical contaminants. EPA culled this list down from a universe of over 7000 contaminants. NRDC submits the following comments on EPA's Draft CCL3.

## I. SUMMARY

NRDC requests that EPA take the following actions concerning the Draft CCL3:

- Delete the pesticide **nitrofen** (CAS # 1836-75-5) from the Draft CCL3. The available information on use, release and potential environmental occurrence of this chemical does not support its inclusion in the CCL3.
- Regulate perchlorate (CAS # 7790-98-9) in drinking water pursuant to the Safe Drinking Water Act (SDWA). NRDC agrees with the inclusion of perchlorate in the CCL3 and supports the promulgation of a fully heath-protective Maximum Contaminant Level (MCL) for perchlorate.
- Regulate perfluorooctanoic acid (PFOA, CAS # 335-67-1) in drinking water pursuant to the Safe Drinking Water Act (SDWA). This chemical is a known endocrine disruptor and drinking water contaminant, and is appropriately included in the Draft CCL3.
- Add the following chemicals to the CCL3:
    - Alkylphenol polyethoxylates (APEs):

- **Alkylphenol mono- to tri-oxylates** (CAS # 68555-24-8)
- **Nonylphenol (NP)** (CAS # 25154-52-3)
- **Nonylphenol ethoxylate (NPE)** (CAS # 9016-45-9)
- **Octylphenol ethoxylate (OPE)** (CAS # 9036-19-5)

- Antibiotics:
  - **Amoxicillin** (CAS # 26787-78-0)
  - **Bacitracin zinc** (CAS # 1405-89-6)
  - **Linezolid** (CAS # 165800-03-3)
  - **Methicillin** (CAS # 61-32-5)
  - **Oxacillin** (CAS # 66-79-5)
  - **Penicillin** (multiple CAS #s)
  - **Spiramycin** (CAS # 8025-81-8)
  - **Tylosin** (CAS # 1401-69-0)
  - **Vancomycin** (CAS # 1404-90-6)
  - **Virginiamycin** (CAS # 11006-76-1)

- **Bisphenol A (BPA)** (CAS # 80-05-7)

- Microbials:
  - **Mycobacterium Avium Complex (MAC)**

- Pesticides:
  - **Aldicarb** (CAS # 116-06-3)
  - **Azinphos-methyl** (CAS # 86-50-0)
  - **Carbaryl** (CAS # 63-25-2)
  - **Chlorpyrifos** (CAS # 2921-88-2)
  - **Dichlorvos (DDVP)** (CAS # 62-73-7)
  - **Dicofol** (CAS # 115-32-2)
  - **Endosulfan** (CAS # 115-29-7)
  - **Linuron** (CAS # 330-55-2)
  - **Phosmet** (CAS # 732-11-6)
  - **Trichlorfon** (CAS # 52-68-6)
  - **Triclocarban** (CAS # 101-20-2)
  - **Triclosan** (CAS # 3380-34-5)

- Phthalates:
  - **Benzyl butyl phthalate (BzBP)** (CAS # 85-68-7)
  - **Di-isononyl phthalate (DiNP)** (CAS # 28553-12-0)
  - **Di-n-octyl phthalate (DnOP)** (CAS # 117-84-0)
  - **Dibutyl phthalate (DBP)** (CAS # 84-74-2)
  - **Dicyclohexyl phthalate (DCHP)** (CAS # 84-61-7)
  - **Diethyl phthalate (DEP)** (CAS # 84-66-2)
  - **Dimethyl phthalate (DMP)** (CAS # 131-11-3)

- Reproductive hormones:
  - **Equilenin** (CAS # 517-09-9)
  - **Equilin** (CAS # 474-86-2)
  - **17α-Ethynyl estradiol** (CAS # 57-63-6)
  - **17 α -Estradiol** (CAS # 57-91-0 70)
  - **17β-Estradiol** (CAS # 50-28-2)
  - **Estriol** (CAS # 50-27-1)
  - **Estrone** (CAS # 53-16-7)
  - **Mestranol** (CAS # 72-33-3)
  - **19-Norethisterone** (CAS # 68-22-4)
  - **Progesterone** (CAS # 57-83-0)
  - **Testosterone** (CAS # 58-22-0)

## II. DETAILED COMMENTS

**The CCL3 contains contaminants that need not be listed at this time.**

EPA listed **nitrofen** (CAS # 1836-75-5) as one of the chemical contaminants on the draft CCL3. However, NRDC does not believe that nitrofen needs to be included on the list. Nitrofen does not appear to pose a threat of contamination to drinking water supplies due to the lack of significant sources of nitrofen releases to the environment and to its rapid biodegradation in the aquatic environment. Nitrofen is no longer sold or manufactured in the United States[1] and all EPA registrations for nitrofen products were cancelled in 1983.[2] Nitrofen in water biodegrades relatively quickly, with about 99% biodegradation occurring within 50 days.[3] A search of the EPA Superfund Information Systems database found no hazardous waste sites proposed, listed, or deleted from the National Priorities List where nitrofen was a contaminant of concern.[4] The *HazDat* database of the Agency for Toxic Substances and Disease Registry (ATSDR), which contains information on the release of hazardous substances from Superfund sites or from emergency events, did not contain listings of any sites where nitrofen was detected.[5] A search of the EPA STORET database back to 1980 found data for only 75 environmental samples of any kind analyzed for

[1] National Library of Medicine. *Hazardous Substances Data Base*. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

[2] U.S. Environmental Protection Agency (U.S. EPA). 1998. *Status of Pesticides in Registration, Reregistration, and Special Review (aka Rainbow Report.* http://www.epa.gov/oppfead1/international/piclist.htm.

[3] Spectrum Laboratories. *Chemical Fact Sheet: CAS # 1836755.* http://www.speclab.com/compound/c1836755.htm

[4] U.S. EPA. *Superfund Information Systems*. http://cfpub.epa.gov/supercpad/cursites/srchsites.cfm.

[5] Agency for Toxic Substances and Disease Registry (ATSDR). *Hazardous Substance Release and Health Effects Database (HazDat)*. http://www.atsdr.cdc.gov/Hazdat.html

nitrofen. All of these were water samples from Dade County in the state of Florida taken between 1997 and 1999. No nitrofen was detected in any of the samples.[6]

The EPA Toxics Release Inventory contains reports of nitrofen disposal and other releases for only three years since reporting began in 1988: 505 pounds were released into the air from the Custom Alloy Corporation facility in High Bridge, NJ in both 2000 and 2001, and 25,300 pounds were disposed of in RCRA Subtitle C (hazardous waste) landfills from a Chemical Waste Management facility in Kettleman City, CA.[7] As such, nitrofen releases appear to be very limited in both time and geographic location.

Currently, the lack of sources of nitrofen releases to the environment suggests that exposure among the U.S. population is through consumption of imported vegetables treated with nitrofen,[8] and not through drinking water. Therefore, EPA should prioritize other, more troubling, chemicals to be listed on the CCL3 and considered for regulation.

**EPA must regulate some of the chemicals listed on the CCL3**

*Perchlorate.* NRDC agrees with the inclusion of **perchlorate** (CAS # 7790-98-9 ) in the CCL3 and supports the promulgation of a fully health-protective Maximum Contaminant Level (MCL) for perchlorate in drinking water that is protective of sensitive subpopulations such as pregnant women, fetuses, infants and children. Perchlorate is known to interfere with the normal function of the thyroid gland. The thyroid gland produces a hormone that is necessary for regulation of many body functions including heart rate, metabolism, energy, mood, cognitive function, and growth and development. Iodide is a necessary ingredient of the thyroid hormone thyroxine ($T_4$). Normally, iodide is transported into the thyroid gland by the sodium-iodide symporter (NIS). Once in the gland, iodide is bound to thyroglobulin. Perchlorate blocks the NIS and prevents uptake of iodide into the gland.

Thyroid hormone deficiency is associated with neurodevelopmental deficits
While there may be other toxic actions and target organs for perchlorate toxicity, it is a scientific certainty that the thyroid is a critical target organ, and inhibition of iodine uptake is a critical mechanism of toxicity. Furthermore, it is well established that thyroid hormones are critically important for normal growth and development of the central nervous system, and therefore that gestation and infancy are periods of vulnerability to perturbations in normal thyroid hormone activity. Adequate levels of thyroid hormone are necessary for correct migration of cortical neurons during brain formation (1st trimester), neuronal proliferation during cerebellar formation (2nd

[6] U.S. EPA. *STORET*. http://www.epa.gov/storet/dbtop.html
[7] U.S. EPA. *Toxics Release Inventory*. http://www.epa.gov/triexplorer.
[8] National Library of Medicine. *Hazardous Substances Data Base*. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

trimester), microtubule formation, and myelin deposition (postnatal).[9] Since the need for adequate thyroid hormone begins early in development, often before a mother may know that she is pregnant, treatment with iodide supplements may be too late to rescue early thryroid-dependent developmental processes.

In infants with early-life or prenatal onset of hypothyroidism, a condition where the thyroid does not produce adequate levels of thyroid hormone, researchers have recorded lasting effects in selective memory and attention deficits, language, hearing, and vestibular function[10]. Congenital hypothyroidism in infants is not uncommon, occurring in one out of every 3,500-5,000 children in North America. Surveys in pregnant women in the U.S. have reported that 2.5 percent of pregnant women have borderline or subclinical hypothyroidism (thyroid stimulating hormone (TSH) concentrations above 6 mU/l), and about 1 percent are estimated to have frank hypothyroidism. Since there are over 4 million babies born annually, this represents 40,000 infants born to mothers with frank hypothyroidism. A 1999 study by Dr. James Haddow, medical director, Foundation for Blood Research, showed that children born to mothers with untreated hypothyroidism during pregnancy score lower on IQ tests than children of healthy mothers.[11] Of the 62 women in Dr. Haddow's study, only 14 were diagnosed and receiving treatment for hypothyroidism before their pregnancies. Of those with untreated hypothyroidism, their children's IQ scores averaged 7 points below the children of mother's with normal thyroid hormone levels, and 19 percent had IQ scores below 85. Children who have an I.Q. less than 85 are more likely to have difficulties in school, and may be less successful in their careers and interpersonal relationships. In a later study researchers reported that pregnant women with borderline or more severe hypothyroidism (TSH levels 6mU/L or greater) have an almost four-times greater risk for miscarriage during the second trimester.[12] This study suggests that 6 out of every 100 late term miscarriages may be attributable to thyroid deficiency during pregnancy.

The World Health Organization recognizes iodine deficiency as the most common preventable cause of mental retardation in the world. Without adequate maternal iodine intake, both the fetus and mother are hypothyroid. Without appropriate diagnosis and treatment with iodide supplements the child may suffer abnormal neurodevelopment, in extreme cases leading to cretinism with mental retardation,

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[9] Glinoer D. Potential consequences of maternal hypothyroidism on the offspring: Evidence and implications. *Horm Res* 55:109-114, 2001.

[10] Rovet JF. Congenital hypothyroidism: an analysis of persisting deficits and associated factors. *Neuropsychol Dev Cogn C Child Neuropsychol.* 2002 Sep;8(3):150-62. Review.

[11] Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, O'Heir CE, Mitchell ML, Hermos RJ, Waisbren SE, Faix JD, Klein RZ. *N Engl J Med.* 1999 Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. Aug 19;341(8):549-55. Comment in: *N Engl J Med.* 1999 Aug 19;341(8):601-2. *N Engl J Med.* 1999 Dec 23;341(26):2015-6; discussion 2017. *N Engl J Med.* 1999 Dec 23;341(26):2015; discussion 2017. *N Engl J Med.* 1999 Dec 23;341(26):2016-7. *N Engl J Med.* 1999 Dec 23;341(26):2016; discussion 2017.

[12] Allan WC, Haddow JE, Palomaki GE, Williams JR, Mitchell ML, Hermos RJ, Faix JD, Klein RZ. Maternal thyroid deficiency and pregnancy complications: implications for population screening. *J Med Screen.* 2000;7(3):127-30.

deaf-mutism and spasticity. The World Health Organization estimated in 1990 that 20 million people worldwide had some degree of brain damage due to iodine deficiency experienced in fetal life. Although iodine deficiency is less common in the United States, the CDC biomonitoring data found that among women of childbearing age, 15% have low urine iodine concentrations (below 5 μg/dl) indicative of iodine deficiency. These women would be expected to be most vulnerable to the toxic effects of perchlorate during pregnancy. CDC reported that iodide deficiency was most common in women living below the poverty level, and people in the Southern U.S.

Because perchlorate crosses the placenta, it has the potential to directly affect the fetus, and may induce hypothyroidism in the fetus and newborn, in addition to its indirect fetal effects through interference with maternal thyroid activity.[13] A 2005 study reported that perchlorate was detected in all 38 samples of breast milk from women living in 18 states across the U.S. Perchlorate was also detected in all but one of the 47 store milk samples from 11 states. Although the study had a limited number of samples, it did report that the breast milk with the highest perchlorate levels (above 10 μg/L) also had the lowest iodide content.[14] These data suggest that perchlorate contamination in breast milk may lower the iodide content, thereby creating a double jeopardy for the breastfeeding infant, robbing its food source of necessary iodide while also dosing it with perchlorate. Most concerning, these researchers reported that in the breast milk samples the average concentration of perchlorate was five times higher than in store milk, raising concern that the healthiest source of food for newborns is in need of regulatory protection.

Several studies have demonstrated exposure and measurable effects of perchlorate exposure in children and adults:

- Blount et al. (2006a). This study found detectable perchlorate levels in all urine samples from 2,820 individuals studied as part of the National Health and Nutrition Examination Survey (NHANES) in 2001 and 2002. Researchers found a median perchlorate level of 3.6 ug/l (3.38 ug/g creatinine) and a 95$^{th}$ percentile level of 14 ug/l (12.7 ug/g creatinine). The estimated doses corresponding to the urinary levels of perchlorate were below the EPA Reference Dose (RfD).[15]

- Blount et al. (2006b). This study involved a portion of the study cohort described in Blount 2006a, cited above. The researchers studied the

[13] Clewell RA, Merrill EA, Yu KO, Mahle DA, Sterner TR, Mattie DR, Robinson PJ, Fisher JW, Gearhart JM. Predicting fetal perchlorate dose and inhibition of iodide kinetics during gestation: a physiologically-based pharmacokinetic analysis of perchlorate and iodide kinetics in the rat. *Toxicol Sci.* 2003 Jun;73(2):235-55.

[14] Kirk AB, Martinelango PK, Tian K, Dutta A, Smith EE, Dasgupta PK. Perchlorate and iodide in dairy and breast milk. *Environ Sci Technol.* 2005 Apr 1;39(7):2011-7

[15] Blount BC, Valentin-Blasini L, Osterloh JD, Mauldin JP, Pirkle JL. Perchlorate Exposure of the U.S. Population, 2001-2002. *J Expo Sci Environ Epidemiol.* 2007 Jul;17(4):400-7.

relationship between low-level perchlorate exposure as indicated by perchlorate concentrations in urine and serum levels of total thyroxine ($T_4$) and thyroid stimulating hormone (TSH) in 2,299 men and women aged 12 and older. The study found that higher perchlorate levels were significantly correlated with lower levels of T4 and higher levels of TSH in women with low urinary iodine (<100 ug/l).[16]

- Brechner et al, 2000. Authors report an association between perchlorate-contaminated drinking water in Yuma, Arizona and abnormal thyroid function in newborns. Their data suggest that even low-level perchlorate may increase risk of thyroid disruption in newborns.[17]

- Schwartz 2001. An unpublished study reported that perchlorate contaminated drinking water in a Southern California community is associated with thyroid disruption in newborns in a dose-dependent manner, with measurable effects at contamination levels of 3 to over 13 μg/L.

The Blount et al. 2006a and 2006b studies cited above were published after EPA issued its 24.5 ppb Drinking Water Equivalent Level (DWEL) for perchlorate. Taken together, these studies provide key evidence about perchlorate interference with thyroid hormones at levels below the EPA Reference Dose (RfD) and demonstrate the inadequacy of the 24.5 ppb DWEL that was calculated based on the RfD.

EPA drinking water monitoring data show that widespread contamination may be exposing millions of people to perchlorate throughout the country. EPA's Unregulated Contaminant Monitoring Rule (UCMR) required all large public water systems (serving a population of over 10,000 people) and a sample of smaller systems to monitor for perchlorate for a period of three years beginning in 2001. Public water systems (PWS) in 26 states and two U.S. territories had reported perchlorate detections as of the January 2005 UCMR data release.[18] Concentrations in the samples that tested positive for perchlorate ranged from 4.0 ppb (the minimum reporting level or MRL) to 420.0 ppb, with an average of 10.0 ppb. Of the 32,877 samples analyzed nationally, 614, or 1.9 percent, contained perchlorate at or above the MRL. A total of 153 of the 3,722 PWS tested, or 4.1 percent, detected perchlorate in their water. These systems served a population of 12.6 million, or 7.0 percent of the population served by all the PWS monitored. California and Arizona had the largest populations served by systems that detected perchlorate, with 5.3 million and 2.7 million, respectively.

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[16] Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. *Environ Health Perspect.* 2006 Dec;114(12):1865-71.

[17] Brechner RJ, Parkhurst GD, Humble WO, Brown MB, Herman WH. Ammonium perchlorate contamination of Colorado River drinking water is associated with abnormal thyroid function in newborns in Arizona. *J Occup Environ Med.* 2000 Aug;42(8):777-82.

[18] U.S. EPA. *Unregulated Contaminant Monitoring Rule*, [January 2005 data release]. http://www.epa.gov/safewater/ucmr/index.html

Some perchlorate detections in PWS seem to correspond closely with the locations of known perchlorate releases, particularly in some sites in California and Arizona, while in other states there is no apparent connection. Unidentified releases may play a role, but since perchlorate contamination can travel long distances in groundwater and surface water, geographic proximity to a release site is not always necessary for a water source to become contaminated. EPA had listed 109 sites of known perchlorate releases in 29 states as of December 10, 2004.[19]

Other agencies have collected perchlorate occurrence data that demonstrate that perchlorate is even more widespread than the UCMR database indicates. NRDC has reviewed the following data sources:

- Arizona: The Arizona Departments of Environmental Quality (ADEQ) and Water Resources (ADWR) conducted a study of perchlorate contamination in water between May and August, 2004, after two earlier studies by ADEQ and the City of Phoenix documented numerous occurrences of perchlorate in ground and surface waters in 1999 and 2000. Researchers analyzed a total of 41 surface water samples, 35 groundwater samples, and 12 samples from underground recharge facilities supplied by Colorado River water. The sampling points included both drinking and non-drinking water sources.[20]

- California: The California Department of Health Services (DHS) began tracking perchlorate occurrence in drinking water wells in 1997, and has required PWS to test for it since 1999. The data produced by the early well tests have been entered together with more recent drinking water monitoring data in a database maintained by the DHS Drinking Water Program. Although the database reporting limit is 4 ppb, it contains results for some samples with perchlorate levels as low as 1 ppb. As of April 2005, the database contained perchlorate sampling results for 1,231 PWS with active water sources. It also contained perchlorate results for 34 agricultural and monitoring sites belonging to 17 systems.[21]

- Massachusetts: The Massachusetts Department of Environmental Protection (DEP) promulgated an emergency regulation in February 2004 that required all community and non-transient, non-community (NTNC) water systems to test for perchlorate at each entry point. Groundwater systems were required to monitor in April and September, 2004. Surface water systems had to test in March 2004 and quarterly during the remainder of 2004. The DEP database contains results as low as 0.19 ppb, but concentrations below 1 ppb were

[19] U.S. EPA. *Known Perchlorate Releases in the U. S. - December 10, 2004.* http://www.epa.gov/fedfac/pdf/detection_with_dates_12_10_04.pdf

[20] Arizona Department of Environmental Quality (ADEQ)., *Perchlorate in Arizona: Occurrence Study of 2004* (revised). http://www.azdeq.gov/function/about/perch.html.

[21] California Department of Health Services (DHS). *California Drinking Water Data* [database on CD], April 2005.

below the limit of quantitation. The concentrations reported for these positive samples are usually laboratory estimates.[22] The DEP database contained monitoring results for 706 PWS as of March 2005.[23]

- Texas: In 2002 Texas Tech University (TTU) Water Resources Center initiated a two-phase study of perchlorate contamination in the High Plains area of western Texas for the Texas Commission on Environmental Quality. In 2003 the second phase of the investigation extended the initial nine-county study area to encompass 54 counties. A total of 560 PWS wells, 29 U.S. Geological Survey (USGS) wells, 99 High Plains Water District (HPWD) wells and 76 private wells were sampled.[24]

- U.S. Government Accountability Office (GAO): In May 2005 GAO published a report on perchlorate contamination and actions taken to address this problem in the U.S. This report listed perchlorate release sites and perchlorate detections in public water systems and private wells.[25]

A review of these data sources conducted by NRDC in 2005 found reports of of 5,369 public water systems sampled, of which 402 (7.5 percent) detected perchlorate in their water. The highest concentrations were reported by systems in Massachusetts and Puerto Rico, where the highest levels found were 1,300 and 420 ppb, respectively. Water systems in California, the state with the most affected systems, had concentrations ranging from 1.0 to 130 ppb, with an average of 9.2 ppb in positive samples

The occurrence, exposure and health effects data discussed above support the establishment of a Maximum Contaminant Level (MCL) for perchlorate. Unlike the existing DWEL, which fails to take into account the demonstrated effects of perchlorate exposure at low doses, the MCL should be protective of sensitive subpopulations such as pregnant women, fetuses, infants and children. In developing the MCL, EPA must consider factors such as body weight and routes and patterns of exposure, and include an appropriate margin of safety.

*Perfluorooctanoic acid.* We are pleased that the Agency included **perfluorooctanoic acid** or PFOA (CAS # 335-67-1) on the draft CCL3. Because of the toxicity and widespread exposure to PFOA, we believe that the time is ripe for EPA to regulate PFOA within this cycle, as required by the SDWA.

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[22] Personal communication from D. Guterman, Massachusetts DEP, April 5, 2005.

[23] Massachusetts Department of Environmental Protection. Perchlorate monitoring results [data provided by Drinking Water Program], March 2005.

[24] W.A. Jackson et al., *Distribution and Potential Sources of Perchlorate in the High Plains Region of Texas: Final Report*, Texas Tech University Water Resources Center, prepared for Texas Commission on Environmental Quality, 2004., http://www.waterresources.ttu.edu/research.htm.

[25] U.S. Government Accountability Office (GAO), *Perchlorate: A System to Track Sampling and Cleanup Results Is Needed,* 2005, GAO-05-462. http://www.gao.gov

The adverse health effects associated with exposure to PFOA are well documented. PFOA binds to serum proteins in blood and acts as an endocrine disruptor (lowering testosterone concentrations while increasing estradiol levels) and developmental toxicant, as found in some animal studies on rats.[26] A study of fish hepatocytes has confirmed the estrogenic properties of PFOA found in rat studies.[27]

A study in female mice found that PFOA decreased IgM antibody synthesis.[28] PFOA has also been found to cause liver damage in mice, which is characterized by multifocal coagulation, liquefaction necrosis, hepatocytomegaly, acidophilic cytoplasm and other cellular changes.[29, 30] This compound also causes liver, testis and pancreatic tumors in rats.[31] PFOA causes changes in gene expression affecting inflammation, cell cycle regulation, and metabolic processes.[32, 33] Neurotoxic effects have also been found in mice exposed neonatally to PFOA.[34]

Studies have indicated effects on humans as well. A study of newborn children in Maryland found an association between PFOA concentrations in cord serum and infants' birth weight and size.[35] In a study of 454 workers occupationally exposed to PFOA, higher levels of serum PFOA were associated with increased total cholesterol, decreased total bilirubin and increased serum aspartate aminotransferase, providing evidence of PFOA effects on the human liver.[36]

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[26] Jensen AA, Leffers H. Emerging endocrine disrupters: perfluoroalkylated substances. *Int J Androl.* 2008 Apr;31(2):161-9.

[27] Liu C, Du Y, Zhou B. Evaluation of estrogenic activities and mechanism of action of perfluorinated chemicals determined by vitellogenin induction in primary cultured tilapia hepatocytes. *Aquat Toxicol.* 2007 Dec 30;85(4):267-77.

[28] Dewitt JC, Copeland CB, Strynar MJ, Luebke RW. Perfluorooctanoic Acid-Induced Immunomodulation in Adult C57BL/6J or C57BL/6N Female Mice. *Environ Health Perspect.* 2008 May;116(5):644-50

[29] Son HY, Kim SH, Shin HI, Bae HI, Yang JH. Perfluorooctanoic acid-induced hepatic toxicity following 21-day oral exposure in mice. *Arch Toxicol.* 2008 Apr;82(4):239-46.

[30] Wolf DC, Moore T, Abbott BD, Rosen MB, Das KP, Zehr RD, Lindstrom AB, Strynar MJ, Lau C. Comparative Hepatic Effects of Perfluorooctanoic Acid and WY 14,643 in PPAR-{alpha} Knockout and Wild-type Mice. *Toxicol Pathol.* 2008 May 8.

[31] Kennedy GL Jr, 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 Jul-Aug;34(4):351-84.

[32] Rosen MB, Abbott BD, Wolf DC, Corton JC, Wood CR, Schmid JE, Das KP, Zehr RD, Blair ET, Lau C. Gene Profiling in the Livers of Wild-Type and PPAR{alpha}-Null Mice Exposed to Perfluorooctanoic Acid (PFOA). *Toxicol Pathol.* 2008 May 8.

[33] Wei Y, Chan LL, Wang D, Zhang H, Wang J, Dai J. Proteomic analysis of hepatic protein profiles in rare minnow (Gobiocypris rarus) exposed to perfluorooctanoic acid. *J Proteome Res.* 2008 Apr;7(4):1729-39.

[34] Johansson N, Fredriksson A, Eriksson P. Neonatal exposure to perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) causes neurobehavioural defects in adult mice. *Neurotoxicology.* 2008 Jan;29(1):160-9.

[35] Apelberg BJ, Witter FR, Herbstman JB, Calafat AM, Halden RU, Needham LL, Goldman LR. Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. *Environ Health Perspect.* 2007 Nov;115(11):1670-6.

[36] Sakr CJ, Leonard RC, Kreckmann KH, Slade MD, Cullen MR. Longitudinal study of serum lipids and liver enzymes in workers with occupational exposure to ammonium perfluorooctanoate. *J Occup Environ Med.* 2007 Aug;49(8):872-9.

In addition to these health effects, concerns about the occurrence and bioaccumulation of PFOA in the general population have existed since the 1990s.[37] Wastewater treatment plants (WWTP) are an important source of PFOA contamination in surface water,[38] which degrades drinking water sources. As a result, drinking water is an important pathway of PFOA exposure.

Elevated concentrations of PFOA have been found near facilities that use perfluorinated compounds or process wastewater containing these chemicals. For example, PFOA concentrations of 253 to 1150 ng/L were detected in the Conasauga River in Georgia. The study location was downstream of a wastewater land application site in Dalton, GA home to a large carpet manufacturing facility that is a source of fluorinated chemicals. Meanwhile, PFOA levels in streams and ponds in the Dalton area ranged from 49.9 to 299 ng/L.[39]

It has been estimated that the daily exposure of Americans to PFOA ranges from 1 to 130 ng/kg(bw)/day, the greater portion of which is due to oral exposure through food and drinking water.[40] A study near a fluoropolymer production facility determined that exposure through drinking water, rather than inhalation exposure, was the determinant factor in serum PFOA levels.[41] A similar German study also concluded that drinking water is a key exposure pathway near PFOA-contaminated sites. In this study, researchers analyzed blood PFOA levels in a study population of 691 individuals aged 6 to 69 years who lived near an agricultural area contaminated by the application of soil conditioner mixed with industrial waste. This population was exposed to PFOA through contaminated drinking water at concentrations of 500-640 ng/L The study found average PFOA levels in blood of 24.6 ug/L (children 5-6 years), 26.7 ug/L (mothers 23-49 years), and 28.5 ug/L (men 18-69 years). These values are 4.5 to 8.3 times higher than concentrations detected in a control population. PFOA concentrations were significantly related to tap water consumption at home.[42]

The 2003–2004 National Health and Nutrition Examination Survey (NHANES) found PFOA levels in 99.7% of the samples of human blood serum collected from the

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[37] U.S. Environmental Protection Agency. *Basic Information on PFOA.* http://www.epa.gov/oppt/pfoa/pubs/pfoainfo.htm

[38] Sinclair E, Kannan K. Mass loading and fate of perfluoroalkyl surfactants in wastewater treatment plants. *Environ Sci Technol.* 2006 Mar 1;40(5):1408-14.

[39] Konwick BJ, Tomy GT, Ismail N, Peterson JT, Fauver RJ, Higginbotham D, Fisk AT. Concentrations and Patterns of Perfluoroalkyl Acids in Georgia, USA Surface Waters Near and Distant to a Major Use Source. *Environ Toxicol Chem.* 2008 Apr 17:1.

[40] Trudel D, Horowitz L, Wormuth M, Scheringer M, Cousins IT, Hungerbühler K. Estimating consumer exposure to PFOS and PFOA. *Risk Anal.* 2008 Apr;28(2):251-69.

[41] Emmett EA, Shofer FS, Zhang H, Freeman D, Desai C, Shaw LM. Community exposure to perfluorooctanoate: relationships between serum concentrations and exposure sources. *J Occup Environ Med.* 2006 Aug;48(8):759-70.

[42] Hölzer J, Midasch O, Rauchfuss K, Kraft M, Reupert R, Angerer J, Kleeschulte P, Marschall N, Wilhelm M. Biomonitoring of perfluorinated compounds in children and adults exposed to perfluorooctanoate-contaminated drinking water. *Environ Health Perspect.* 2008 May;116(5):651-7.

2,094 study participants. The geometric mean PFOA concentration was 3.9 ug/L (95% confidence interval: 3.6 – 4.3 ug/L). This study population was representative of the general U.S. population above 12 years of age.[43] In addition, a study of 299 newborn children born in Baltimore, MD, determined that PFOA was present in 100% of the cord serum samples. The geometric mean concentration was 1.6 ng/mL.[44]

PFOA is persistent both in the environment and in the human body. In a study of retired perfluorochemical workers, the arithmetic and geometric mean elimination half-life of PFOA in blood serum was found to be 3.8 years, respectively, indicating a long persistence in the organism.[45]

Given the adverse health effects associated with exposure to PFOA, as well as the widespread PFOA contamination in the environment, EPA must determine to regulate levels of this chemical in drinking water, which will meaningfully reduce health risks for those served by public water systems.

**EPA has not included some contaminants on the CCL3 that should be listed**

Despite the appearances of having a comprehensive process for creating the CCL3 – by first looking at the universe of contaminants and then culling that list down – EPA failed to include some important categories of contaminants that are posing significant risk of adverse health effects in drinking water.

*Alkylphenol polyethoxylates (APEs).* These compounds include:

- **Alkylphenol mono- to tri-oxylates** (CAS # 68555-24-8)
- **Nonylphenol *(NP)*** (CAS # 25154-52-3)
- **Nonylphenol ethoxylate *(NPE)*** (CAS # 9016-45-9)
- **Octylphenol *(OP)*** (CAS # 27193-28-8)
- **Octylphenol ethoxylate *(OPE)*** (CAS # 9036-19-5)

[43] Calafat AM, Wong LY, Kuklenyik Z, Reidy JA, Needham LL. Polyfluoroalkyl chemicals in the U.S. population: data from the National Health and Nutrition Examination Survey (NHANES) 2003-2004 and comparisons with NHANES 1999-2000. *Environ Health Perspect.* 2007 Nov;115(11):1596-602.

[44] Apelberg BJ, Goldman LR, Calafat AM, Herbstman JB, Kuklenyik Z, Heidler J, Needham LL, Halden RU, Witter FR. Determinants of fetal exposure to polyfluoroalkyl compounds in Baltimore, Maryland. *Environ Sci Technol.* 2007 Jun 1;41(11):3891-7

[45] Olsen GW, Burris JM, Ehresman DJ, Froehlich JW, Seacat AM, Butenhoff JL, Zobel LR. Half-life of serum elimination of perfluorooctanesulfonate,perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. *Environ Health Perspect.* 2007 Sep;115(9):1298-305.

An estimated 450,000,000 pounds of alkylphenol polyethoxylates (APEs) are produced annually in the United States, and about half that amount is estimated to be released to wastewater. Alkylphenols were first reported to be estrogenic in the 1930s. In 1991, publication of the effects of nonylphenol on cultured human breast cancer cells led to health concerns. Estrogenic effects have also been shown in the mouse. Estrogenic effects are present at tissue concentrations of 0.1 μM for octylphenol and 1 μM for nonylphenol. A recombinant yeast screen using the human estrogen receptor has shown similar results.[46]

Alkylphenol polyethoxylates do not break down effectively in sewage treatment plants or in the environment. Instead they degrade to alkylphenols and alkylphenol ethoxylates, which persist for longer. Nonylphenol and its ethoxylates, and other alkylphenols, have been detected in wastewater and in waterways.[47]

*Antibiotics*. In March 2008, the Associated Press released a report on finding pharmaceuticals in drinking water that garnered considerable press across the country, despite EPA being cognizant of this problem for at least a decade. Currently, there are no pharmaceuticals listed on any of the CCLs. In light of the widespread presence of these chemicals in our drinking water, EPA must act now and include a subset of the chemicals on the CCL3.

Widespread exposure to **antibiotics** is contributing to the growth of bacterial resistance, and this problem is of grave concern. In the past several decades almost every bacteria that can cause infections in humans has developed resistance to at least one antibiotic, and some are resistant to multiple antibiotics. The Centers for Disease Control and Prevention (CDC) have identified antibiotic resistance as one of the most pressing public health problems to face our nation.[48] Infections caused by bacteria with resistance to at least one antibiotic have been estimated to kill over 60,000 hospitalized patients each year.[49]

Antibiotic resistance is caused by a number of factors including repeated and improper use of antibiotics in both humans and animals. Scientists also agree that exposure to low levels of antibiotics actually promotes bacterial resistance by exerting selective pressure for genes that promote resistance. Antibiotics are found in wastewater because the body does not completely metabolize all drugs, so both the metabolized and unmetabolized drug are excreted by humans into wastewater. For

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[46] Ying GG, Williams B, Kookana R. Environmental fate of alkylphenols and alkylphenol ethoxylates--a review. *Environ Int*. 2002 Jul;28(3):215-26.

[47] Gatidou G, Thomaidis NS, Stasinakis AS, Lekkas TD. Simultaneous determination of the endocrine disrupting compounds nonylphenol, nonylphenol ethoxylates, triclosan and bisphenol A in wastewater and sewage sludge by gas chromatography-mass spectrometry. *J Chromatogr A*. 2006 Oct 27.

[48] Centers for Disease Control and Prevention (CDC). *Campaign to Prevent Antimicrobial Resistance in Healthcare Settings*. http://www.cdc.gov/drugresistance/healthcare/problem.htm

[49] Health Care Without Harm. *Antibiotic Resistance and Agricultural Overuse of Antibiotics*, 2005. http://www.noharm.org/details.cfm?ID=938&type=document

example, when amoxicillin is ingested, 60-75% of the antibiotic is excreted unchanged into the urine. This antibiotic, now in the environment, may encounter other bacteria and promote resistance. It is unknown how much of an impact current low levels of antibiotics in drinking water are having on the problem of bacterial resistance. However, the potential has been recognized for many years.[50]

Massive quantities of antibiotics are used in agriculture both to treat infections and as food additives to promote growth and to compensate for conditions that contribute to infection. Animals raised in Concentrated Animal Feeding Operations (CAFOs) are at increased risk for infection due to close confinement and stress. In fact, it has been estimated that 70% of the antibiotics used in the U.S. are for animal husbandry.[51] Improper use and overuse of antibiotics in livestock and poultry can cause resistance in strains of bacteria that can infect humans. Furthermore, half of the antibiotics used in livestock are in the same classes of drugs that are used in humans. As a result the U.S. Institute of Medicine (IOM) and the World Health Organization (WHO) both stated that the widespread use of antibiotics in agriculture is contributing to antibiotic resistance in humans.[52]

Large animal feeding operations generate a large amount of waste that can potentially contaminate groundwater and waterways contributing to antibiotic resistance and contamination of waterways with steroid hormones.[53] As occurs in humans, some portion of the antibiotics administered to livestock will pass unchanged through their bodies and will be excreted in their waste. It has been estimated that between 25-75% of antibiotics are excreted unchanged in feces and can persist in the soil after land application.[54] Manure is applied in large quantities as fertilizer in farm fields. In

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[50] USA Today, in an 11/8/00 news article stated, "Experts fear that even low levels of antibiotics fouling the nations water supply may help create super-bugs: micro organisms that have evolved to survive an antibiotic's lethal assault."

[51] Mellon et al. *Hogging It: Estimates of Antimicrobial Abuse in Livestock*. Union of Concerned Scientists: Cambridge MA. 2000.

[52] Quotes from the Healthcare Without Harm factsheet. *Antibiotic Resistance and Agricultural Overuse of Antibiotics*. 2005. http://www.noharm.org/us/food/issue

*U.S. Institute of Medicine/National Academy of Science:* "Clearly, a decrease in antimicrobial use in human medicine alone will have little effect on the current [antibiotic-resistant] situation. Substantial efforts must be made to decrease inappropriate overuse in animals and agriculture as well."

*World Health Organization*: "There is clear evidence of the human health consequences due to resistant organisms resulting from non-human usage of antimicrobials. These consequences include infections that would not have otherwise occurred, increased frequency of treatment failures (in some cases death) and increased severity of infections."

[53] Gilchrist MJ, Greko C, Wallinga DB, Beran GW, Riley DG, Thorne PS. The potential role of concentrated animal feeding operations in infectious disease epidemics and antibiotic resistance. *Environ Health Perspect*. 2007 Feb;115(2):313-6.

Wallinga D, Mellon M, Roach S. Antibiotic use in swine farms in Alberta. *Can Vet J*. 2006 Dec;47(12):1153; author reply 1153-4.

Wallinga D. Public health advocate. Prev Vet Med. 2006 Feb 24;73(2-3):221-8. Epub 2005 Oct 28.

[54] Chee-Sanford, J.C., et al. Occurrence and Diversity of Tetracycline Resistance Genes in Lagoons and Groundwater Underlying Two Swine Production Facilities. *Applied and Environmental Microbiology*, April 2001. Vol. 6 no. 4, pp. 1494-1502.

addition to potentially contaminating the food supply with antibiotic resistant bacteria, antibiotics in manure can persist in soil and promote the development of more antibiotic resistant bacteria. Animal waste and its associated contaminants can enter waterways through groundwater contamination, overflow of waste lagoons into surface water or by over-application of manure as fertilizer in farm fields. A recently published study found evidence of fecal contamination and increased levels of antibiotic resistant bacteria downstream of a swine concentrated feeding operation.[55] Other studies have found antibiotic resistance in groundwater underlying a swine waste lagoon.[56]

As such, antibiotics that are used both for human medical needs and in large-scale agriculture operations at low levels in animal feed to promote animal growth must be included on the CCL3 and must be regulated. These antibiotics include **bacitracin zinc, spiramycin, tylosin, and virginiamycin.** Notably, these antibiotics were all banned for agricultural use in the European Union in 1998.

Infections among hospital patients (nosocomial infections) from enterococci bacteria are very common. Such infections that result in human disease can be fatal, particularly those caused by strains of vancomycin-resistant enterococci (VRE). During 2004, VRE caused about one of every three infections in hospital intensive-care units, according to the Centers CDC. As of 2007, the U.S. had reported seven cases of vancomycin-resistant *Staphylococcus aureus* (VRSA) infection. Therefore, **vancomycin** must be included on the CCL3.

Beta-lactam antibiotics are a broad class of antibiotics which include penicillin derivatives, cephalosporins, monobactams, carbapenems and Beta-lactamase inhibitors. Methicillin, a form of penicillin, had been relied upon as an common effective treatment for *Staphylococcus aureus* infections but now many strains of *S. aureus* bacteria are resistant to methicillin. These are now called MRSA, or 'methicillin-resistant *Staphylococcus aureus*'. Unfortunately, MRSA is actually resistant to much of the entire class of penicillin-like antibiotics called beta-lactams. Therefore, EPA must include **penicillin, amoxicillin, oxacillin and methicillin** on the CCL3.

Linezolid resistance in *Staphylococcus aureus* was reported in 2003. Community-acquired MRSA (CA-MRSA) has now emerged as an epidemic that is responsible for rapidly progressive, fatal diseases including necrotizing pneumonia, severe sepsis and necrotizing fasciitis. Outbreaks of CA-MRSA infections have been reported in correctional facilities, among athletic teams, among military recruits, in newborn nurseries, and among active homosexual men. Therefore, **linezolid** must be included on the CCL3.

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[55] Sapkota AR, et al. Antibiotic-resistant enterococci and fecal indicators in surface water and groundwater impacted by a concentrated Swine feeding operation. *Environ Health Perspect.* 2007 Jul;115(7):1040-5.

[56] Chee-Sanford, J.C., et al. Occurrence and Diversity of Tetracycline Resistance Genes in Lagoons and Groundwater Underlying Two Swine Production Facilities. *Applied and Environmental Microbiology*, April 2001. Vol. 6 no. 4, pp. 1494-1502.

*Bisphenol A (BPA).* **Bisphenol A** (4,4'-(1-Methylethylidene)bisphenol or 4,4'-Isopropylidenediphenol), (CASRN 80-05-7), is a monomer used as the building block of polycarbonate plastics and other plastics including epoxy resins. BPA is found in a wide variety of everyday consumer products, such as the coating of food and drink packaging, dental sealants, baby bottles, water bottles, microwave ovenware and eating utensils. As these products age, the polycarbonate polymer breaks down, releasing the BPA monomer. BPA is produced at over one million pounds per year and is frequently found in the environment. BPA releases to the environment in the U.S. totaled 1.4 million pounds in 2006, including 3,410 pounds released directly to water and 108,805 pounds released to the air.[57]

A number of recent studies have revealed that early life exposures to low-doses of BPA result in adverse effects later in life. The developing fetus is especially vulnerable. Although many of these studies were done in laboratory animals, the exposures occurred at concentrations currently found in the human population.[58]

- In rats, *in utero* exposure to BPA causes long-term effects on development of mammary tissue, causing preneoplastic lesions, increased susceptibility to cancer and increased sensitivity to a chemical known to cause breast cancer.[59, 60]
- Perinatal exposure to low levels of BPA causes precancerous prostate lesions (prostatic intraepithelial neoplasia) in rats. The effect appears to result from the failure in exposed animals of a gene to become hypermethylated as the rats age.[61]
- Experiments with mice reveal that chronic adult exposure to BPA causes insulin resistance, a common problem in humans that can lead to Type II diabetes and heart disease.[62]
- BPA has been shown to cause aneuploidy in mouse oocytes. Meiotic aneuploidy is the most common cause of miscarriage in women.[63]

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[57] U.S. EPA, *Toxics Release Inventory*, http://www.epa.gov/triexplorer.

[58] Calafat AM, Ye X, Wong LY, Reidy JA, Needham LL. Exposure of the U.S. population to bisphenol A and 4-tertiary-octylphenol: 2003-2004. *Environ Health Perspect.* 2008 Jan;116(1):39-44.

[59] Durando M, Kass L, Piva J, Sonnenschein C, Soto AM, Luque EH, Muñoz-de-Toro M. Prenatal Bisphenol A Exposure Induces Preneoplastic Lesions in the Mammary Gland in Wistar Rats. *Environ Health Perspect*, 2007 Jan;115(1):80-6.

[60] Murray TJ, Maffini, MV, Ucci AA, Sonnenschein C and Soto AM. Induction of mammary gland ductal hyperplasias and carcinoma in situ following fetal bisphenol A exposure. *Reprod Toxicol.* 2007 Apr-May;23(3):383-90.

[61] Ho SM, Tang WY, Belmonte de Frausto J, and Prins GS. Developmental exposure to estradiol and bisphenol A increases susceptibility to prostate carcinogenesis and epigenetically regulates phosphodiesterase type 4 variant 4. *Cancer Res.* 66(11):5624-32 (2006).

[62] Alonso-Magdalena P, Morimoto S, Ripoll C, Fuentes E and Nadal A. The estrogenic effect of bisphenol A disrupts pancreatic beta-cell function in vivo and induces insulin resistance. *Environ Health Perspect.*114(1):106-12 (2006).

[63] Hunt PA, Koehler KE, Susiarjo M, Hodges CA, Ilagan A, Voigt RC, Thomas S, Thomas BF, and Hassold TJ. Bisphenol A exposure causes meiotic aneuploidy in the female mouse. *Curr Biol.* 13(7):546-53 (2003).

- In a small prospective study, researchers in Japan found women with a history of repeated spontaneous miscarriages had higher levels of BPA. The researchers found evidence of aneuploidy in several of the miscarried fetuses in concordance with previous studies showing BPA causes meiotic aneuploidy.[64]
- BPA lowers sperm count in adult rats even at extremely low levels.[65]

Recently, a group of 38 scientists issued a consensus statement expressing their concern that current levels of BPA exposure were contributing to the human health conditions of neurobehavioral problems, obesity, infertility and reproductive cancers.[66] In addition, the U.S. National Toxicology Program has issued a draft report expressing "some concern" that BPA could cause neurobehavioral abnormalities, early onset puberty, and reproductive cancers, especially in fetuses, infants and children who are exposed.[67]

BPA is a water contaminant. A study in Germany found BPA in surface water (0.0005 to 0.41 ug/L), in sewage effluents (0.018 to 0.702 ug/L), in sediments (0.01 to 0.19 mg/kg) and in sewage sludge (0.004 to 1.363mg/kg dw).[68] Cousins et al. (2002) reviewed previously published monitoring data for the United States and found a median reported water concentration of 0.5 ug/l (below the detection limit of the studies) and a 90$^{th}$ percentile of 4.4 ug/l. The same study also suggested a half-life for BPA of 4.5 days in surface water, indicating that BPA can be transported hundreds of kilometers in rivers before levels fall below detection limits.[69]

*Microbials.* **Mycobacterium Avium Complex (MAC)** causes lung infections in immunocompromised individuals.[70] Mycobacteria are able to survive and grow in

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[64] Sugiura-Ogasawara M, Ozaki Y, Sonta S, Makino T and Suzumori K. Exposure to bisphenol A is associated with recurrent miscarriage. *Hum Reprod.* 20(8):2325-9 (2005).

[65] Sakaue, M, S Ohsako, R Ishimura, S Kurosawa, M Kurohmaru, Y Hayashi, Y Aoki, J Yonemoto and C Tohyama. Bisphenol-A Affects Spermatogenesis in the Adult Rat Even at a Low Dose. *J Occup Health* 43:185 -190 (2001).

[66] vom Saal FS, Akingbemi BT, Belcher SM, Birnbaum LS, Crain DA, Eriksen M, Farabollini F, Guillette LJ Jr, Hauser R, Heindel JJ, Ho SM, Hunt PA, Iguchi T, Jobling S, Kanno J, Keri RA, Knudsen KE, Laufer H, LeBlanc GA, Marcus M, McLachlan JA, Myers JP, Nadal A, Newbold RR, Olea N, Prins GS, Richter CA, Rubin BS, Sonnenschein C, Soto AM, Talsness CE, Vandenbergh JG, Vandenberg LN, Walser-Kuntz DR, Watson CS, Welshons WV, Wetherill Y, Zoeller RT. Chapel Hill bisphenol A expert panel consensus statement: integration of mechanisms, effects in animals and potential to impact human health at current levels of exposure. *Reprod Toxicol.* 2007 Aug-Sep;24(2):131-8

[67] Draft NTP brief on Bisphenol A. Released April 14, 2008.
http://cerhr.niehs.nih.gov/chemicals/bisphenol/BPADraftBriefVF_04_14_08.pdf

[68] Fromme H, Kuchler T, Otto T, Pilz K, Muller J, and Wenzel A. Occurrence of phthalates and bisphenol A and F in the environment. *Water Res.* 36(6):1429-38 (2002).

[69] Cousins IT, Staples CA, Klecka GM, Mackay1 D. Multimedia assessment of the environmental fate of bisphenol A. *Human and Ecological Risk Assessment* 2002 8(5):1107-1135.

[70] Centers for Disease Control, *Mycobacterium avium* Complex.
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/mycobacteriumavium_t.htm

aquatic environments due to their protective outer coating, which also makes them resistant to chlorine treatment of water. Environmental sources are thought to be the main route of transmission of these pathogens. These bacteria are widely present in water sources and can also be found in biofilms that form on the inside of water pipes.[71]

About 20 to 30 percent of people with AIDS become infected with MAC. Although adults usually do not get MAC disease until their T-cell count drops below 50, children can get it earlier. People with disseminated MAC disease develop fever, night sweats, weight loss, abdominal pain, tiredness, and diarrhea. EPA researchers estimate that approximately 1500 individuals with advanced AIDS ingest tap water with detectable concentrations of MAC organisms each day.[72] A related species typically considered MAC, *Mycobacterium avium intracellulare*, has been listed in Contaminant Candidate Lists (CCLs) 1 and 2. MAC should be included again in CCL3. The health effects and demonstrated occurrence in drinking water of MAC support the establishment of an MCL for this microbial contaminant.

*Pesticides*. **Aldicarb** (CAS # 116-06-3) is an N-methyl carbamate insecticide that causes reversible red blood cell and plasma cholinesterase inhibition. This pesticide is classified as Toxicity Category 1 because of its high toxicity through all routes of exposure (oral, dermal and inhalation). Symptoms of acute aldicarb exposure observed in animal studies include decreased motor activity, lacrimation, tremors, salivation, pinpoint pupils, and decreased grip strength. A rat study by EPA/ORD demonstrated that young animals are more susceptible to aldicarb-induced brain cholinesterase inhibition than adults.[73] Although it is generally believed that acute high level exposure to aldicarb will not cause chronic health effects, one case study by Grendon et al. (1994) in Washington State documented long-term health problems in men and sheep resulting from a single poisoning incident.[74]

EPA has not assessed the risks of chronic exposure to aldicarb in its 2006 Revised Human Health Risk Assessment (HRA). The Agency reasoned that since cholinesterase inhibition due to aldicarb exposure is reversed in less than 24 hours, such an assessment is unnecessary and chronic exposure can be treated as a series of acute exposures.[75] However, EPA mentioned in the Revised HRA that effects such as pale kidneys and hydroceles in the oviducts occurred in dams in a developmental study, symptoms that suggest chronic damage not seen in acute single-exposure

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[71] U.S. EPA, *Mycobacteria: Drinking Water Fact Sheet*, EPA-822-F-02-002. http://www.epa.gov.

[72] Rice G, Wright JM, Boutin B, Swartout J, Rodgers P, Niemuth N, Broder M. Estimating the frequency of tap-water exposures to Mycobacterium avium complex in the U.S. population with advanced AIDS. *J Toxicol Environ Health A*. 2005 Jun 11-25;68(11-12):1033-47.

[73] U.S. EPA, *Aldicarb, HED Revised Preliminary Human Health Risk Assessment for the Reregistration Eligibility Decision Document (RED)*. May 12, 2006.

[74] Grendon J, Frost F, Baum L. Chronic health effects among sheep and humans surviving an aldicarb poisoning incident. *Vet Hum Toxicol*. 1994 Jun;36(3):218-23.

[75] U.S. EPA 2006, supra.

cases. In addition, some studies suggest that chronic exposure to aldicarb may have longer-term effects on the immune and nervous systems. Fiore et al (2006) analyzed immune function in two groups of women, one exposed to aldicarb at environmental concentrations in groundwater at levels below 61 ppb (23 subjects), and an unexposed group (27 subjects). No women in either group had known reasons for immune problems. The researchers found a significant association between aldicarb exposure and abnormalities in T-cell subset ratios.[76] Hajoui et al. (1992) also found changes in the percentages of certain T-cell subsets after subchronic, but not chronic exposure.[77] The results of a rat study by Smulders et al. (2003) suggest that exposure to carbamates such as aldicarb may also lead to chronic changes in the nervous system resulting from the inhibition of neuronal nicotinic acetylcholine receptors.[78] A similar study of the carbamates fenoxycarb, carbaryl, and S-ethyl N,N-dipropylthiocarbamate (EPTC), which have the same mechanism of action, showed that increasing the pesticide dose or the length of exposure reduced the rate of reversal of acetylcholine receptor inhibition.[79] Therefore, two mechanisms, cholinesterase inhibition and acetylcholine receptor inhibition may lead to chronic neurotoxicity from exposure to carbamate pesticides such as aldicarb. This raises concerns about chronic low-level exposure such as may result from aldicarb contamination of drinking water.

EPA placed aldicarb under Special Review in 1984 due to concerns about groundwater contamination.[80] Aldicarb degradation in groundwater is slow. This chemical is persistent and mobile in soil, and degrades in the environment to aldicarb sulfoxide and aldicarb sulfone, both of which are cholinesterase inhibitors. In 1991 EPA established MCLs of 0.003 ppb for aldicarb, 0.004 ppb for aldicarb sulfoxide and 0.002 ppb for aldicarb sulfone, but these MCLs never went into effect. Instead, EPA issued a 7 ppb health advisory for each of the aldicarb species and for combined aldicarb residues.

EPA based its drinking water risk assessment in the HRA on the highest aldicarb concentrations in groundwater found in eight regions where aldicarb was used. The concentrations ranged from 0 to 24 ppb. The region with no aldicarb detections was removed from the analysis. Surface water concentrations, on the other hand, were derived from models for lack of sufficient monitoring data.

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[76] Fiore MC, Anderson HA, Hong R, Golubjatnikov R, Seiser JE, Nordstrom D, Hanrahan L, Belluck D. Chronic exposure to aldicarb-contaminated groundwater and human immune function. *Environ Res.* 1986 Dec;41(2):633-45.

[77] Hajoui O, Flipo D, Mansour S, Fournier M, Krzystyniak K. Immunotoxicity of subchronic versus chronic exposure to aldicarb in mice. *Int J Immunopharmacol.* 1992 Oct;14(7):1203-11.

[78] Smulders CJ, Bueters TJ, Van Kleef RG, Vijverberg HP. Selective effects of carbamate pesticides on rat neuronal nicotinic acetylcholine receptors and rat brain acetylcholinesterase. *Toxicol Appl Pharmacol.* 2003 Dec 1;193(2):139-46.

[79] Smulders CJ, Van Kleef RG, de Groot A, Gotti C, Vijverberg HP. A noncompetitive, sequential mechanism for inhibition of rat alpha4beta2 neuronal nicotinic acetylcholine receptors by carbamate pesticides. *Toxicol Sci.* 2004 Nov;82(1):219-27.

[80] U.S. EPA, 49 FR 28320, 1984, and 53 FR 24630, 1988.

Acute dietary exposure estimates from food alone exceeded the level of concern for children 1 to 2 years old (159% of the acute Population Adjusted Dose, or aPAD), and children 3 to 5 years old (129% aPAD), so that any additional exposures from drinking water would increase these risks of concern. The highest exposure from groundwater calculated for the regions where this pesticide was detected was 945% aPAD for the 95th percentile of the most exposed population sub-group. For the general U.S. population and other sub-groups, exposure ranged from 20% aPAD to 393% aPAD.[81]

It is clear from EPA's own analysis that aldicarb is a water contaminant that poses health risks of concern at levels found in food and drinking water. Given that food exposure alone exceeds levels of concern for children, drinking water exposure creates an additional unacceptable risk. EPA must move to establish a protective MCL for aldicarb.

**Azinphos-methyl** (CAS # 86-50-0) is an organophosphate pesticide classified as toxicity category 1 for oral exposure. Exposure to azinphos-methyl causes plasma, red blood cell and brain cholinesterase inhibition, with symptoms including headache, nausea, vomiting, dizziness, anxiety, muscle tremors and weakness. Studies by Souza et al. (2004, 2005) found that azinphos-methyl affected human placental enzymatic activity, which may have adverse consequences for fetal development.[82, 83] Exposure to organophosphate pesticides (OPs) such as azinphos-methyl has been associated with lower performance on neurobehavioral tests in exposed adults.[84] Children are more vulnerable than adults to the neurotoxic effects of OPs and may suffer developmental effects from low-level chronic exposures.[85]

Azinphos-methyl has a high potential to pollute surface waters due to runoff and spray drift.[86, 87] Data on environmental concentrations of azinphos-methyl in the

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[81] U.S. EPA, 2006, supra.

[82] Souza MS, Magnarelli de Potas G, Pechen de D'Angelo AM. Organophosphorous and organochlorine pesticides affect human placental phosphoinositides metabolism and PI-4 kinase activity. *J Biochem Mol Toxicol*. 2004;18(1):30-6.

[83] Souza MS, Magnarelli GG, Rovedatti MG, Cruz SS, De D'Angelo AM. Prenatal exposure to pesticides: analysis of human placental acetylcholinesterase, glutathione S-transferase and catalase as biomarkers of effect. *Biomarkers*. 2005 Sep-Oct;10(5):376-89.

[84] Rothlein J, Rohlman D, Lasarev M, Phillips J, Muniz J, McCauley L. Organophosphate pesticide exposure and neurobehavioral performance in agricultural and non-agricultural Hispanic workers. *Environ Health Perspect*. 2006 May;114(5):691-6.

[85] Rohlman DS, Arcury TA, Quandt SA, Lasarev M, Rothlein J, Travers R, Tamulinas A, Scherer J, Early J, Marin A, Phillips J, McCauley L. Neurobehavioral performance in preschool children from agricultural and non-agricultural communities in Oregon and North Carolina. *Neurotoxicology*. 2005 Aug;26(4):589-98.

[86] U.S. EPA, *Interim Reregistration Eligibility Decision for Azinphos-Methyl*, Case No. 0235. October 30, 2001.

[87] Dabrowski JM, Bennett ER, Bollen A, Schulz R. Mitigation of azinphos-methyl in a vegetated stream: comparison of runoff- and spray-drift. *Chemosphere*. 2006 Jan;62(2):204-12.

United States are limited, but studies in South Africa suggest that under certain conditions azinphos-methyl may also reach high concentrations (>40 ppb) in groundwater.[88, 89]

EPA indicated in its drinking water assessment in the Interim Reregistration Eligibility Decision (IRED) document for azinphos-methyl that the estimated environmental concentration (EEC) of this pesticide in surface water is 16 ppb at typical application rates in peaches. This concentration is over three times the acute drinking water level of comparison (DWLOC)[90] the agency calculated for infants less than a year old (5 ppb), and over twice the DWLOC for children 1-6 years (6 ppb). The highest annual mean concentrations in surface water according to monitoring data and EPA models ranged from 0.27 ppb to 7.2 ppb. The latter concentration exceeds the chronic DWLOC the agency calculated for infants less than a year old (7 ppb).

While EPA argued in the IRED that the phase-out of azinphos –methyl use on peaches will eliminate drinking water risks of concern, EPA is still allowing the use of azinphos-methyl on apples (the most frequently treated crop) at application rates equal to or higher than those for peaches (1.0-1.5 lb ai/A per application, 4.5 lb ai/A per year maximum on apples vs. 1.125 lbs ai/A per application, 4.5 lbs ai/A per year maximum on peaches). Furthermore, the total amount of azinphos-methyl used on apples (890,000 lb active ingredient) is over seven times the amount used on peaches (120,000 lb). Therefore, the EPA assessment indicates that azinphos-methyl poses a risk to drinking water supplies. While EPA has issued a four-year limited registration for azinphos-methyl use on apples and seven other crops, the Agency has stated that these registrations may be extended, thus creating the need to regulate azinphos-methyl as a drinking water contaminant.

**Carbaryl** (CAS # 63-25-2) is an N-methyl carbamate pesticide that acts as a neurotoxic acetylcholinesterase inhibitor and a "likely" carcinogen according to the Office of Pesticide Programs Cancer Assessment Review Committee. The systemic effects of carbaryl include headache, dizziness, weakness, shaking, nausea, stomach cramps, diarrhea, and sweating. Effects may also include loss of appetite, weakness, weight loss, and general malaise. Carbaryl is particularly toxic to the developing nervous system of fetuses, infants, and young children. Exposure to elevated levels of

[88] Loewy RM, Carvajal LG, Novelli M, de D'Angelo AM. Effect of pesticide use in fruit production orchards on shallow ground water. *J Environ Sci Health B*. 2003 May;38(3):317-25.

[89] Loewy RM, Carvajal LG, Novelli M, Pechen de D'Angelo AM. Azinphos methyl residues in shallow groundwater from the fruit production region of northern Patagonia, Argentina. **J Environ Sci Health B**. 2006;41(6):869-81.

[90] The drinking water level of concern (DWLOC) is the amount of allowable risk left for exposure through drinking water, after considering the contribution from food to the total allowable dietary risk. The DWLOC is compared with the drinking water estimated environmental concentration (EEC) to determine whether drinking water exposure risks are of concern.

carbaryl may cause developmental neurotoxicity and "significant changes in some of the morphometric measurements of the brain".[91, 92]

Approximately 3.9 million pounds of carbaryl active ingredient are used annually in the U.S. When EPA issued its Revised Risk Assessment for carbaryl in 2003, its water assessment did not consider non-agricultural sources of carbaryl, which constitute a total of 40% of carbaryl use by weight, and which are the dominant sources of carbaryl pollution in surface water. Despite ignoring non-agricultural uses, the carbaryl health risk assessment in the *Interim Reregistration Eligibility Decision* (IRED) found that acute surface water risks presuming maximum label application rates exceeded the drinking water level of concern (DWLOC) for children and the general population when combined with estimated food exposures.[93]

U.S. Geological Survey National Water-Quality Assessment (USGS NAWQA) monitoring data presented in the carbaryl assessment demonstrated that streams draining urban areas had both higher concentrations of carbaryl and more frequent detections, when compared with streams draining agricultural or mixed land use areas. It is clear that contamination of water is predominantly from non-agriculture uses of carbaryl, and that by not considering these uses, the Agency dramatically underestimated the amount of carbaryl in drinking water (Estimated Environmental Concentration, or EEC), which is likely to be two-times higher than EPA estimates. Twenty-one (21) percent of surface water samples in the NAWQA database contained detectable levels of carbaryl.

EPA discussed in its IRED the limitations of existing monitoring data:

> "Carbaryl is fairly mobile, but is not likely to persist or accumulate in the environment. As such, it is difficult for monitoring studies to detect peak concentrations that can occur. EPA determined that currently available monitoring studies for carbaryl are limited in this regard, and did not use them to define peak values for carbaryl."

As a result of these data limitations, EPA used models to estimate drinking water EECs for currently registered uses in the carbaryl IRED. The Agency reported that the acute drinking water EECs ranged from 23 to 410 ppb for acute exposure, and from 1.3 to 23 ppb for chronic exposure, which exceeded the acute DWLOC for children 1-2 years old (7.4 ppb) and for the general population (200 ppb). This is especially concerning, given that these calculations are likely to underestimate risk by excluding non-agricultural uses of carbaryl, which comprise 40% of total carbaryl

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[91] Brenda Tarplee, U.S. EPA Health Effects Division, C*arbaryl Reassessment Report of the FQPA Safety Factor Committee*, Memorandum, December 13, 1999, Tox Review No. 013891.

[92] Brenda Tarplee, U.S. EPA Health Effects Division, *Carbaryl - 2nd Reassessment Report of the FQPA Safety Factor Committee*, Memorandum, April 30, 2001, Tox Review No. 014553.

[93] U.S. EPA, *Interim Reregistration Eligibility Decision for Carbaryl*, Case No. 0080. Revised October 22, 2004.

used. Therefore, it is likely that actual EEC's are even higher, possibly 40% higher, than what the Agency calculates. The high toxicity of carbaryl, coupled with the high exceedances of acceptable levels in drinking water, make this level of risk to infants and children unacceptably high.

Given the limitations in the monitoring data that the Agency has acknowledged, and the fact that the highest EEC estimated by EPA models was 55 times the acute DWLOC for children 1 to 2 years old, it is clear that carbaryl presents risks of concern from drinking water exposure and should be regulated as a drinking water contaminant by establishing an MCL.

**Chlorpyrifos** (CAS # 2921-88-2) is an organophosphate pesticide used at approximately 21-24 million pounds active ingredient (a.i.) annually in the United States. Most chlorpyrifos is used in agriculture on crops such as corn and cotton, but other uses include golf courses, road medians, food processing plants, manufacturing plants, ship holds, railroad boxcars, and non-structural wood treatments. Chlorpyrifos is applied aerially, by chemigation, groundboom, hand wand, airblast sprayer, and other methods.[94]

With chlorpyrifos and other developmental neurotoxic chemicals, risk to the fetus, infant, and child comes primarily from the timing of exposure. Even a very small dose, for even a short duration, during a developmental period of vulnerability will result in permanent neural dysfunction. There is no demonstrated reliable threshold of safety for this highly toxic chemical, as indicated in the IRED, where a no-effect level could not be determined for developmental neurotoxicity. However, there is demonstrated evidence of neuropathology and increased vulnerability of fetuses when exposed to chlorpyrifos[95]. EPA has acknowledged this susceptibility in the chlorpyrifos Human Health Risk Assessment:

> "In conclusion, the weight of the evidence raises concern for an increase in both the sensitivity and susceptibility of the fetus or young animal to adverse biochemical, morphological, or behavioral alterations from chlorpyrifos treatment during brain development. With respect to cholinesterase inhibition, an increase in sensitivity of the young compared to adults was seen all along the dose response curve, even at relatively low doses."[96]

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[94] U.S. EPA, *Interim Reregistration Eligibility Decision for Chlorpyrifos*. 2002.

[95] Makris S, Raffaele K, Sette W, Seed J. *A retrospective analysis of twelve developmental neurotoxicity studies submitted to the USEPA Office of Prevention, Pesticides, and Toxic Substances (OPPTS)*. Draft November 12, 1998.

[96] U.S. EPA. *Human Health Risk Assessment: Chlorpyrifos*. 2000.

Although EPA said in the IRED that the drinking water risk is below the level of concern, the Agency noted that there have been cases of high levels of drinking water well contamination associated with localized applications of chlorpyrifos as a subterranean termiticide. This was addressed, EPA said, by eliminating all termiticidal uses. However, despite EPA's assertions that only termiticidal use leads to water contamination problems, USGS and others have found contamination of ground and surface water with chlorpyrifos and its metabolites, and EPA's own modeling shows that it is likely that in certain areas of heavy use, chlorpyrifos (and its metabolites) present significant water risks. There is no evidence that the water risks of chlorpyrifos and its metabolites are limited to termiticidal use.

There is extensive evidence of the potential of chlorpyrifos to contaminate surface and groundwater. Combined USGS data for state, local, national, and multi-state studies that measured chlorpyrifos concentrations in surface water detected the pesticide at 7 of 108 (6%) sites sampled.[97] Chlorpyrifos has medium runoff potential due to its relatively low water solubility, 2 mg/L[98,99]. A chlorpyrifos flux as a percentage of use of 0.15 has been measured in the Minnesota River.[100] Chlorpyrifos is also used in non-agricultural settings and can drift or runoff directly into surface water bodies in areas of high population density.

Data from the Mid-Continent Pesticide Study[101] show that chlorpyrifos was present in the ground water in 4.2% of the wells sampled.[102] Chlorpyrifos has been detected in 0.6% of wells sampled, according to the U.S. EPA's Pesticides in Ground Water Database.[103] Long (1989) detected chlorpyrifos in the ground water of 30% of 56 sites examined beneath pesticide mixing and loading facilities in Illinois.[104] The maximum concentration detected was 0.5 ppb.

Water monitoring sample sites are not necessarily correlated with chlorpyrifos use sites, and in particular, may miss sites where multiple fields are treated with chlorpyrifos resulting in pooled runoff into a common water source. In fact, the

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[97] Larson, Steven J., Capel, Paul D., and Majewski, M.S., 1997, *Pesticides in Surface Waters: Distribution, Trends, and Governing Factors. Chelsea*, MI: Ann Arbor Press, 373 p. 19.

[98] Becker, R.L., Herzfeld, D., Ostlie, K.R., and Stamm-Katovich, E.J., 1989, *Pesticides: Surface runoff. leaching, and exposure concerns*, University of Minnesota, Minnesota Extension Service Publication AG-BU-3911, 32 p.

[99] Goss, DW. Screening procedure for soil and pesticides relative to potential water quality impacts: *Weed Technol.* 1992 6:701-8.

[100] Larson et al, 1997, supra.

[101] Burkart MR, Kolpin DW. Hydrologic and land-use factors associated with herbicides and nitrate in near-surface aquifers. *J. Environ. Qual.* 1993 22(4):646-56.

[102] Barbas, JE, Resek, EA. 1996, *Pesticides in Ground Water: Distribution, Trends, and Governing Factors*. Chelsea, MI: Ann Arbor Press, 588 p., at p. 98-9

[103] Barbas & Resek, supra, at p. 167

[104] Long, T., 1989, Groundwater contamination in the vicinity of agrichemical mixing and loading facilities, in *Illinois Agricultural Pesticides Conference: Proceedings*: University of Illinois, College of Agricultural Consumer and Environmental Services, Urbana-Champaign, Ill., pp. 139-149; Barbas & Resek at 327.

IRED states, "it is not clear that they [monitoring data] represent the most vulnerable groundwater where chlorpyrifos is used most intensively" (IRED p.18). Monitoring of surface water is likely to be subject to the same problem. Levels of chlorpyrifos in pooled runoff sites are likely to be many times higher than single field sites. Similarly, data collection is not timed to correspond with worst-case scenarios, such as closely following chlorpyrifos applications, or following large storm runoff events, and thus most often misses these highly toxic environmental exposures.

Using the PRZM/EXAMS screening model, EPA estimated that 90-day average and peak chlorpyrifos concentrations were 6.7 and 40 ppb respectively. Meanwhile, acute DWLOCs for infants less than a year old, children 1-6 years and females 13 to 50 years ranged from 0.9 to 9 ppb. Chronic DWLOCs for these population groups ranged from 0.2 to 0.72 ppb. EPA's modeling estimates therefore show that chlorpyrifos exposure in drinking water has the potential to expose vulnerable groups of the population to unacceptable levels of this chemical.

**Dichlorvos** (CAS # 62-73-7), or DDVP, is an organophosphate insecticide widely used in agriculture. Like other organophosphates, dichlorvos is an acetylcholinesterase inhibitor. DDVP exposure may cause symptoms such as nausea, vomiting, dizziness, muscle spasms, and seizures. According to a 2000 EPA Cancer Assessment review, there is suggestive evidence that dichlorvos may cause cancer.[105] The National Toxicology Program has stated that there is "clear evidence" of carcinogenic activity of dichlorvos in a mice study.[106] One study has linked dichlorvos exposure to leukemia in children under 15.[107] Another study has also found an association between dichlorvos exposure and leukemia in adult men.[108] Furthermore, EPA has determined that "dichlorvos has been shown to be a direct acting mutagen by common *in vitro* bacterial genetic toxicity assays and *in vitro* mammalian test systems."[109]

Dichlorvos is soluble in water and may enter surface waters in runoff. However, no data on its occurrence in surface waters has been collected; there is also little data on dichlorvos in groundwater. Two other pesticides, naled and trichlorfon, degrade to dichlorvos in the environment and represent additional inputs of dichlorvos to water. However, monitoring data on these two pesticides is also very limited.

Given the lack of monitoring data, EPA used IR-PCA PRZM/EXAMS models to

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[105] U.S. EPA, *Dichlorvos (DDVP) – Report of the Cancer Assessment Review Committee*. 2000.

[106] National Toxicology Program. *NTP Toxicology and Carcinogenesis Studies of Dichlorvos (CAS No. 62-73-7) in F344/N Rats and B6C3F1 Mice (Gavage Studies)*. National Toxicology Program Technical Report Series 1989;342:1-208

[107] Leiss JK, Savitz DA. Home pesticide use and childhood cancer: a case-control study. *Am J Public Health*. 1995; 85:249-52

[108] Brown LM, Blair A, Gibson R, et al. Pesticide exposures and other agricultural risk factors for leukemia among men in Iowa and Minnesota. *Cancer Res*. 1990;50(20):6585-91

[109] U.S. EPA. HED Preliminary Risk Assessment for Dichlorvos. October 11, 2000.

calculate estimated drinking water concentrations (EDWCs) of dichlorvos in surface water. The models produced estimates that were below the EPA level of concern.[110] However, the complete lack of monitoring data raises questions about whether an exclusive reliance on modeling results is appropriate for a neurotoxic and potentially carcinogenic pesticide such as dichlorvos. EPA should collect data monitoring data for dichlorvos by requiring such data from the registrants or commissioning its own studies to better assess drinking water risks and set an MCL if necessary.

**Dicofol** (CAS # 115-32-2) is an organochlorine pesticide used in agriculture, primarily on cotton and citrus crops. Approximately 860,000 pounds of active ingredient are used every year. Animal studies have found that dicofol causes toxicity in the liver, adrenal glands, kidneys, thyroid, reproductive organs, heart and stomach. Liver and thyroid effects occurred at relatively low doses (100 ppm and 10 ppm, respectively). Dicofol is a possible human carcinogen.[111] Dicofol has shown endocrine disruptor activity *in vivo* and *in vitro*.[112, 113, 114] This chemical has been shown to interfere with blastocyst implantation in rats.[115]

EPA used its SCI-GROW model to estimate dicofol concentrations in groundwater and calculated a 90-day average peak concentration of 0.069 ppb. An overall mean surface water concentration of 0.5 ppb was estimated with the PRZM-EXAMS model. Both concentrations were below the Drinking Water Levels of Comparison (DWLOCs) for children and the general U.S. population for both acute and chronic exposure. However, there are some important shortcomings in EPA's assessment of dicofol exposure and risk.

The first problem with the assessment is related to the way EPA calculated the Reference Dose (RfD). EPA is supposed to apply an additional safety factor of 10x to the RfD calculation to protect infants and children, who may have increased susceptibility to health effects from chemical exposures compared to adults. The Agency reduced the FQPA safety factor of 10x to 3x based on the lack of increased pre-natal or post-natal susceptibility to dicofol in developmental toxicity studies. However, EPA stated that a developmental neurotoxicity study was necessary because dicofol produced neurotoxicity in rats and such a study might identify an

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[110] U.S. EPA. Interim Reregistration Eligibility Decision for Dichlorvos (DDVP), 2006.

[111] U.S. EPA. *Reregistration Eligibility Decision, Dicofol*, 1998.

[112] Hoekstra PF, Burnison BK, Garrison AW, Neheli T, Muir DC. Estrogenic activity of dicofol with the human estrogen receptor: Isomer- and enantiomer-specific implications. *Chemosphere*. 2006 Jun;64(1):174-7. Epub 2005 Dec 7.

[113] Thibaut R, Porte C. Effects of endocrine disrupters on sex steroid synthesis and metabolism pathways in fish. *J Steroid Biochem Mol Biol*. 2004 Dec;92(5):485-94. Epub 2004 Dec 21.

[114] Ishihara A, Sawatsubashi S, Yamauchi K. Endocrine disrupting chemicals: interference of thyroid hormone binding to transthyretins and to thyroid hormone receptors. *Mol Cell Endocrinol*. 2003 Jan 31;199(1-2):105-17.

[115] Jadaramkunti UC, Kaliwal BB. Possible mechanisms for the anti-implantation action of dicofol in albino rats. *J Basic Clin Physiol Pharmacol*. 2001;12(3):217-26.

endpoint for dietary risk. Despite lacking such a study, EPA improperly reduced the safety factor to 3x. If the 10x factor had been applied as mandated by the Food Quality Protection Act, a more protective acute RfD of 0.015 mg/kg $day^{-1}$ would have been chosen instead of the 0.05 mg/kg $day^{-1}$ dose EPA used in its assessment. Had EPA applied the 10x safety factor, dicofol exposure from food alone would have exceeded the acute RfD and the EPA level of concern for all population groups (see Table 1). This would have resulted in a DWLOC of zero (0), so that any drinking water exposure would have been of concern.

**Table 1. Comparison of acute dietary exposure values from food at the 99.9th percentile**

| Population | Exposure (mg/kg/day) | With 3x safety factor RfD = 0.05 mg/kg/day % of Acute RfD | With 10x safety factor RfD = 0.015 mg/kg/day % of Acute RfD |
|---|---|---|---|
| U.S. Population | 0.017523 | 35 | 117 |
| Non-nursing infants (<1 year old) | 0.044923 | 90 | 299 |
| Children (1-6 years old) | 0.034919 | 70 | 233 |
| Children (7-12 years old) | 0.024705 | 49 | 165 |

The unwarranted reduction of the FQPA safety factor also affected the outcome of the chronic dietary exposure assessment. As shown in Table 2, if the 10x factor had been applied, chronic exposures from food alone for infants and children 1 to 6 years old would have exceeded the level of concern. Therefore, any drinking water exposure would have been of concern as well.

**Table 2. Chronic dietary food exposure and risk estimate from Dicofol (in food alone)**

| Population | Exposure (mg/kg/day) | With 3x safety factor RfD = 0.0004 mg/kg/day % of Chornic RfD | With 10x safety factor RfD = 0.00012 mg/kg/day % of Chronic RfD |
|---|---|---|---|
| U.S. Population | 0.000076 | 19 | 63 |
| Non-nursing infants (<1 year old) | 0.000129 | 32 | 108 |

| | | | |
|---|---|---|---|
| Children (1-6 years old) | 0.00015 | 38 | 125 |
| Children (7-12 years old) | 0.000104 | 26 | 87 |

Another shortcoming in the EPA assessment is that the Agency relied on models to estimate environmental concentrations in surface and groundwater, but did not have a robust set of monitoring data. EPA should require the collection of surface and groundwater monitoring data in areas where dicofol is applied. The Agency should use these data to corroborate its exposure estimates and make a regulatory determination for dicofol under the SDWA.

**Endosulfan** (CAS # 115-29-7) is an organochlorine insecticide and acaricide. Technical grade endosulfan is made of both alpha and beta stereoisomers whose toxicity is manifested through blockage of inhibitory GABA (gamma amino butyric acid) gated chloride channels, resulting in over-stimulation of the central nervous system. Endosulfan is a recognized neurotoxin[116] and endocrine disruptor[117], making even extremely low-dose exposures of very great concern, especially to vulnerable populations such as children and fetuses.

Endosulfan is similar in its acute oral toxicity to the related insecticides aldrin and dieldrin, except that it is slightly more toxic than these substances in female laboratory animals.[118] Inhalation of endosulfan dust by humans has been associated with slight nausea, confusion, excitement, flushing, and dry mouth[119]. Nine employees who had been working with 50-percent water-wettable endosulfan powder for only a few days had convulsions[120].

Endosulfan is a significant endocrine disruptor and reproductive toxicant. This pesticide increases the rate of testosterone breakdown and excretion.[121] In immature rats, endosulfan causes significant dose-related decreases in sperm counts, and causes sperm deformities at low exposure levels.[122] In fish, endosulfan elevates levels of

[116] Lakshmana MK, Raju TR. 1994. Endosulfan induces small but significant changes in the levels of noradrenaline, dopamine, and serotonin in the developing rat brain and deficits. *Toxicology*, 91(2): 139-150.

[117] Willey JB, Krone PH. 2001. Effects of endosulfan and nonylphenol on the primordial germ cell population in pre-larval zebrafish embryos. *Aquat Toxicol*, 54(1-2): 113-123

[118] OSHA comments from the January 19, 1989 *Final Rule on Air Contaminants Project* extracted from 54 FR 2332 et. seq.

[119] State of California: Department of Industrial Relations/Ex. 1-8

[120] Association of American Pesticide Control Officials, Inc. 1969, as cited in ACGIH 1986/Ex. 1-3, p. 230

[121] Wilson V, LeBlanc GA. Endosulfan elevates testosterone biotransformation and clearance in CD-1 mice. *Toxicol Appl Pharmacol* 148:158-168, 1998.

[122] Sinha N, Narayan R, Saxena DK. Effect of endosulfan on the testis of growing rats. Bulletin Environ Contamination Toxicol 58:79-86, 1997. Sinha N, Narayan R, Shanker R, Saxena DK. Endosulfan-induced biochemical changes in the testis of rats. *Veterinary and Human Toxicol* 37:547-549, 1995.

thyroxine and suppresses levels of triiodothyronine, probably by inhibiting the conversion of thyroxine to T3.[123] The developing brain is potentially most severely affected by this pesticide via altered levels of critical neurotransmitters such as dopamine, noradrenaline and serotonin; the altered neurotransmitter levels are associated with deficits in learning and memory.[124]

The EPA estimates that 1.4 million pounds of endosulfan are applied annually to U.S. crops. According to the EFED risk assessment for the RED on endosulfan, monitoring data show widespread contamination of surface water. EPA modeled surface water contamination and calculated acute estimated environmental concentrations ranging from 4.49 ppb to 23.86 ppb. Chronic EECs ranged from 0.53 ppb to 1.5 ppb. The acute and chronic EEC for endosulfan in groundwater was 0.012 ppb. EPA concluded in the RED that "residues of endosulfan in drinking water are of concern" for acute exposure for infants less than one year old and for children 1-6 years old. EPA determined that exposure from food alone created risks of concern for children 1 to 6 years old and set a DWLOC of zero (0) ppb for this population.[125]

EPA proposed mitigation measures to address risks from endosulfan contamination of drinking water (110-foot setbacks for ground applications, 3-foot vegetative buffers, and reductions in application rates). However, the implementation of required mitigation measures to reduce pesticide risks is rarely monitored or enforced. Given the risk indicated in the drinking water exposure assessment, EPA should require more widespread monitoring for endosulfan and take regulatory action to establish an MCL for endosulfan.

**Linuron** (CAS # 330-55-2) is an urea-based herbicide used primarily on soybeans (79 percent of usage). It has been shown to cause non-malignant testicular and liver tumors in animals.[126] Investigation of the testicular tumors revealed that this herbicide acts by blocking the function of male androgens. In animals, at relatively low doses, linuron is a recognized anti-androgen. This chemical has been shown in laboratory studies to decrease male sex organ weights, cause testicular atrophy, delay puberty, and increase estrogen levels in males.[127] [128]

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[123] Sinha N, Lal B, Singh TP. Pesticides induced changes in circulating thyroid hormones in the freshwater catfish clarias batrachus. *Comparative Biochem Physiol* 100C: 107-110, 1991.

[124] Lakshmana MK, Raju TR. Endosulfan induces small but significant changes in the levels of noradrenaline, dopamine and serotonin in the developing rat brain and deficits in the operant learning performance. *Toxicology* 91:139-150, 1994.

[125] U.S. EPA, *Reregistration Eligibility Decision for Endosulfan*. 2002.

[126] Extension Toxicology Network (EXTOXNET), *Pesticide Information Profiles*. June 1996. http://extoxnet.orst.edu/pips/linuron.htm.

[127] Cook JC, Mullin LS, Frame SR, Biegel LB. Investigation of a mechanism for Leydig cell tumorigenesis by linuron in rats. *Toxicol Appl Pharmacol* 119:195-204, 1993.

[128] Gray LE Jr, Wolf C, Lambright C, Mann P, Price M, Cooper RL, Ostby J. Administration of potentially antiandrogenic pesticides (procymidone, linuron, iprodione, chlozolinate, p,p'-DDE, and ketoconazole) and toxic substances (dibutyl- and diethylhexyl phthalate, PCB 169, and ethane dimethane sulphonate) during

About 400,000 pounds of linuron are used in U.S. agriculture each year. This herbicide persists for 1-5 months in soil, and has been shown to run off of fields into surface and groundwater supplies. EPA concluded in its Reregistration Eligibility Decision (RED) that linuron exceeded the Levels of Concern (LOC) for groundwater quality. EPA also expressed "moderate concerns" for drinking water supply systems relying on surface water sources.[129]

Several factors in EPA's drinking water exposure assessment raise concerns about groundwater contamination. In the groundwater portion of the assessment, data were present for only four states: Georgia, Missouri, Virginia, and Wisconsin. In Georgia linuron was found in groundwater in concentrations up to 5 ppb. EPA later cast doubt on the reliability of the data and removed it from consideration in the final RED, basing its decision on new information received from the State of Georgia.

Valid groundwater detections in Missouri (up to 1.9 ppb), Virginia (up to 1.31 ppb in 4 of 8 wells) and Wisconsin (up to 2.7 ppb) may seriously underestimate linuron levels throughout the country because these three states are not among the 16-20 states where linuron is most heavily used. The sixteen states listed on page 3 of EPA's Overview of Linuron Risk Assessment appear to account for well over 80% of linuron use in the United States,[130] so the complete absence of any data on groundwater in any of these states is a critical data gap. The USGS has also reported on areas where linuron is most heavily used on a per-acre basis. The USGS maps indicate that Indiana, Ohio, Michigan, Delaware, and Maryland are heavy use states.[131] These states are not among the ones from which groundwater data are available. Strangely, only one of these (Michigan) is listed by EPA as among heavy use states.

Casting further doubt on EPA's estimates of the risks of linuron in drinking water sources is the fact that the model used for surface water assessment was not tested against any data whatsoever. The exposure estimates (18 ppb) for infants and children exceed EPA's chronic DWLOC (6 ppb) by three-fold. This result is of particular concern in light of the serious flaws in the drinking water risk assessment that conspire to underestimate the actual risk. EPA admits that "residues of linuron and its metabolites in drinking water may represent a chronic human health risk…"

Since linuron is not regulated under the Safe Drinking Water Act (SDWA), water supply systems are not required to sample or analyze for it. This is a particular problem because EPA admits that drinking water treatment is unlikely to remove

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sexual differentiation produces diverse profiles of reproductive malformations in the male rat. *Toxicol Ind Health*. 1999 Jan-Mar;15(1-2):94-118.

[129] U.S. EPA. *Reregistration Eligibility Decision for Linuron*, 1995.

[130] U.S. EPA., *Overview of Linuron Risk Assessment*. 2002.
http://www.epa.gov/oppsrrd1/reregistration/linuron/linuron_overview_5-31-02.PDF.

[131] U.S. Geological Survey (USGS). *1992 Pesticide Use Maps*.
http://ca.water.usgs.gov/pnsp/pesticide_use_maps/show_map.php?year=92&map=m1993

linuron and its degradates. The Agency must move rapidly to collect more data on linuron in water and must make a high priority of regulating linuron under the SDWA.

**Phosmet** (CAS # 732-11-6) is an organophosphate pesticide used primarily on apples, peaches, walnuts, almonds and pears. Approximately 1.25 million pounds of active ingredient are applied every year. Phosmet is a neurotoxicant that causes red blood cell, plasma, serum and brain cholinesterase inhibition. It also shows mutagenic activity.[132, 133] Phosmet interferes with human placental enzymatic activity, which may affect fetal development.[134] EPA has stated in its Interim Reregistration Eligibility Decision (IRED) for phosmet that there is "suggestive evidence of carcinogenicity" based on increased incidence of liver adenomas and carcinomas in male mice, and of mammary gland tumors in females.[135]

Phosmet is mobile in runoff and has the potential to contaminate drinking water sources. EPA has done a drinking water risk assessment for phosmet as part of the pesticide reregistration process. The EPA IRED used modeling estimates to assess phosmet exposure through drinking water due to the limited amount of monitoring data available. Estimated environmental concentrations ranged from 0.4 to 140 ppb. While EPA concluded that drinking water exposure through surface and groundwater was not of concern, there are several flaws in the EPA analysis that undermine that conclusion, as explained below. The IRED drinking water assessment should not be relied upon to decide whether to regulate phosmet under the SDWA

EPA determines whether the drinking water risks of a pesticide are of concern as part of its dietary risk assessment for that chemical. For drinking water risk to remain below the Agency's level of concern, the sum of food and drinking water exposures must be less than the Population Adjusted Dose (PAD).[136] The IRED risk summary for phosmet indicates that dietary risk, acute and chronic, is below the Agency's level of concern. However, the Agency had initially determined that acute dietary exposures were of great concern for infants and children, with up to 2000% of the

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[132] Vlckova V, Miadokova E, Podstavkova S, Vlcek D. Mutagenic activity of phosmet, the active component of the organophosphorus insecticide Decemtione EK 20 in Salmonella and Saccharomyces assays. *Mutat Res*. 1993 Jul;302(3):153-6.

[133] Hasegawa R, Cabral R, Hoshiya T, Hakoi K, Ogiso T, Boonyaphiphat P, Shirai T, Ito N. Carcinogenic potential of some pesticides in a medium-term multi-organ bioassay in rats. *Int J Cancer*. 1993 May 28;54(3):489-93. Erratum in: *Int J Cancer* 1993 Sep 30;55(3):528.

[134] Souza MS, Magnarelli GG, Rovedatti MG, Cruz SS, De D'Angelo AM. Prenatal exposure to pesticides: analysis of human placental acetylcholinesterase, glutathione S-transferase and catalase as biomarkers of effect. *Biomarkers*. 2005 Sep-Oct;10(5):376-89.

[135] U.S. EPA, Interim *Reregistration Eligibility Decision for Phosmet*, Case No. 0242. October 30, 2001.

[136] The PAD is a term that expresses the dietary risk of a chemical, and reflects the Reference Dose, either acute or chronic, that has been adjusted to account for the FQPA safety factor (i.e., RfD/FQPA safety factor). A risk estimate that is less than 100% of the acute or chronic PAD does not exceed the Agency's risk concern.

acute Reference Dose (aRfD) consumed[137]. Such an exceedance in exposure from food alone means that any additional exposure from drinking water would create additional unacceptable risks.

The assessment of food exposure was subsequently revised using a newly submitted acute neurotoxicity study by the registrant[138], reviewed by the Agency in February 1999,[139] and by the hazard identification assessment review committee (HIARC) in July, 1999.[140] This new acute neurotoxicity study in rats was used to raise the No Observable Adverse Effects Level (NOAEL) to 4.5 mg/kg/day, from the 1.1 value that had been used, based on a chronic toxicity study in rats. The result was a four-fold change, which also resulted in an increase in the PAD. The HIARC executive summary of the study states that "no effects of treatment were seen in the 3.0 or 4.5 mg/kg group", which is in agreement with the registrants conclusions. However, the study DER[141] finds some critical problems with this study:

- "Extremely high variability was noted in the data from the motor activity testing, raising questions about the sensitivity of the procedures used in this study. For example, an increase in subsession activity approaching 300% above control levels was not found to be statistically significantly different from controls."
- "There was also some large variability in some of the blood cholinesterase measurements (especially for the red blood cells), such that decreases of 25% were not statistically significant. Again, it is possible that true differences caused by exposure to phosmet might be obscured by the high variability of the measure." In fact, the DER states that "the smallest statistically significant change detected in blood measures was 40% (DER p. 10)
- "no information is available regarding the dose response curves for cholinesterase inhibition or behavioral effects. This is especially relevant since similar levels of inhibition (60-75%) were seen in brain and red blood cell cholinesterase at the high dose, with brain inhibition persisting throughout the study."

NRDC suggests that this study is not sufficient to establish a NOAEL, since the variability in cholinesterase inhibition was so great that the study design did not provide any statistical power to detect treatment effects. Therefore, the increase in the

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[137] Swartz, C., U.S. EPA. *Phosmet. HED review of the Gowan Co. probabilistic (Monte Carlo) acute dietary exposure risk assessment.* July 30, 1999

[138] *Phosmet: Acute neurotoxicity study.* (GD Cappon, lead investigator; Gowan Co., Yuma, AZ, sponsor). MRID No. 44673301. WIL Research Labs, Ashland OH. Oct 8, 1998.

[139] Raffaele K. 1999. *Phosmet: Acute neurotoxicity study.* U.S. EPA. DER of study MRID 44673301. Obtained by FOIA #RIN 0593-02, to Jennifer Sass, Jan. 16, 2002

[140] Taylor LL. 1999. *Phosmet: Revised report of the hazard identification assessment review committee on phosmet.* HED Doc No. 013604. August 4, 1999.

[141] Raffaele K. 1999. *Phosmet: Acute neurotoxicity study.* U.S. EPA. DER of study MRID 44673301. Obtained by FOIA #RIN 0593-02, to Jennifer Sass, Jan. 16, 2002. Discussion and conclusions, p. 13-14

PAD that made it possible for food and drinking water exposures to remain below the level of concern was not scientifically supported.

Notwithstanding EPA's previous determination that phosmet in drinking water does not pose risks of concern (which, as noted above, was based on a flawed study), phosmet should be regulated as a water contaminant under the SDWA and an MCL should be established.

**Trichlorfon** (CAS # 52-68-6) is an organophosphate insecticide with agricultural non-food and feed crop uses (e.g. agricultural non-cultivated areas, ornamental trees, etc.), as well as indoor and outdoor residential use. Usage volume data for these registered uses is not available.[142]

Like the other organphosphates, trichlorfon is a neurotoxicant and cholinesterase inhibitor. Trichlorfon exposure is associated with kidney, lung and gastrointestinal abnormalities in animal studies. Anemia has also been reported, as well as benign pheochromocytomas. A statistically significant increase in mononuclear cell leukemia was also observed. Incidences of alveolar/bronchiolar adenomas, renal tubular adenomas and alveolar/bronchiolar carcinomas, while not statistically significant, occurred with frequencies "well outside of the historical control range for all three tumor types."[143] While EPA decided to classify trichlorfon in Group E for carcinogenicity arguing that the statistically significant increases in tumors in the studies were seen in the lower but not the higher doses, we argue that the evidence remains suggestive given that separate studies found significant increases in the same types of tumors.

In the studies analyzed by EPA during the reregistration process, trichlorfon also showed developmental toxicity in animals (decreased fetal body weight, delayed or reduced ossification) and mutagenic activity in an in vitro cytogenetic study in mammalian cells.

Trichlorfon is highly mobile in soil, but EPA did not assess its groundwater contamination potential during the reregistration process for lack of appropriate data. Trichlorfon can enter surface waters in ground spray and runoff. Well samples from Georgia in the EPA Pesticides in Ground Water Database showed trichlorfon detections in 12 of 179 wells with concentration up to 10 ppb. EPA did not consider these samples useful, citing analytical uncertainties.

Trichlorfon has a half-life in soil of 1 to 27 days, depending on soil type, which increases its potential to contaminate surface waters. However, the trichlorfon RED does not address drinking water risks. Despite the cancellation of feed and food crop uses, trichlorfon still has registered agricultural and residential outdoor uses that pose

[142] U.S. EPA. *Reregistration Eligibility Decision for Trichlorfon*, List A, Case 0104. 1997.

[143] U.S. EPA, 1997, supra.

a risk of surface and possibly groundwater contamination. The scarcity of monitoring data on environmental concentrations should not lead to an assumption of negligible risk. The known toxicity of trichlorfon, its mobility and extended half-life in soil all make it a likely water contaminant in high use areas. EPA should require the collection of monitoring data for these areas to enable the Agency to assess water contamination risks and make a regulatory decision concerning trichlorfon.

**Triclocarban** (Urea, N-(4-chlorophenyl)-N'-(3,4-dichlorophenyl) 3,4,4'-Trichlorocarbanilide), CAS # 101-20-2, an antimicrobial pesticide also known as TCC, is a possible endocrine disruptor that has been widely detected in effluent from wastewater treatment plants (WWTPs) in the United States. TCC has also been frequently detected in environmental water samples. An animal study indicates that triclocarban exposure enhanced the effects of testosterone both in vitro and in vivo in male rats.[144]

The half-life of TCC in sediment is 540 days. One study predicted the magnitude and frequency of TCC contamination nationwide based on experimental and modeling data to be 1150 ng/L and 60%, respectively; much higher than previously recognized by EPA (240 ng/L, 30%).[145] Another study in the Greater Baltimore area found an average TCC level of 6.75 ug/L in wastewater samples, while river water samples had concentrations of up to 5.6 ug/L.[146] These concentrations are higher than the Predicted Environmental Concentrations (PEC) calculated by the TCC Consortium in a report submitted to EPA in 2003 as part of the High Production Volume Chemical program, which estimated PECs from 0.0013 to 0.050 μg/L.[147] The actual measurements from the Greater Baltimore area study also exceed the TCC Consortium's Predicted No Effect Concentration of 0.146 μg/L.[148]

A study of a 684 million liter per day typical activated sludge WWTP found a concentration of 6.1 ± 2.0 ug/L in the influent and 0.17 ± 0.03 ug/L in the effluent. Approximately 127 ± 6 g/d exited the plant in the effluent, a clear indication that conventional wastewater treatment may leave considerable levels of TCC in the

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[144] Chen J, Ahn KC, Gee NA, Ahmed MI, Duleba AJ, Zhao L, Gee SJ, Hammock BD, Lasley BL. Triclocarban enhances testosterone action: a new type of endocrine disruptor? *Endocrinology*. 2008 Mar;149(3):1173-9.

[145] Halden RU, Paull DH. Co-occurrence of triclocarban and triclosan in U.S. water resources. *Environ Sci Technol*. 2005 Mar 15;39(6):1420-6.

[146] Halden RU, Paull DH. Analysis of triclocarban in aquatic samples by liquid chromatography electrospray ionization mass spectrometry. *Environ Sci Technol*. 2004 Sep 15;38(18):4849-55.

[147] TCC Consortium. *High Production Volume (HPV) Chemical Challenge Program Data Availability and Screening Level Assessment for Triclocarban*. 2002.
http://www.epa.gov/chemrtk/pubs/summaries/tricloca/c14186.pdf

[148] TCC Consortium. *High Production Volume (HPV) Chemical Challenge Program Data Availability and Screening Level Assessment for Triclocarban*. 2002.
http://www.epa.gov/chemrtk/pubs/summaries/tricloca/c14186.pdf

water.[149] Because of this, TCC concentrations tend to be higher downstream of WWTPs.[150] The most important sources of triclocarban to the aquatic environment were estimated to be activated sludge treatment plants (contributing 39-67%), followed by trickling filters (31-54%), combined sewer overflows (2-7%) and sanitary sewer overflows (<0.2%).[151]

Given these data, triclocarban should be added to the CCL3.

**Triclosan (5-chloro-2-(2,4-dichlorophenoxy)-phenol)** (CAS # 3380-34-5), is a broad spectrum antimicrobial pesticide that is widely used in personal care products such as soaps, toothpastes, cosmetics, skin creams and deodorants; kitchen accessories such as cutting boards and utensils; and in textiles such as sportswear, shoes and carpets.

Triclosan is produced at over one million pounds per year. The chemical structure of triclosan is similar to other endocrine disrupting compounds and potential breakdown products of triclosan include dioxins.[152]

Recently, low levels of triclosan were found to interfere with the metamorphosis of frogs. Exposure to as little as 0.15 micrograms/l triclosan caused an earlier metamorphosis than normal, with effects on the tadpole brain and tail.[153] Triclosan activates the human pregnane X receptor (hPXR), which is involved in the enzymatic metabolism of steroids and xenobiotics.[154]

Triclosan has been found in wastewater treatment effluent and drinking water sources.[155] Triclosan was detected in Louisiana sewage treatment plant effluent at 10-21 ng/l.[156] Boyd (2004) reported triclosan concentrations of ND – 29 ng/l in two

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[149] Heidler J, Sapkota A, Halden RU. Partitioning, persistence, and accumulation in digested sludge of the topical antiseptic triclocarban during wastewater treatment. *Environ Sci Technol.* 2006 Jun 1;40(11):3634-9.

[150] Sapkota A, Heidler J, Halden RU. Detection of triclocarban and two co-contaminating chlorocarbanilides in US aquatic environments using isotope dilution liquid chromatography tandem mass spectrometry. *Environ Res.* 2007 Jan;103(1):21-9.

[151] Halden RU, Paull DH. Co-occurrence of triclocarban and triclosan in U.S. water resources. *Environ Sci Technol.* 2005 Mar 15;39(6):1420-6.

[152] Latch DE, Packer JL, Stender BL, VanOverbeke J, Arnold WA, and McNeill K. Aqueous photochemistry of triclosan: formation of 2,4-dichlorophenol, 2,8-dichlorodibenzo-p-dioxin, and oligomerization products. *Environ Toxicol Chem.* 24(3):517-25 (2005).

[153] Veldhoen N, Skirrow RC, Osachoff H, Wigmore H, Clapson DJ, Gunderson MP, Van Aggelen G, and Helbing CC. The bactericidal agent triclosan modulates thyroid hormone-associated gene expression and disrupts postembryonic anuran development. *Aquat Toxicol.* 80(3):217-27 (2006).

[154] Jacobs MN, Nolan GT, Hood SR. Lignans, bacteriocides and organochlorine compounds activate the human pregnane X receptor (PXR). *Toxicol Appl Pharmacol.* 2005 Dec 1;209(2):123-33.

[155] Greyshock AE, Vikesland PJ. Triclosan reactivity in chloraminated waters. *Environ Sci Technol.* 2006 Apr 15;40(8):2615-22.

[156] Boyd GR, Reemtsma H, Grimm DA, Mitra S. Pharmaceuticals and personal care products (PPCPs) in

stormwater canals in New Orleans.[157] Triclosan has also been detected in raw and finished drinking water samples from Southern California.[158]

*Phthalates*. Phthalates are endocrine disruptors that have been found to cause developmental and reproductive abnormalities in animal studies.[159] Furthermore, studies have found an association between phthalate metabolite concentrations and obesity, insulin resistance and thyroid hormone levels in humans.[160] Stahlhut et al. (2007) analyzed urinary concentrations of seven phthalate metabolites in 1,443 adult men and found a statistically significant positive association between concentrations of the metabolites MBzP, MEHHP, MEOHP and MEP and abdominal obesity. Concentrations of MBP, MBzP and MEP were positively and significantly associated with insulin resistance.[161] In a different study, baby boys exposed to the phthalates, DMP, DEP or BBP, in their mother's breast milk were found to have hormonal disturbances at 3 months of age.[162] Studies have found that di-isononyl phthalate (DiNP) is an anti-androgenic endocrine disruptor with developmental and reproductive toxicity. Exposures in pregnant rats have been shown to adversely affect development of the male reproductive tract. Adverse effects include a cluster of outcomes that has been called "phthalate syndrome" and includes underdeveloped or absent reproductive organs, retained nipples, cryptorchidism, decreased anogenital distance (AGD), hypospadias, and decreased or abnormal sperm. DINP does not bind to the androgen receptor and these effects are likely mediated through interference with testosterone synthesis.[163, 164]

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surface and treated waters of Louisiana, USA and Ontario, Canada. *Sci Total Environ*. 2003 Jul 20;311(1-3):135-49.

[157] Boyd GR, Palmeri JM, Zhang S, Grimm DA. Pharmaceuticals and personal care products (PPCPs) and endocrine disrupting chemicals (EDCs) in stormwater canals and Bayou St. John in New Orleans, Louisiana, USA. *Sci Total Environ*. 2004 Oct 15;333(1-3):137-48.

[158] Loraine GA and Pettigrove ME. Seasonal variations in concentrations of pharmaceuticals and personal care products in drinking water and reclaimed wastewater in southern California. *Environ Sci Technol*. 40(3):687-95 (2006).

[159] Centers for Disease Control and Prevention. T*hird National Report on Human Exposure to Environmental Chemicals*. Atlanta (GA): CDC, 2005.

[160] Meeker JD, Calafat AM, Hauser R. Di(2-ethylhexyl) phthalate metabolites may alter thyroid hormone levels in men. *Environ Health Perspect*. 2007 Jul;115(7):1029-34.

[161] Stahlhut RW, van Wijngaarden E, Dye TD, Cook S, Swan SH. Concentrations of urinary phthalate metabolites are associated with increased waist circumference and insulin resistance in adult U.S. males. *Environ Health Perspect*. 2007 Jun;115(6):876-82.

[162] Main KM, Mortensen GK, Kaleva MM, Boisen KA, Damgaard IN, Chellakooty M, Schmidt IM, Suomi AM, Virtanen HE, Petersen DV, Andersson AM, Toppari J, Skakkebaek NE. Human breast milk contamination with phthalates and alterations of endogenous reproductive hormones in infants three months of age. *Environ Health Perspect*. 2006 Feb;114(2):270-6.

[163] Gray LE Jr, Wilson VS, Stoker T, Lambright C, Furr J, Noriega N, Howdeshell K, Ankley GT, and Guillette L. Adverse effects of environmental antiandrogens and androgens on reproductive development in mammals. *Int J Androl*. 29(1):96-108 (2006).

[164] Gray LE Jr, Ostby J, Furr J, Price M, Veeramachaneni DN, and Parks L. Perinatal exposure to the phthalates DEHP, BBP, and DINP, but not DEP, DMP, or DOTP, alters sexual differentiation of the male rat. *Toxicol Sci*.58(2):350-65 (2000).

Phthalates enter the environment as a result of releases from industrial facilities that manufacture or use these compounds, from waste disposal sites, through the use of phthalate-containing products by consumers and through discharge of municipal wastewaters containing phthalates. Phthalates have been found in numerous hazardous waste sites: diethyl phthalate (DEP) has been identified at 348 sites, dibutyl phthalate (DBP) at 602 sites, dimethyl phthalate (DMP) at 167 sites, benzyl butyl phthalate (BzBP) at 413 sites, dicyclohexyl phthalate (DCHP) at one site, and di-n-octyl phthalate (DnOP) at 433 sites, among other phthalates.[165]

Phthalates have been detected in environmental water samples across the United States, which raises concerns about drinking water as a route of exposure. The following data were found in a search for stream water samples analyzed for phthalates in the EPA STORET database. Results are for the period January 2000 through May 2008:[166]

- **Benzyl butyl phthalate (BzBP)** was present in 167 of 677 stream water samples analyzed for this chemical, with a maximum concentration of 3.6 ug/L.
- **Di-isononyl phthalate (DiNP)** – No data available.[167]
- **Di-n-octyl phthalate (DnOP)** was found in 42 (8%) of 497 stream water samples, with a maximum concentration of 0.85 ug/L.
- **Dibutyl phthalate (DBP)** was found in 221 (34%) of 659 stream water samples for that period, with a maximum concentration of 7.4 ug/L.
- **Diethyl phthalate (DEP)** was detected in 264 (35%) of the 748 stream water samples analyzed. The maximum concentration found was 10.14 ug/L. DEP levels were $\geq$ 1 ug/L in 79 (11%) of the samples tested.
- **Dimethyl phthalate (DMP)** was present in 49 (7%) of 678 stream water samples, with a maximum of 3.2 ug/L.

Phthalates are ubiquitous in the U.S. population. Although significant exposure can occur due to consumer products, the contribution of drinking water to overall exposure deserves to be examined. The NHANES measured the concentrations of 12

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[165] Agency for Toxic Substances and Disease Registry (ATSDR). *Hazardous Substance Release and Health Effects Database (HazDat)*. http://www.atsdr.cdc.gov/Hazdat.html

[166] U.S. EPA. *STORET*. http://www.epa.gov/storet/

[167] The Institute for Health and Consumer Protection (IHCP) of the Europen Chemicals Bureau estimated a half life in surface water for DINP of 50 days. According to the IHCP, 7 percent of the DINP in the influent in sewage treatment plants will be released in the effluent. *See* European Commission Joint Research Centre, Institute for Health and Consumer Protection, *1,2-Benzenedicarboxylic acid,Di-C8-10-Branched Alkyl Esters, C9-Rich and Di-"Isononyl" Phthalate (DINP), CAS Nos: 68515-48-0 and 28553-12-0, EINECS Nos: 271-090-9 and 249-079-5, Summary Risk Assessment Report*, 2003. http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/SUMMARY/dinpsum046.pdf. Given the widespread use and high production volumes of DINP, these releases could pose risks for water quality.

phthalate metabolites in the urine of over 2,500 children and adults. The highest average concentration was 163 ug/g creatinine for MEP, a metabolite of the plasticizer diethyl phthalate (see Table 3). The Centers for Disease Control and Prevention (CDC) did not report what percentage of samples had detectable concentrations of each of the metabolites, but nine of the metabolites were found in the urine of at least half of the individuals.[168]

**Table 3. CDC report of phthalate concentrations in urine; NHANES 1999 – 2000 and 2001 - 2002**

| Phthalate metabolite | Sample size | Concentration in urine (creatinine corrected) | |
|---|---|---|---|
| | | Geometric mean (ug/g creatinine) | Median (ug/g creatinine) |
| Mono-ethyl phthalate (MEP) | 2536 | 163 | 141 |
| Mono-n-butyl phthalate (MBP) | 2541 | 22.4 | 21.9 |
| Mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)* | 2782 | 18.8 | 16.6 |
| Mono-benzyl phthalate (MBZP) | 2541 | 14.0 | 13.3 |
| Mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP)* | 2772 | 12.6 | 11.2 |
| Mono-2-ethylhexyl phthalate (MEHP)* | 2541 | 3.12 | 3.08 |
| Mono-3-carboxypropyl phthalate (MCPP) | 2772 | 2.57 | 2.45 |
| Mono-isobutyl phthalate (MIP) | 2772 | 2.53 | 2.44 |
| Mono-methyl phthalate (MMP) | 2772 | 1.08 | 1.33 |
| Mono-cyclohexyl phthalate (MCHP) | 2541 | ** | <LOD |
| Mono-n-octyl phthalate (MOP) | 2541 | ** | <LOD |
| Mono-isononyl phthalate (MINP) | 2541 | ** | <LOD |
| * This is a metabolite of di-2-ethyhexyl phthalate (DEHP). EPA has set a drinking water standard for DEHP.<br>** = Not calculated due to high number of non-detects<br>LOD = Level of detection | | | |

[168] Centers for Disease Control and Prevention. T*hird National Report on Human Exposure to Environmental Chemicals*. Atlanta (GA): CDC, 2005.

| Table 4. Frequency of detection of phthalate metabolites in human urine samples, United States | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Study | Subjects | Sample size | Metabolite | Percent of individuals in sample with detectable concentrations | | | | | | |
| | | | | < 25 | 25 – 49 | 50 – 74 | 75-84 | 85 – 89 | 90-94 | 95 – 100 |
| Wolff et al. (2007)[169] | Girls<br><br>Age: 6 – 8 yrs | 90 | MECPP | | | | | | | 100% |
| | | | MEHHP | | | | | | | 100% |
| | | | MEOHP | | | | | | | 100% |
| | | | MEHP | | | | | | 94.4% | |
| | | | MEP | | | | | | | 100% |
| | | | MBP | | | | | | | 99.8% |
| | | | MBZP | | | | | | | 93.0% |
| | | | MIBP | | | | | | | 95.7% |
| | | | MCPP | | | | | | | 100% |
| | | | MMP | 20% | | | | | | |
| Meeker et al (2007)[170] | Men at fertility clinic<br><br>Age: 18 – 55 yrs | 408 | MEP | | | | | | | 100% |
| | | | MBP | | | | | | | 97% |
| | | | MBZP | | | | | | 94% | |
| | | | MEHP | | | | 85% | | | |
| | | 208 | MEHHP* | | | | | | | 95% |
| | | | MEOHP* | | | | | | | 95% |
| Stahlhut et al. (2007)[171] | Men in NHANES 1999-2002 study<br><br>Age: >18 yrs | 1443 | MBP* | | | | | | | 95% |
| | | | MBZP* | | | | | | | 95% |
| | | | MEHP | | | | 80% | | | |
| | | | MEP* | | | | | | | 95% |
| | | 780 | MEHHP* | | | | | | | 95% |
| | | | MEOHP* | | | | | | | 95% |
| Silva et al. (2007)[172] | Adults | 129 | MIDP | 10% | | | | | | |
| | | | MCINP | | | | | | | 98% |
| | | | MHIDP | | | | | | | 96% |
| | | | MOIDP | | | | | 85% | | |
| Adibi et al. (2003)[173] | Pregnant women in prenatal clinic in NY<br><br>Age: 18 – 35 yrs | 25 | MEP | | | | | | | 100% |
| | | | MBP | | | | | | | 100% |
| | | | MBZP | | | | | | | 100% |
| | | | MEHP | | | | | | | 100% |
| | | | MCHP | Frequency not given; reported to be "largely nondetected values" | | | | | | |
| | | | MOP | Frequency not given; reported to be "largely nondetected values" | | | | | | |
| | | | MINP | Frequency not given; reported to be "largely nondetected values" | | | | | | |
| | | | MMP | Frequency not given; reported to be "largely nondetected values" | | | | | | |

[169] Wolff MS, Teitelbaum SL, Windham G, Pinney SM, Britton JA, Chelimo C, Godbold J, Biro F, Kushi LH, Pfeiffer CM, Calafat AM. Pilot study of urinary biomarkers of phytoestrogens, phthalates, and phenols in girls. *Environ Health Perspect.* 2007 Jan;115(1):116-21.

[170] Meeker JD, Calafat AM, Hauser R. Di(2-ethylhexyl) phthalate metabolites may alter thyroid hormone levels in men. *Environ Health Perspect.* 2007 Jul;115(7):1029-34.

[171] Stahlhut RW, van Wijngaarden E, Dye TD, Cook S, Swan SH. Concentrations of urinary phthalate metabolites are associated with increased waist circumference and insulin resistance in adult U.S. males. *Environ Health Perspect.* 2007 Jun;115(6):876-82.

[172] Silva MJ, Reidy JA, Kato K, Preau JL Jr, Needham LL, Calafat AM. Assessment of human exposure to di-isodecyl phthalate using oxidative metabolites as biomarkers. *Biomarkers.* 2007 Mar-Apr;12(2):133-44.

[173] Adibi JJ, Perera FP, Jedrychowski W, Camann DE, Barr D, Jacek R, Whyatt RM. Prenatal exposures to phthalates among women in New York City and Krakow, Poland. *Environ Health Perspect.* 2003 Nov;111(14):1719-22.

**Table 4. Frequency of detection of phthalate metabolites in human urine samples, United States (continued)**

| Study | Subjects | Sample size | Metabolite | Percent of individuals in sample with detectable concentrations | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | < 25 | 25 – 49 | 50 – 74 | 75-84 | 85 – 89 | 90-94 | 95 – 100 |
| Blount et al. (2000)[174] | Adults in NHANES 1988-1994<br><br>Age: 20 – 60 yrs | 289 | MEHP* | | | | >75% | | | |
| | | | MEP* | | | | >75% | | | |
| | | | MBZP* | | | | >75% | | | |
| | | | MBP* | | | | >75% | | | |
| | | | MINP* | >75% | | | | | | |
| | | | MCHP* | >75% | | | | | | |
| | | | MOP* | >75% | | | | | | |
| * = Exact percentage not reported | | | | | | | | | | |

Therefore, the following phthalate compounds should be added to the CCL 3:

- **Benzyl butyl phthalate (BzBP)** (CAS # 85-68-7)
- **Di-isononyl phthalate (DiNP)** (CAS # 28553-12-0)
- **Di-n-octyl phthalate (DnOP)** (CAS # 117-84-0)
- **Dibutyl phthalate (DBP)** (CAS # 84-74-2)
- **Dicyclohexyl phthalate (DCHP)** (CAS # 84-61-7)
- **Diethyl phthalate (DEP)** (CAS # 84-66-2)
- **Dimethyl phthalate (DMP)** (CAS # 131-11-3)

*Reproductive hormones.* The U.S. Geological Survey (USGS) conducted a study of 139 streams in 30 states that found widespread presence of estrogenic compounds, ovulation inhibitors and other reproductive hormones in surface water near urbanized and agricultural areas (see Table 5).[175]

While each of these compounds is generally found at low concentrations, the potential effects on human health of mixtures of these compounds are unknown. Based on the individual effects of these chemicals, possible risks include defects of the reproductive system in individuals exposed during critical stages of development (e.g. testosterone)[176], decreased fertility (ovulation inhibitors such as mestranol, 19-norethisterone), and increased risk of breast cancer (e.g. equilenin, equilin)[177], among others.

[174] Blount BC, Silva MJ, Caudill SP, Needham LL, Pirkle JL, Sampson EJ, Lucier GW, Jackson RJ, Brock JW. Levels of seven urinary phthalate metabolites in a human reference population. *Environ Health Perspect.* 2000 Oct;108(10):979-82.

[175] Kolpin DW, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB, Buxton HT. Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999-2000: a national reconnaissance. *Environ Sci Technol.* 2002 Mar 15;36(6):1202-11.

[176] Hotchkiss AK, Lambright CS, Ostby JS, Parks-Saldutti L, Vandenbergh JG, Gray LE Jr. Prenatal testosterone exposure permanently masculinizes anogenital distance, nipple development, and reproductive tract morphology in female Sprague-Dawley rats. *Toxicol Sci.* 2007 Apr;96(2):335-45.

[177] Ding S, Shapiro R, Geacintov NE, Broyde S. Equilenin-derived DNA adducts to cytosine in DNA duplexes: structures and thermodynamics. *Biochemistry.* 2005 Nov 8;44(44):14565-76.

**Table 5. Concentrations of reproductive hormones in U.S. streams (USGS, 2002)**

| Compound | CAS # | Compound type | Frequency of detection | Median concentration (ug/L) | Maximum concentration (ug/L) |
|---|---|---|---|---|---|
| Equilenin | 517-09-9 | estrogen replacement | 2.8 | 0.14 | 0.278 |
| Equilin | 474-86-2 | estrogen replacement | 1.4 | 0.147 | 0.147 |
| 17α-Ethynyl estradiol | 57-63-6 | ovulation inhibitor | 15.7 | 0.073 | 0.831 |
| 17 α -Estradiol | 57-91-0 70 | reproductive hormone | 5.7 | 0.03 | 0.074 |
| 17β-Estradiol* | 50-28-2 | reproductive hormone | 10.6 | 0.16 | 0.2 |
| 17 β –Estradiol* | 50-28-2 | reproductive hormone | 10.0 | 0.009 | 0.093 |
| Estriol | 50-27-1 | reproductive hormone | 21.4 | 0.019 | 0.051 |
| Estrone | 53-16-7 | reproductive hormone | 7.1 | 0.027 | 0.112 |
| Mestranol | 72-33-3 | ovulation inhibitor | 10.0 | 0.074 | 0.407 |
| 19-Norethisterone | 68-22-4 | ovulation inhibitor | 12.8 | 0.048 | 0.872 |
| Progesterone | 57-83-0 | reproductive hormone | 4.3 | 0.11 | 0.199 |
| Testosterone | 58-22-0 | reproductive hormone | 2.8 | 0.116 | 0.214 |

* Water samples were tested for 17β-estradiol by two different methods.

Wastewater treatment plants (WWTPs), the likely sources of most of these chemicals, do not treat sewage for these pollutants. Furthermore, drinking water treatment plants do not generally test or treat water for these contaminants, so the frequency of occurrence of these chemicals in treated drinking water and the degree of human exposure are not known. Additional monitoring of water sources and drinking water are necessary to determine the full extent of the contamination, to assess risks to human health, and to determine acceptable levls of exposure and appropriate regulatory action. Therefore, **equilenin, equilin, 17α-ethynyl estradiol, 17 α – estradiol, 17β-estradiol, estriol, estrone, mestranol, 19-norethisterone, progesterone and testosterone** should be added to the CCL3.

## III. RECOMMENDATIONS

We urge EPA to add the contaminants recommended above by NRDC to the CCL3. These contaminants meet EPA's criteria to be listed in CCL3. Their health effects, use patterns and known or likely environmental occurrence in drinking water sources should make them candidates for regulation under the SDWA. Furthermore, NRDC also recommends that EPA delete the pesticide **nitrofen** (CAS # 1836-75-5) from the Draft CCL3. The available information on this chemical does not support its inclusion in the CCL3.

NRDC agrees with the inclusion of perchlorate and perfluorooctanoic acid (PFOA) in the Draft CCL3 and requests that EPA act promptly to regulate these endocrine disruptors in drinking water pursuant to the Safe Drinking Water Act (SDWA).

Finally, we recommend that the Agency act to promptly assess the risks associated with other contaminants nominated to the CCL3 and take appropriate regulatory action under the SDWA to establish Maximum Contaminant Levels (MCLs) as necessary.

Respectfully submitted,

/s/

Mae Wu

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VIA ELECTRONIC SUBMISSION

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May 21, 2008

Re: 3M Comments on Draft Third Candidate Contaminant List
(Docket No. EPA-HQ-OW-2007-1189)

Dear Mr. Carpenter:

3M Company is pleased to submit the attached comments on EPA's Draft Third Candidate Contaminant List. Please feel free to contact me if you have any questions.

Sincerely,

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Encl.

# COMMENTS OF 3M COMPANY ON EPA'S INCLUSION OF PFOA ON THE THIRD CONTAMINANT CANDIDATE LIST (CCL 3)

## INTRODUCTION

3M Company (3M) appreciates the opportunity to comment on the U.S. Environmental Protection Agency's (EPA) inclusion of perfluorooctanoic acid (PFOA) on the Draft Third Drinking Water Candidate Contaminant List (CCL 3). 73 Fed. Reg. 9628 (Feb. 21, 2008). 3M supports the mission of the CCL process to protect our Nation's drinking water. As discussed below, however, 3M believes that in assessing PFOA for inclusion on the CCL 3, EPA should use more relevant information to characterize PFOA's potential human health effects and exposure levels. To ensure a clear and accurate record, it is important that EPA properly characterize PFOA health effects and exposure during the CCL 3 process. 3M offers the following comments for EPA's consideration.

## DISCUSSION

### 1. A More Relevant Study Should Be Used to Characterize the Potency and Severity of PFOA Health Effects

According to the PFOA Contaminant Information Sheet[1], EPA used a 1 mg/kg/day LOAEL included in EPA's 2005 Draft Risk Assessment of PFOA[2] to characterize the potential for PFOA to cause adverse health effects. For the reasons explained below, 3M believes this LOAEL should not be used to characterize the potency and severity of PFOA health effects in laboratory animals.

EPA's use of the 1 mg/kg/day LOAEL value reported in the Draft Risk Assessment fails to properly capture the nature and intent of that document. The Draft Risk Assessment reported multiple endpoints and did not purport to determine a particular "critical effect" and effect level for regulatory or formal listing purposes. In its review of the Draft Risk Assessment, the EPA Science Advisory Board (SAB) agreed with EPA's inclusion of multiple endpoints in the "current draft", and did not render an opinion as to appropriateness of any single value for use in characterizing PFOA health effects.[3] In fact, the Draft

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1 *See* EPA, Contaminant Information Sheets for the Draft CCL 3 Chemicals (February 2008), Docket ID No. EPA-HQ-OW-2007-1189-0043, p. 151-52.

2 EPA, Draft Risk Assessment of the Potential Human Health Effects of Associated with Exposure to Perfluorooctanoic Acid and its Salts, Office of Pollution Prevention and Toxics, Risk Assessment Division (January 4, 2005). (Hereinafter "Draft Risk Assessment").

3 *See* EPA, SAB Review of EPA's Draft Risk Assessment of Potential Human Health Effects Associated with PFOA and its Salts (May 30, 2006), EPA-SAB-06-006.

Risk Assessment calculated two margins of exposure (MOEs) for PFOA in adult animals -- one based on a LOAEL from a two-generation study of rats and another based on a LOAEL from a study of cynomolgus monkeys -- and did not render an opinion as to whether one was more appropriate than the other. (EPA also separately calculated MOEs for developmental effects).

Studies based on primates are a better model than rats for human risk assessment in the case of PFOA. Notably, the only agency to establish a drinking water criterion for PFOA through rulemaking -- the Minnesota Department of Health -- based its interim Health Risk Level for PFOA on an effect level from the monkey study.[4] Primates are preferable to rats because PFOA is known to act, at least in part, through a mechanism of action in rodents that is much less operative in humans.

EPA calculated margins of exposure from the monkey study in its Draft Risk Assessment, but has not derived a Reference Dose from the monkey study. EPA's risk assessment guidance calls for the use of a benchmark dose for determining the point of departure and Reference Dose when such a benchmark dose is available. In a published risk assessment for PFOA, 3M and co-authors (Butenhoff *et al.* 2004a) have calculated benchmark doses for endpoints in the monkey study (Butenhoff *et al.* 2002). The benchmark dose for liver-weight-to-brain-weight ratio is 3.9 mg/kg/day. 3M believes this is a more relevant point of departure.

Indeed, not only are rats less relevant for human risk assessment than non-human primates, but the particular point of departure used in the draft EPA risk assessment for the rat study is not appropriate. The 1 mg/kg/day point of departure chosen by EPA during the CCL 3 process is based on a reduction in male post-weaning body weight in the first-generation pups in a two-generation reproductive study in rats reported in York (2002) and Butenhoff *et al.* (2004b). Although the Draft Risk Assessment did base one of the MOE calculations on this effect, the Draft Risk Assessment itself acknowledges that the "significance of reduced body weight for human health is not clear."[5] 3M agrees that the effects on male body weights in this study are not of clear significance for human health and therefore urges that EPA not use this effect to characterize PFOA health effects in the CCL 3 process.

### 2. A Default Relative Source Contribution Value of 20% Should Not Have Been Used in the Calculation of a PFOA Health Reference Level

3M believes that the relative source contribution (RSC) value that EPA used to calculate the health reference level (HRL) for PFOA as part of the CCL 3

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[4] *See* 32 Minn. Reg. 374 (Aug. 27, 2007).

[5] Draft Risk Assessment at 96.

process does not follow EPA guidance. Although 3M recognizes that EPA used this HRL for CCL screening purposes only, we are concerned that EPA's calculation approach could influence future regulatory activity. Accordingly, EPA should follow the procedures for calculating HRL values provided in its own guidance.

In Step Three of the CCL 3 process (Classification to the CCL), EPA used a default 20% (0.2) RSC value for PFOA.[6] The RSC is a factor used to describe the proportion of the total permissible dose that is derived from the ingestion of water, versus other exposure routes. EPA guidance on the derivation of water quality criteria, referenced in the CCL,[7] allows RSC values in the range of 0.2 to 0.8, with a default value of 0.2 applied in the absence of data supporting a different RSC. (20% relative source contribution used "unless there are data to suggest that the 20% is inappropriate)."[8] In fact, there are data which show that a 20% RSC for PFOA is inappropriate. As described below, a comparison of exposures in persons with and without known drinking water PFOA exposure shows that where there is drinking water exposure, it is the major source of exposure -- well above 20% of the total exposure.

Background exposures in the general population, which generally does not have drinking water exposure, have been well documented in a number of studies published by both the Centers for Disease Control and Prevention (CDC) and 3M.

- 3M's studies have used American Red Cross samples from adult blood donors. 3M has published data on Red Cross samples from a variety of geographic locations in the U.S., including Minneapolis-St. Paul donors (Olsen *et al.*, 2003). The levels in this study are also consistent with levels in studies of children from twenty states, and with levels found in a separate study of the elderly (Olsen *et al.*, 2004a and 2004b).

- The 3M national study has been confirmed by published Centers for Disease Control data based on a statistically representative sample of the U.S. population. (Calafat *et al.*, 2007a).

- 3M has also published a more recent study of levels of PFOA in Minneapolis-St. Paul blood donors, showing a decline in general population exposures (Olsen *et al.*, 2007). CDC's data also show a

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6 *See* EPA, Draft: Contaminant Candidate List 3 Chemicals: Classification of the PCCL to CCL, EPA 815-R-08-004, February 2008 (hereinafter "Classification to CCL") at p. 61.

7 EPA, Methodology for deriving ambient water quality criteria for the protection of human health. Office of Water, EPA-822-B-00-004, October, 2000, p. 1-7.

8 Classification to CCL at 61.

decline in PFOA concentrations in the general population (Calafat, *et al.*, 2007b).

Data on persons known to be exposed to PFOA in drinking water are available from three sources: 1) a peer-reviewed University of Pennsylvania study of a community exposed to PFOA in drinking water in West Virginia (Emmett *et al.*, 2006a, 2006b); 2) recently published study of a German population exposed to PFOA in drinking water (Holzer, *et al.*, 2008); and 3) exposure data on persons living in Washington County, Minnesota, presumably exposed to PFOA in municipal or private well water prior to the installation of treatment.[9] Exposure data for both the general population and persons exposed through drinking water are summarized in Table 1, below.

**Table 1. Geometric Mean Serum/Plasma Concentrations of PFOA (ppb)**

| Sample Source | Location | Year | PFOA (ppb) |
|---|---|---|---|
| *Background General Population Exposure* | | | |
| CDC | National | 2000 | 5.2 |
| 3M/Am. Red Cross | National | 2000 | 4.6 |
| 3M/Am. Red Cross | Mnpls/St. Paul | 2000 | 4.5 |
| 3M/Am. Red Cross | Mnpls/St. Paul | 2005 | 2.2 |
| Holzer *et al.* | Siegen, Germany | 2006 | 2.6-6.3* |
| *Persons with Drinking Water Exposure* | | | |
| Taft, Stettinius & Hollister | Oakdale, MN | 2005 | 36.5 |
| U. of PA (Emmett *et al.*) | WVa/OH | 2004-5 | 354 (median) |
| Holzer *et al.* | Arnsberg, Germany | 2006 | 22.1 – 25.3* |

* Range reported for children, mothers and adult men.

Although we must assume that people who live in Oakdale were exposed via the consumption of Oakdale municipal drinking water, the number of samples is sufficient to demonstrate a marked difference between the serum concentrations in the Oakdale population with exposure through city water and the general population in the Minneapolis/St. Paul metropolitan area or the U.S. general population. These data show that background serum concentrations based on non-drinking water exposures (serum ranging from 2.2 to 5.2 ppb) account for between 6 and 14 % of the serum concentrations in persons exposed via drinking water (whose mean serum concentration is 36.5 ppb). Thus, in persons exposed through drinking water, drinking water accounts for between 86 and 94% of exposures.[10]

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9 Blood sampled by attorneys (Taft, Stettinius & Hollister LLP) who are suing 3M in private litigation. Data available in EPA FYI Docket No. AR 226.

10 The proportion for the German population studied in Holzer *et al.* (2008) is similar – 75 to 88%.

The Oakdale blood data, while unpublished, are consistent with the published data on the West Virginia/Ohio population exposed to PFOA. In studying the association of drinking water concentrations with serum concentrations of PFOA in a population in West Virginia/Ohio, University of Pennsylvania researchers similarly found that drinking water was the major source of exposure. Emmett *et al.* (2006a, 2006b). This study concluded that serum PFOA concentrations "depended on the source of residential drinking water, and not potential air exposure," and that "[r]esidential water source was the primary determinant of serum (PFOA)."

In that study, serum concentrations among 291 residents using Little Hocking, Ohio city water were, on average, 105 times the residential drinking water concentration. PFOA concentrations in Oakdale city well samples averaged 0.3 to 0.8 ppb between October 2005 and March 2006, before 3M provided treatment. Therefore, the reported 2005 geometric mean Oakdale serum PFOA concentration of 36.5 ppb is consistent with the relationship between drinking water and serum PFOA concentrations observed in the University of Pennsylvania study.

Finally, in the German study (Holzer, *et al.*, 2008), persons consuming municipal water currently containing 0.5 ppb PFOA in drinking water had serum levels elevated 4.5-8.3 times the reference population. The authors concluded that drinking water consumption is a significant predictor of serum levels.

These facts provide strong, objective evidence that exposures from sources other than water are low and declining, and that the higher concentrations observed in the Oakdale population and the University of Pennsylvania study in West Virginia/Ohio, are most certainly due to the drinking water source.

Based on these data, EPA guidance would lead to a RSC of 50-80% rather than the 20% based on a default assumption. 3M believes that because data are available showing that the default 20% RSC value is inappropriate for PFOA, EPA should not use the default value in the CCL 3 process or in other regulatory proceedings.

3. <u>An Inappropriate Measure Was Used to Classify PFOA Occurrence</u>

3M believes the information used to classify PFOA occurrence in Step Three of the CCL 3 process also is inappropriate. To define the magnitude aspect of PFOA's occurrence in drinking water, EPA used the highest public drinking water level reported for Little Hocking, OH (7.2 µg/l) cited in Emmett *et al.* (2006a). Because Emmett *et al.* does not contain prevalence data for PFOA, EPA described the prevalence of PFOA using data for "Select Minnesota Municipal Wells" as described in a February 27, 2006 presentation by the Minnesota Department of Health (MDH) to the Minnesota Senate Environment

and Natural Resources Committee.[11] In using Minnesota prevalence data and West Virginia magnitude data, EPA has derived a measure of occurrence for PFOA that does not actually exist in the environment, which creates an artificial and inaccurate impression of the extent of PFOA's occurrence in drinking water. 3M believes that it is more scientifically appropriate to use occurrence and magnitude data that actually occur simultaneously in the environment.

In addition, 3M believes EPA's characterization of the MDH prevalence data used in deriving a measure of PFOA occurrence is somewhat misleading. As noted by EPA in the PFOA Contaminant Information Sheet, the MDH presentation indicates that 6 of 37, or 16.2%, of municipal wells sampled contained detectable levels of PFOA.[12] However, MDH sampled 37 municipal wells in seven Minnesota communities (Cottage Grove, Hastings, Lake Elmo, St. Paul, North St. Paul, Woodbury and Oakdale) and all six wells with PFOA detections were located in a single community, Oakdale, which has known contamination. No PFOA was detected in the other six communities' municipal wells. Thus, the positive occurrence data relied upon by EPA are linked to a single location, and therefore do not support the prevalence of PFOA in Minnesota suggested by the 16.2% figure. Indeed, the aggregate of Minnesota well samples, which includes data from non-community wells and private wells is only 8.2%, even with the bias introduced by the Oakdale data. Moreover, the 6 out of 37 wells with PFOA is an artificially high proportion, and not representative of more widespread prevalence because all wells sampled were in Washington County, which was chosen specifically because PFOA from waste sites was expected to be found in the drinking water.

## CONCLUSION

As explained above, 3M believes that, in the process of assessing PFOA for inclusion on the CCL 3, EPA did not use the most relevant information to characterize PFOA's potential human health effects and exposure levels. A clear and accurate record of the CCL 3 process with respect to PFOA is important, in our view, particularly given that determinations made in the process may influence other regulatory or formal listing determinations. 3M hopes that EPA finds the foregoing comments useful in helping to ensure a clear and accurate CCL 3 record.

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11 MDH (H. Goeden and J. Kelly), "Perfluorochemicals in Minnesota" (February 27, 2006), EPA Docket ID No. EPA-HQ-OW-2007-1189-0027.

12 *See Id.* at slide 17.

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