Comments on the U.S. EPA's Amended Cryolite Final Work Plan Registration Review

Prepared for the
U.S. Environmental Protection Agency

February 21, 2012

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1. Introduction

The Fluoride Action Network (FAN) would like to take this opportunity to respond to the Amended Cryolite Final Working Plan for Cryolite. We understand that EPA must make numerous difficult decisions concerning the Registration Review for cryolite, and appreciate the concerted effort that has thus far gone into determining whether cryolite continues to meet the Federal Insecticide, Fungicide, and Rodenticide Act (FIRFA) standard for registration.

Cryolite as a pesticide has been scientifically neglected to the advantage of aluminum producers, and to the belief system advocated by EPA's Office of Drinking Water and CDC's Oral Health Division that putting fluoride in drinking water is beneficial for oral health. However, studies published since the 1996 RED for cryolite confirm the need for a more thorough study of its adverse effects.

While FAN applauds the decision by EPA's EFED to include an avian reproduction study (850.2300) for cryolite, numerous other concerns were raised by FAN in our previous submission (FAN, 5 Jul 2011) that were not adequately addressed prior to release of the Amended Cryolite Final Work Plan Registration Review (EPA, December 2011). Several of these concerns are reiterated and expounded upon below.

2. Response to EPA's Documents Concerning the Registration Review for Cryolite

2.1. EPA has failed to acknowledge that OPP must discontinue its promulgation of cryolite, as it does not meet the safety standard in FFDCA Section 408 regarding fluoride.

Cryolite is the only regulated pesticide to leave fluoride residues in and/or on fresh fruits and vegetables. Aside from kiwifruit (fluoride tolerance of 15 ppm), all other cryolite-treated foods have a fluoride tolerance of 7 ppm (US CFR, 2012), including:

> Apricot, Blackberry, Blueberry (huckleberry) Boysenberry, Broccoli, Brussels Sprouts, Cabbage, Cauliflower, Collards, Cranberry, Dewberry, Eggplant, Grape, Kale, Kohlrabi, Lettuce (head & leaf), Loganberry, Melon, Nectarine, Peach, Pepper, Plum (prune, fresh), Pumpkin, Raspberry, Squash (summer & winter), Strawberry, Tomato, Youngberry.
>
> Citrus Fruit*: Calamondin, Citrus citron, Citrus hybrids (chironja, tangelo, tangor), grapefruit, kumquat, lemon, lime, mandarin (tangerine), orange (sweet & sour), pummelo, satsuma mandarin
>
> *Note: the Citrus fruit category has recently expanded. See Citrus Fruit Group 10 and its definitions at http://ir4.rutgers.edu/other/CropGroup.htm

According to the EPA Office of Water (OW), children younger than age 7 are routinely

exposed to fluoride levels that exceed the "safe" dose recently proposed by OW (RfD=0.08 mg/kg/day; EPA OW, 2010a). Even when exposure estimates are recalculated to exclude the fluoride contribution from sulfuryl fluoride (as proposed by EPA OPP; FR, 2011b), the aggregate exposure to fluoride for this major identifiable population subgroup (children) does not meet the safety standard in FFDCA Section 408. Although the main source of fluoride for most Americans is still drinking water, Rankin et al. (2011) found that children 24-60 months of age consume an average of 36-39 percent of dietary fluoride from solid foods, with some children receiving as much as 85-88 percent of their dietary fluoride from solid foods.

Fluoride remains in the body for an extended period of time, with a half-life of approximately 20 years in the human bone (NRC, 2006, page 92). It is estimated that for daily fluoride exposure, a healthy body will retain approximately 50 percent, which is mainly sequestered in the bone. When a person eats food treated with cryolite, some of the fluoride consumed will remain in the body for the entire lifespan.

Fluoride retained in bones over time after eating one serving of a Cryolite-treated fruit or vegetable at 1 year of age

At age (years)	Percent of F from cryolite retained in bone
20	50%
40	25%
60	12.5%
80	6.3%
100	2.2%
120	1.1%

In addition to teeth and bones, fluoride also accumulates in the pineal gland (Luke, 2001), and may impact numerous physiological systems. It is irresponsible of EPA to allow the use of any pesticide when it or its constituents are known to accumulate and persist in the human body.

While EPA's Office of Drinking Water makes the assumption that dental fluorosis is the most sensitive endpoint for fluoride exposure, the NRC report (2006) identified not one, but three adverse effects with the current maximum contaminant level of 4 ppm fluoride in drinking water:

1. Bone Fractures
2. Clinical stage II skeletal fluorosis—associated with chronic joint pain, arthritic symptoms, calcification of ligaments, and osteosclerosis of cancellous bones
3. Severe dental fluorosis

Numerous other adverse effects have been reported in the scientific literature at or below those levels found to cause dental fluorosis. Among these are neurological effects (e.g.

brain damage and reduced IQ in children), endocrine effects (e.g. altered thyroid function), bone disorders (e.g. changes in bone density, bone fractures), osteosarcoma, and reproductive effects.

2.2. EPA has refused to establish tolerances for aluminum from cryolite on food.

After 50 years of use of cryolite as a pesticide in the United States, there is a lot we still do not know about this chemical. As stated by EPA (2011b):

> Its exact mechanism of action is not yet well understood. (p.7)
>
> Although the use of cryolite should have negligible impacts on ground and surface water quality, cryolite applications in acidic soils or aquatic environments may contribute to Al^{3+} toxicity in plants and aquatic organisms (p.10)
>
> In the hydrolysis study, aluminum speciation with fluoride or hydroxide was not determined, equilibrium constants were not measured, and the results were not compared with those from scientific literature (p.10).

Like fluoride, aluminum remains in the body for an extended period of time. According to ATSDR's (2008, p.112) report on aluminum, "a half-life of about 50 years was estimated (Priest 2004)". Thus, i*n addition to tolerances for fluoride, EPA should issue tolerances for aluminum as a dietary residue of cryolite, and should calculate aggregate aluminum exposures to determine if the aluminum from cryolite adds unnecessarily to an already over-exposed population. In its response to FAN's comments, EPA states that "Most foods that have been tested were found to contain 0.1-10 ppm aluminum" (EPA, 6 Sept 2011, p.2). EPA should determine if foods treated with cryolite have higher levels of aluminum than untreated foods.*

EPA's statement that "a much larger source of oral exposure to aluminum is reportedly from antacids and buffered analgesics" is by no means an acceptable or scientific rationale for not issuing tolerances for aluminum. ATSDR (2008) notes the following for those exposed to antacids and buffered analgesics:

> Growth reduction, hypotonia, muscle weakness, and craniosynostosis (premature ossification of the skull and obliteration of the sutures) have been observed in healthy infants following prolonged used of oral antacids for the treatment of colic (Pivnick et al., 1995). (page 122)
>
> Osteomalacia has been observed in healthy individuals following long-term use of aluminum-containing antacids and in individuals with kidney disease. There are numerous case reports of osteomalacia and rickets in otherwise healthy infants and adults using aluminum-containing antacids for the treatment of gastrointestinal illnesses (i.e., ulcers, gastritis, colic)… (page 71)

For those consuming antacids or oral analgesics, any additional aluminum ingested from

food with unregulated levels could pose an even more serious health threat than may already be present.

EPA may only promulgate a pesticide tolerance determined to be "safe"—meaning that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information" (FDA, 2009). OPP must therefore begin to phase out cryolite, based on the same rationale as recently stated for sulfuryl fluoride (FR, 2011b).

2.3. EPA has failed to address valid concerns of the neurological effects of fluoride and aluminum from cryolite.

Mundy et al. (2009) at EPA's Neurotoxicology division classify fluoride as a developmental neurotoxicant. Aluminum is a well-known neurotoxicant, and according to Hänninen et al. (1994) and others, the brain is one of the recognized target organs for its toxicity.

> In the cases in which human aluminum toxicity has occurred, the target organs appear to be the lung, bone, and the central nervous system (page 117)... The molecular mechanism of aluminum bone and neurotoxicity has not been established. (ATSDR, 2008, p.99)

According to Walton (2012), "More aluminum enters the brain than leaves, resulting in a net increase in intraneuronal aluminum with advancing age." While many studies report that aluminum enters and stays in the brain (e.g. House et al., 2012), it is not well known what substances enable it to get there. We know that alumina nanoparticles can cross the blood-brain barrier (Dong et al., 2012). In our July submission (FAN, 2011) we cited a relevant and important low-dose, long-term rat study by Varner et al. (1998). The authors of this study suggest that fluoride facilitated the aluminum in the rat chow to cross the blood brain barrier as explanation for the high aluminum levels in the brains of the fluoride-exposed rats. Yokel (2006) suggested many complex transporters.

The neurotoxic effects of cryolite have the potential to be greater than that of fluoride or aluminum alone, as indicated in the following:

> Effects were "more pronounced in animals given fluoride and aluminum together ...it can be concluded that aluminum appears to enhance the neurotoxic hazards caused by fluoride." (Kaur et al., 2009)

> The toxic effects of cryolite are largely due to its content of aluminum and fluoride. Thus, its toxic effects, if not known, have to be based on known adverse effects of aluminum and fluoride. (Soderlund, 1995)

> The overall weight of evidence strongly indicates that oral exposure to aluminum

> results in functional and cognitive alterations. Motor function and sensory function are affected by aluminum exposure. (ATSDR, 2008, page 80)

Especially susceptible to adverse neurological effects of aluminum are those in which the brain is still forming.

> Infants and children should not be viewed as 'small adults' with regard to toxicological risk as their unique physiology makes them much more vulnerable to toxic insults. (Tomljenovic and Shaw, 2012)

> For most brain regions analyzed the highest aluminum concentrations were found in young rats, which would indicate that early stages of the life cycle must be considered for enhanced brain aluminum accumulation. (Dominigo et al., 1996)

Three developmental neurotoxicity tests were performed for cryolite (US EPA, 1996). They were all crude, one was unacceptable, and none performed an examination of the animal brains. These studies include:

- Rats exposed by gavage to 0, 750, 1500 or 3000 mg/kg/day during gestation days 6-15 inclusive (MRID 00128112): "the only observation was whitening of the teeth of dams". This 1983 unpublished study was prepared by Science Applications, Inc., and submitted by Agchem Div., Pennwalt Corp.
- Mice exposed by gavage to 0, 30, 100 or 300 mg/kg/day with bent ribs and limbs in fetuses at the highest dose (MRID 42297902). Undated, little information available.
- Rabbits exposed by gavage at dose levels of 0, 10, 30, 100, 300 or 1000 mg/kg/day (MRID 42297901). This study was deemed "unacceptable" because it "suggested that severe maternal toxicity occurred at lower doses than external developmental toxicity." Unpublished 1992 study prepared by WIL Research Labs, Inc.

The European Chemicals Agency (2010b) comment on these and two other critical studies:

> The database contains five developmental toxicity studies and one 2-generation study, and they are all very poorly reported.

It appears that no cryolite study performed thus far has included histological examinations of the brain. All cryolite studies should be made available to the public. According to ATSDR (2008):

> Recent biological monitoring data, particularly for aluminum in blood and urine, are limited. More recent information would be useful in assessing current

> exposure levels… The Department of Health and Human Services and EPA have not evaluated the human carcinogenic potential of aluminum… Data on health effects of ingested aluminum in humans are unsuitable for MRL [minimal risk levels] consideration because studies have centered on specific patient populations (i.e., dialysis, neurodegenerative disease) and are not the types typically used in risk evaluation.
>
> The oral intake of aluminum tends to be higher for children than for adults (Greger 1992). Calculations based on the FDA's Total Diet Study suggest that 2-year-old children (13 kg body weight) consumed almost 3 times as much aluminum per kg body weight as adult males (75 kg body weight) or adult females (60 kg body weight), respectively (0.48 versus 0.18 and 0.15 mg aluminum/kg body weight, respectively) (Greger 1992). Infants fed milk-based or soy-based infant formulas can be exposed to higher concentrations of aluminum than infants fed breast milk or cows' milk (see Section 6.4.4).

Of the numerous studies reporting the neurotoxicity of aluminum, some include:

- Abd El-Rahman, 2003
- Abu-Taweel et al., 2012
- Akila et al., 1999
- Bondy, 2010
- Bowdler et al., 1979
- Cui et al., 2012
- Domingo et al., 1996
- Dong et al., 2011
- Erazi et al., 2010
- Gómez et al., 2008
- Hänninen et al., 2004
- House et al., 2012
- Itoh et al., 2008
- Jin et al., 2009, 2010, 2011
- Julka et al., 1995
- Kaizer et al., 2008
- Kaur et al., 2006a, 2006b, 2009
- Kim et al., 2007
- Kumar et al., 2008, 2009a, 2009b
- Lemire & Appanna, 2011
- Lipman et al., 1988
- Liu et al., 2008
- Markesbery et al., 1984
- Meyer-Baron et al., 2007
- Miu et al., 2003
- Niu et al., 2007
- Pendlebury et al., 1987, 1988
- Platt et al., 2001
- Provan et al., 1992
- Ribes et al., 2008, 2010
- Sánchez-Iglesias et al., 2009
- Sethi et al., 2008
- Sharma and Sharma, 2012
- Shaw et al., 2009
- Solomon et al., 1988
- Tomljenovic et al., 2012
- Tripathi et al., 2009
- Walton, 2007, 2012
- Xing et al., 2012
- Yang et al., 2006
- Yokel, 1985, 1987,1994
- Yuan et al., 2011
- Yumoto et al., 2009

Furthermore, several published reports have found that aluminum exposure may affect learning and memory, including:

- Abu-Taweel et al., 2012
- Cui et al., 2012
- Jin et al., 2009, 2010, 2011
- Julka et al., 1995

- Kaur et al., 2006
- Lipman et al., 1988
- Pendlebury et al. 1987
- Platt et al., 2001
- Provan et al., 1992
- Ribes et al., 2010
- Sethi et al., 2008
- Solomon et al., 1988
- Xing et al., 2012
- Yokel, 1985
- Yokel et al., 1994

As previously mentioned, Kaur et al. (2009) state that "aluminum appears to enhance the neurotoxic hazards caused by fluoride." There are now 26 published papers associating exposure to fluoride with lowered IQ in children (Appendix A). Our concern remains for the synergistic effects of co-exposure to the neurotoxicants in cryolite: fluoride and aluminum, especially for infants and children.

We are exposed to aluminum in many ways. Tariq (1993) reported the following:

> According to recent studies in the United States of America the average adult American diet includes 20-60 mg aluminum d-1, whereas daily consumption of aluminum in the United Kingdom is 6-8 mg. The majority of this aluminum is reported to be ingested from the food ingredients which are generally recognized as safe.

Walton (2007) reported:

> According to the World Health Organization, oral ingestion of aluminum additives is the main form of aluminum exposure for the general public. Aluminum salts are added to a range of commercially-prepared foods and beverages: to clarify drinking water, make salt free-pouring, color snack/dessert foods, and make baked goods rise. In the present study, six Wistar rats chronically consumed aluminum from 16 months of age to the conclusion of their lifespan (averaging 29.8 months) in an amount (1.5mg/kg bodyweight) equivalent to the high end of the total aluminum range ingested daily by humans living in contemporary urban society…Four out of six rats continued to perform the memory task in old age without significant deficit. The remaining two obtained significantly lower mean memory scores in old age than in middle age and exhibited soft signs associated with dementia. Their hippocampal neurons stained for aluminum, showing some but not all features of aluminum accumulation that occur in human hippocampal neurons.

The occupational exposure of workers to aluminum and fluoride is also of concern. Meyer-Baron et al. (2007), Akila et al. (1999), and Hänninen et al. (1994) reported effects on cognitive performance from occupational exposure to aluminum, and many more studies on impaired performance on neurobehavioral tests are cited by ATSDR (2008, p.15). Calvert et al. (1998) reported "significantly reduced performance on the Pattern Memory Test" for structural fumigators using sulfuryl fluoride.

(Concerning occupational exposures, EPA states that there are no incidence reports for

cryolite in their database, and therefore there does not appear to be a concern at this time that would warrant further investigation. It should be noted, however, that the majority of people who do have reactions to pesticides do not know that they should report their effects.)

When one substance contains two neurotoxicants and is used on the foods we eat, the public expects EPA to act in its best interest to ensure that the necessary studies are performed to protect from adverse health effects. The recommendation for a 90-Day Inhalation Toxicity Test, as stated in the Amended Cryolite Final Work Plan (US EPA, Dec 2011) is inadequate. EPA must require a developmental neurotoxicity test for cryolite.

Furthermore, EPA must mandate the testing of cryolite-treated food to determine which commodities uptake aluminum and/or its fluoroaluminum compound, which are known to be bioavailable. Although "aluminum is found naturally in a great number of foods" (ATSDR, 2008, p.125), EPA should not allow even greater exposure to this neurotoxicant, which readily accumulates in the human body.

2.4. EPA has failed to address valid concerns of endocrine effects of fluoride from cryolite.

EPA acknowledges that "as required by FFDCA section 408(p), cryolite is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP)" (EPA, Dec 2011, p.9). However, it is also stated that "Cryolite is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. (EPA, Dec 2011, p.10). Nor is cryolite or fluoride included among the Second List of Chemicals for Tier 1 Screening (EPA, 2012). (http://www.epa.gov/endo/pubs/prioritysetting/draftlist2.htm).

According to the National Research Council's 2006 report, *Fluoride in Drinking Water: A Scientific Review of EPA's Standards*, fluoride is "an endocrine disruptor in the broad sense of altering normal endocrine function or response" (NRC, 2006, p. 266). In addition to altering thyroid function, NRC (2006, p. 256) states that "fluoride is likely to cause decreased melatonin production and to have other effects on normal pineal function, which in turn could contribute to a variety of effects in humans."

In light of research findings, NRC (2006) offered the following recommendation: "The effects of fluoride on various aspects of endocrine function should be examined further, particularly with respect to a possible role in the development of several diseases or mental states in the United States." (p. 267). OPP should therefore require that cryolite and its degradation products and complexes immediately undergo testing for endocrine disruption potential, instead of waiting for cryolite to be included among the pesticides being tested by EPA's Endocrine Disruptor Screening Program (EDSP).

2.5. EPA has refused to consider the potential for aluminofluoride complexes to affect G proteins and cellular signaling pathways.

EPA states that "The assumption that cryolite will not cause higher levels of aluminum, sodium, or fluoride in water or soil beyond what is normally found as background levels in water and soil does not hold true for exposure to plants via contact with leaves" (EPA, Dec 2011, p.3).

EPA also acknowledges that "The fluoro-complexes are only predominate in acidic environments (pH<6.4)," and that "data indicate the fluoro-complexes of aluminum should be important in acidic environments" (EPA, 20 Sept 2011, p.2).

It is feasible that these "higher levels" of aluminum and fluoride from cryolite applied directly to plants, may persist on the leaves at the time of consumption, and that the acidic environment of the stomach would allow for the formation of fluoro-complexes. Furthermore, acidic soils are found in many regions of the United States, including parts of California (Atlas of the Biosphere, 1998), where cryolite use is prevalent.

Manoharan et al. (2007) reported:

> Increasing rates of F additions to soil significantly increased the soil solution concentrations of aluminium (Al) and F irrespective of the initial adjusted soil pH, which ranged from 4.25 to 5.48. High rates of F addition severely restricted root growth; the effect was more pronounced in the strongly acidic soil. Speciation calculations demonstrated that increasing rates of F additions substantially increased the concentrations of Al-F complexes in the soil. Stepwise regression analysis showed that it was the combination of the activities of AlF2(1+) and AlF(2+) complexes that primarily controlled barley root growth. The results suggested that continuous input of F to soils, and increased soil acidification, may become an F risk issue in the future.

Numerous studies have identified altered form and/or function of various cells and tissues in response to aluminum, fluoride and aluminofluoride complexes (Strunecká and Patočka, 2012). Among these findings:

- Brain:
    - *Mimic effects of calcium-mobilizing hormones, which suggests coupling of hormone receptors to phosphoinositide breakdown through G proteins (Rana and Hokin, 1990)*
    - *Greater hydrolysis of phosphoinositides when aluminum chloride and sodium fluoride were present together in rat cerebral cortical membranes (Candura et al., 1991)*
    - *Accumulation of inositol phosphates in suprachiasmatic nuclei region of rat hypothalamus when incubated with aluminofluoride complexes (Nadakavukaren et al, 1990)*
    - *Aluminofluoride complexes blocked the increase in camp stimulation*

by forskolin (Morgan et al., 1991)

- *Liver*
  - *Activation of phosphorylase and inactivation of glycogen synthase in response to fluoride in the presence of aluminum chloride in hepatocytes (Blackmore et al., 1985)*
- *Kidney*
  - *Ion transporting processes affected by aluminofluoride complexes in kidney tubular cells: stimulation of adenylate cyclase; inhibition of amiloride-sensitive Na/H exchange regulated by camp-dependent protein kinase; enhanced epidermal growth factor-stimulated prostaglandin production; mimicked vasopressin and bradykinin induced calcium mobilization (Zhou et al., 1990)*
- *Blood cells*
  - *Induced shape changes and aggregation in platelets (Rendu et al., 1990)*
  - *Impaired polymerization-depolymerization cycle of tubulin (Chabre, 1990)*
  - *RBCs lost membrane material, size decreased (Strunecka et al., 1991)*
- *Osteoblasts and osteoclasts*
  - *Enhanced stimulation of inorganic phosphate transport in osteoblasts (Caverzasio et al., 1996)*
  - *Exposure of osteoclasts to aluminofluoride complexes resulted in a marked concentration-dependent inhibition of bone resorption (Moonga et al., 1993)*
- *Energy metabolism*
  - *Inhibited mitochondrial ATPase activity in the presence of aluminofluoride complexes (Lunardi et al., 1988)*

EPA states that "cryolite has already been evaluated in a number of toxicity studies…The oral exposure to cryolite in the many toxicity studies with different animal species has allowed evaluation of the toxicity potential for cryolite and its aluminum and fluoride degradation products and complexes" (EPA, 6 Sept 2011, p.2). However, EPA fails to realize that the toxicity tests conducted thus far for cryolite could not possibly have analyzed the numerous physiological and biochemical actions of aluminofluoride complexes in various cells and tissues, especially with reference to the effects on G proteins and cellular signaling pathways.

2.6. According to EPA's Cryolite Final Work Plan Registration Review, "EPA also solicited comments, through PWP, on three specific topics: environmental justice, water body impairment, and trade irritants" but that "No comments or information were received during the comment period concerning these issues" (EPA, Dec 2011, p.4).

FAN's previous submission included substantive comments on both environmental justice and water body impairments.

Section 3.6 of FAN's submission is reproduced here in its entirety:

According to OPP (EPA OCSPP, 2011b, p. 9), "The Office of Pesticide Programs (OPP) typically considers the highest potential exposures from the legal use of a pesticide when conducting human health risk assessments, including, but not limited to, people who obtain drinking water from sources near agricultural areas, the variability of diets within the U.S. (including different ages, regions, and ethnicities), and people who may be exposed when harvesting crops." However, there are a number issues regarding fluoride exposure that fall within the realm of environmental justice concerns that OPP has not addressed. Several sub-populations have been shown to be disproportionately harmed by fluoride's toxicity, including low-income people, certain minority groups, and infants and children.

OPP's recent aggregate risk assessment for fluoride was based on OW's analysis of fluoride, which included flawed methodology, inappropriate assumptions, and refusal to consider the voluminous scientific evidence indicating that the harmful effects of fluoride exposure extend beyond just the teeth. The decision by OPP to reduce the FQPA Safety Factor for fluoride to 1X was determined via similar parameters, based largely on OW's findings.

However, as discussed in Section 2.4., OW's use of a safety factor of 1 is scientifically unjustified. OW defends their use of an uncertainty factor of 1 as follows:

> In establishing an estimated oral RfD for fluoride, data on nutritional benefit were assessed in combination with the data on severe dental fluorosis to define a level that provides anticaries protection without causing severe dental fluorosis when consumed daily for a lifetime. Conventional application of uncertainty factors is not always appropriate when carrying out a risk assessment for nutrients and other beneficial substances, especially when there is a relatively small difference between the levels that satisfy need and those that cause adverse effects. For this reason the total uncertainty factor applied was 1. (EPA OW, 2010a, p. 105)

By using a safety factor of 1, OW is claiming that the full range of sensitivity to fluoride among the American population in 2011—with its vast spectrum of racial, ethnic, and socioeconomic groups—was completely accounted for by a study of approx 5000 children in the 1930s. This is quickly countered by the fact that all children in the Dean (1942) study were white. However, numerous studies indicate that black children are more susceptible to dental fluorosis (and probably other harmful effects of fluoride) than are white children. Using an uncertainty factor of 1 here is tantamount to perpetrating environmental *in*justice against black children.

The National Research Council 1993 Review (NRC, 1993) reported four earlier studies showing that ethnicity plays a role in the effects of fluoride:

- Russell (1962), in the Grand Rapids fluoridation study, noted that fluorosis was twice as prevalent among African-American children as white children.
- In the Texas surveys in the 1980s, the odds ratio for African-American children having dental fluorosis, compared with Hispanic and non-Hispanic white

children, was 2.3 (Butler et al., 1985).

- Dental fluorosis also tended to be more severe among African-American children than white children in the Georgia study (Williams and Zwemer, 1990), although the difference was not statistically significant.
- In Kenya, prevalence and number of severe cases were unexpectedly high when related to fluoride concentrations in drinking water (Manji et al., 1986), although nutritional factors could have confounded these results. The reasons for these findings are unknown and do not seem to have been explored further.

Data published in CDC's Morbidity and Mortality Weekly Report in 2005 (Beltrán-Aguilar et al., 2005) show that Black and Mexican Americans have significantly higher levels of the worst forms of dental fluorosis than do Whites, as shown in Table 5.

TABLE 23. Enamel fluorosis* among persons aged 6–39 years, by selected characteristics — United States, National Health and Nutrition Examination Survey, 1999–2002

	Unaffected		Questionable		Very mild		Mild		Moderate/Severe	
Characteristic	%†	SE§	%	SE	%	SE	%	SE	%	SE
Age group (yrs)										
6–11	59.81	4.07	11.80	2.50	19.85	2.12	5.83	0.73	2.71	0.59
12–15	51.46	3.51	11.96	1.84	25.33	1.98	7.68	0.93	3.56	0.59
16–19	58.32	3.30	10.21	1.70	20.79	1.78	6.65	0.67	4.03	0.77
20–39	74.86	2.28	8.83	1.23	11.15	1.22	3.34	0.58	1.81	0.39
Sex										
Male	67.65	2.63	9.99	1.45	15.65	1.52	4.58	0.54	2.12	0.39
Female	66.97	2.84	9.83	1.34	15.58	1.36	4.84	0.61	2.78	0.49
Race/Ethnicity¶										
White, non-Hispanic	69.69	3.13	10.43	1.62	14.09	1.56	3.87	0.60	1.92	0.48
Black, non-Hispanic	56.72	3.30	10.40	2.16	21.21	2.16	8.24	0.82	3.43	0.54
Mexican-American	65.25	3.89	8.95	1.29	15.93	2.24	5.05	0.72	4.82**	1.81
Poverty status††										
<100% FPL	68.02	3.21	10.67	1.64	14.28	1.73	4.07	0.69	2.97	0.66
100%–199% FPL	66.92	2.91	9.11	1.79	16.11	1.46	5.21	0.78	2.65	0.56
≥200% FPL	66.88	2.75	10.73	1.33	15.56	1.56	4.83	0.50	2.00	0.37
Total	**67.40**	**2.65**	**9.91**	**1.35**	**15.55**	**1.37**	**4.69**	**0.49**	**2.45**	**0.40**

* Using Dean's index. All estimates are adjusted by age (single years) and sex to the U.S. 2000 standard population, except sex, which is adjusted only by age.
† Weighted prevalence estimates.
§ Standard error.
¶ Calculated using "other race/ethnicity" and "other Hispanic" in the denominator.
** Unreliable estimate: the standard error is 30% the value of the point estimate, or greater.
†† Percentage of the Federal Poverty Level (FPL), which varies by income and number of persons living in the household.

Table 5. Enamel fluorosis* among persons aged 6-39 years, by selected characteristics—United States, National Health and Nutrition Examination Survey, 1999-2002. Source: Beltrán-Aguilar et al., 2005.

While EPA acknowledges the results of a study by Sohn et al. (2001) that "Fluid intake was significantly associated with age, sex, socioeconomic status, and race and ethnicity," OW failed to include this association in its risk assessment (EPA OW, 2010a). Sohn et al. (2001) states "The effect of race or ethnicity and socioeconomic status (SES) on fluid consumption were particularly noticeable," with African American children consuming significantly more plain water and less milk than other racial or ethnic groups (white children consumed the least amount of total fluid and plain water), and children from the low SES group consuming significantly more plain water and less milk than higher SES groups. A paper in the 2009 *Journal of Public Health Dentistry* reviewed the available research and concluded that "African-American children, and/or children of lower SES, are
ingesting significantly more fluoride than children who are higher on the social scale.

They may be therefore at higher risk for fluorosis." (Sohn et al., 2009)

There may be several reasons why black children are more susceptible to developing dental fluorosis than white children. In addition to ingesting more fluoride (as indicated above) it may also reflect dietary differences. Some black children are lactose intolerant and therefore have less protective calcium and less vitamin D in their diets. Dark pigmentation reduces the synthesis of Vitamin D in the skin at a given level of sunlight, and reduction of sunlight by inner-city pollution may be a further factor. Another possible association was raised by Leite et al. (2011). In this study the authors found that rats treated with both lead and fluoride had worse dental fluorosis than rats treated with fluoride alone. Thus it is possible that children from inner city areas that have already been compromised with lead exposure will be more susceptible to developing dental fluorosis. One can only assume that OW did not recognize the lack of Environmental Justice inherent in its use of an uncertainty factor of 1. However, whether it realized it or not, in developing this RfD in this manner, OW simply failed to protect vulnerable minorities in the population. This is clearly in violation of a U.S. Executive Order (12898,
1994) and one of the stated goals of EPA administrator Lisa Jackson (EPA, 2011a).

OPP should be aware that there are gross disparities in the racial and socioeconomic demographics of agricultural laborers—those most directly affected by the application of cryolite to crops. Approximately 97% of all agricultural usage of cryolite in the United States is in California (GfK Kynetec, 1998-2008; EPA OCSPP, 2010, p. 2). According to the National Agricultural Workers Survey of 2005, 99% of all farmworkers interviewed in
California were Hispanic. Forty-three percent of all individual farmworkers, and 30% of farmworker families earned less than $10,000 per year, and 22% of California farmworkers had annual incomes below the federal poverty level (Aguirre International, 2005).

Regarding the issue of water body impairments, Section 1 (Introduction) of FAN's (2011) submission states:

> OPP states that "Cryolite is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act" (EPA OCSPP, 2011a, p.22). However, it should be acknowledged that two of the degradation products of cryolite, aluminum and fluoride, are among the major causes of impairment of water bodies in the United States. Aluminum (TMDLs: 1974) is second only to iron as the most frequent cause of impairment in the Specific State Pollutants that make up the National Metals (other than mercury) Pollutant group (EPA, 2011b), while fluoride (TMDLs: 78) is the most frequent cause of impairment in the Specific State Pollutants that make up the National Toxic Inorganics Pollutant group (EPA, 2011c). According to EPA, agriculture is indicated as a probable source contributing to impairments affecting more rivers, streams, lakes, reservoirs, ponds, and wetlands that virtually any other source (EPA, 2011d, National Probable Sources Contributing to Impairments). Among

the probable sources that make up the National Agricultural Probable Source Group is runoff from agricultural lands.

Cryolite contains approximately 55% fluorine and 13% aluminum (EPA OCSPP, 2011a, Table 4, p. 10). Thus, the more than 1.2 million pounds of active ingredient used on agricultural crops (EPA, 2010b, p. 2) contribute over 660,000 pounds of fluorine and more than 156,000 pounds of aluminum to the environment each year. These estimates do not include use of cryolite on ornamental plants, unreported registered usage (e.g. small acerage crops), or non-agricultural use sites (e.g. turf, post-harvest, mosquito control, etc.). In fact, according to EPA "There are no usage data for cryolite from our available sources on ornamental plants and nursery crops" (EPA OCSPP, 8 Sept 2010, p.3), although the California Department of Pesticide Regulation estimates that 1,850 pounds of cryolite were used on nursery stocks in 2008.

2.7. Despite declarations in previous documents that "most present day supplies of cryolite pesticide products are synthetically produced" (EPA OCSPP, 2011a, p. 9), EPA's Final Work Plan (EPA, Dec 2011) seems to ignore this fact completely.

EPA's Final Work Plan states that "Cryolite is a naturally-occurring mineral of sodium aluminum fluoride, and is part of the inorganic fluorine chemical family" (EPA, Dec 2011, p.3). While EPA acknowledged FAN's comments on the synthetic nature of cryolite used for agricultural applications, stating that "[FAN] believe the synthetic cryolite is chemically different than natural cryolite due to the presence of impurities" (EPA, 20 Sept 2011), EPA failed to respond to this concern.

As "the type of cryolite (synthetic cryolite versus natural cryolite; cryolite, which is fine ground versus cryolite consisting of larger particles) also influences amount of oral absorption" (ECHA Annex 1, 2010), we request that EPA make public the type (natural or synthetic) of cryolite used in all animal studies and ecological risk assessments, and distinguish for the public those crops which are treated with naturally-occurring cryolite and those treated with synthetic cryolite.

3. Conclusions

While FAN applauds the decision by EPA's EFED to include an avian reproduction study (850.2300) for cryolite, numerous other concerns were raised by FAN in our previous submission (FAN, 5 Jul 2011) that were not adequately addressed prior to release of the Amended Cryolite Final Work Plan Registration Review (EPA, December 2011).

FAN thus requests the following:

1. EPA to phase out the use of cryolite as it does not meet the safety standard in FFDCA

Section 408.

2. EPA to mandate Developmental Toxicity Tests via oral administration of synthetic cryolite to enable it to study the effects of fluoride, aluminum, and the fluoroaluminum compounds. The animal lab chow that is fed to the animals must contain the lowest levels of fluoride and aluminum possible. A histological examination of the brains, kidney, and bone should accompany the requirements for these tests.

3. A field study needs to be undertaken that involves various vegetables and fruits that have cryolite tolerances. This food should be grown in soil with and without cryolite and at the end of the growing season this food should be analyzed for its aluminum content. The level of ph and aluminum content of the soil should be recorded.

4. EPA to release to the public all animal studies performed with cryolite.

5. EPA to release its documents in a format that allows the public to search them.

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APPENDIX A

Twenty-six human studies that report an association of lowered IQ with fluoride exposure.

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