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[Personally Identifiable
Information Redacted]

Dear NTP/OHAT Report Members

July 10, 2016

We are requesting NTP withdraw the July 2016 NTP Research Report, "Systematic Literature Review on the Effects of Fluoride on Learning and Memory in Animal Studies," and correct material flaws before republishing. This NTP Report has a high level of bias and is not a balanced review of literature. The NTP report should not include the promotion and in effect "marketing" of fluoride. Effectiveness for humans is not a part of a literature review on learning and memory in animals. If the evidence on effectiveness of fluoride is raised, the same objective rigor without bias demanded of "safety" must equally be applied for effectiveness. A balanced presentation of science must be made without blindly relying on flaws of government agencies.

The NTP Report relies heavily on trust of "authorities" rather than holding a strict line to measured science. Trust but verify. If you do not have primary measured evidence, say so.

SOURCES OF EXPOSURE:

The question of sources is relatively insignificant. A more important concept is measured data of individual concentration of fluoride in each person's tissues, serum, urine, brain, liver, kidney, bones and teeth. Determine normal and desired fluoride tissue concentrations. Then determine desirable dosage to achieve the desired concentration. After all, we are not treating water, instead our intent is to treat teeth; however, we are also exposing all human tissues, all brains, all organs, all enzymatic systems, hormone production, thyroid, mitochondria, reproductive organs, and all cells.

1. We need to know a range of normal human tissue fluoride concentrations, not just the mean, median, average or 90th percentile water consumption as the EPA presents. The EPA is focused on water concentrations. NTP must focus on animal and human tissue concentrations, which is inclusive of all exposure and absorption. NTP must be protective of everyone, even the most vulnerable and chemically sensitive. What is "normal" for each tissue?

Remember, the 90th percentile adult drinks about 2 liters of water and some drink more than 5 times that amount of water each day. EPA assumes fluoride in foods, fluoride medications, fluoride pesticide and post-harvest, fluorine, and industrial fluoride intake is the same for everyone. EPA is not protective when they use a safety factor and margin of error and confidence factor of 1:1. 1:1 provides no uncertainty for intra or inter species variations, no age or gender considerations, no nutritional, socioeconomic or race considerations, no margin of safety for chemically sensitive individuals, diet variations or synergistic effects with other chemicals. The NTP report makes no mention of these and other EPA flaws in EPA's proposal to raise the "safe" exposure from 0.06 mg/kg-d to 0.08 mg/kg-d. The NTP Report must use measured tissue concentrations, not fluoride water concentrations or EPA estimates.

2. With new and improved research, we are learning that fluoride is more toxic than originally estimated and we are exposed to more fluoride than previously. EPA's proposal that fluoride is safer than we thought is not supported by research.

3. Decades ago in science history, scientists like the EPA estimated fluoride exposure and made assumptions. Now good researchers actually measure fluoride concentrations, using hard data from various tissues and each individual. NTP and EPA are historic and still discussing vague, estimates of assumptions, guessing and hoping, bending to traditions. NPT needs to step up to the plate and require measured evidence for exposure and be protective of all.

4. Historically, some scientists (especially those in my dental and public health professions) confused dosage with concentration. NTP has fallen into their trap. The concentration of water is not a dosage for humans or human tissue. NTP must use individual measured data on blood serum, urine, bone, teeth, brain, pineal gland, kidney, etc. The historic assumption of exposure is crude and lacks scientific precision.

5. In the "INTRODUCTION, Sources of Exposure" the NTP Report glosses over the age at which fluoride is most likely to have a toxic effect on the developing neurological system, i.e. infants under six months of age, the developing fetus and the mother's egg and father's sperm.

6. The NTP Report does not accurately report the EPA RSC from Table 1. The **NTP Report** states, "The relative source contribution from drinking water was . . . 70% in children less than 1 year old." The **EPA RSC report** actually states 70% for infants 0.5-<1 year of age. The NTP report includes the first six months of life while the EPA omits and ignores these most vulnerable infants. Virtually all fluoride infants receive, is from water mixed with formula and the dosage is unacceptable — if formula is made with fluoridated water. The brutal fact that most samples of mother's milk contains no detectible fluoride is the standard of nutrition against which all other supplements must be compared. For those samples of mother's milk which fluoride is detected the concentration is 0.004 ppm in unfluoridated communities.

What primary studies, secondary studies, or reviews does the NTP Report provide on exposure of fluoride for infants and fetus during a most critical time for their developing brain, prior to six months of age? None. Actual tissue concentrations must be measured.

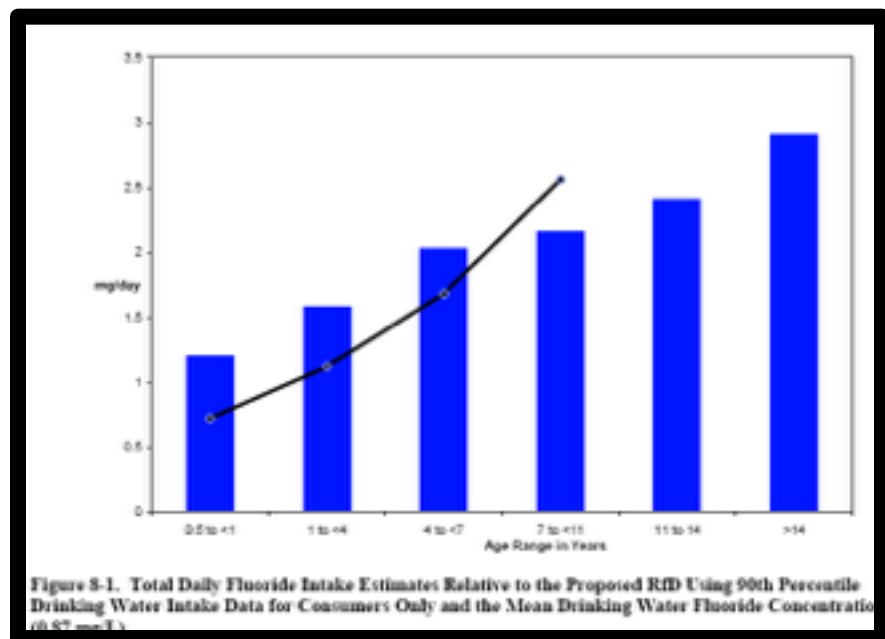
For example, infants up to 6 months drink on average 25 oz of milk a day, 0.75 liters and some drink over 1 liter/day. A 3 kg infant on formula made with fluoridated water and drinking 1 liter a day would have a dosage of 0.43 mg/kg-d. Most infants ingest several times more fluoride than EPA's RfD of 0.06 mg/kg-d or the proposed 0.08 mg/kg-d. It is no surprise that over 40% of adolescents have dental fluorosis, a biomarker of toxic fluoride exposure during development of the tooth. I diagnose dental fluorosis almost every day on patients. Treatment is costing each tens of thousands of dollars, grief and pain.

Most infants (about 80%) receive all or part of their nutrition from formula. Following the EPA's RfD, an infant should not ingest more than 200 ml of water a day, 0.85 cups. Infants only consuming 0.85 cups of formula would develop kwashiorkor. NTP and EPA expect infants to starve in order to stay within the RfD. No wonder EPA omits infants under six months of age.

NTP's failure to include infant fluoride exposure, or at least critically acknowledge the lack of research, is a fatal flaw in the NTP Report. The brains of infants must be protected. If we err on the side of safety rather than effectiveness, we can fix teeth but we cannot fix brains.

7. The NTP Report cherry picked evidence from the EPA Relative Source Contribution 2010 report. Instead of protecting the public, the EPA proposed increasing the "safe" exposure amount of fluoride by 33% which will not reduce dental caries or dental fluorosis or neurologic harm. In order to justify such a huge increase, the EPA did not include infants under six months of age or the fetus. The EPA then also ignored 10% of the population drinking the most water and only accepted 90%. Even with kicking out infants and 10% of the population, the EPA reported about a third of children will still ingest more than EPA's proposed RfD. And then the EPA determined there was no need for any margin safety or uncertainty factor.

What is the "normal" concentration of fluoride for all tissues? EPA and the NTP Report are silent. The EPA's RSC Figure 8-1 reproduced here, clearly shows about a third of children will be exposed to more than the proposed RfD. And the EPA avoided the fetus, infants to six months of age, 10% of the population drinking the most water, and provides no consideration for variations in range of fluoride from other sources.



This NTP Report completely omitted the EPA's RSC limitations. The NTP Report must provide balanced scientific evidence and not simply find evidence and cherry pick evidence, to protect fluoride.

What primary studies or hard measured data, plasma, urine or saliva concentrations, does this NTP Report provide to establish the exposure range of the fetus and infant on mother's milk versus formula made with water containing fluoride? What hard measured scientific evidence does this report provide for plasma fluoride concentrations in the population at large?

This NTP Report must not trust opinions from government agencies or organizations who have staked their reputation on fluoridation. Only use measured data with caution and require better, protecting all with a margin of safety.

EFFECTIVENESS:

1. The NTP Report "INTRODUCTION" claims "Use of Fluoride to Prevent Tooth Decay." The NTP Report promotes the assumed benefits of fluoride without reservation. The wording of the NTP Report sets the reader's mind to both have biased judgment in favor of fluoride's alleged benefit and to protect, defend and recommend fluoride for health. Judgment for a reader considering fluoride's risks will be clouded through the bias with "absolute unchallenged" confidence of benefit. Benefit of fluoride ingestion is controversial and NTP must withdraw promotion of this unapproved drug. Congress has not charged the NTP, EPA, HHS, ADA, AMA, or PHS to determine efficacy, safety or dosage of any substance intended to prevent, treat or cure disease in man or animals.

The NTP report states, "Fluoride from community water fluoridation . . . is intended to prevent dental caries primarily through topical remineralization of tooth surfaces." Fluoride is a drug unapproved by the FDA.

"Topical:"

1. The NTP Report is partly correct, potential benefit of fluoride is topical, on the surface rather than systemic, swallowed. However, the fluoride in water contact time is too short and concentration too low to have benefit topically. Get a glass of cool water and take a swallow. Feel the cold on your teeth? How long was the contact time of the water on your teeth? A second? Two? Five seconds? Did you notice the cold on your bottom teeth? Not much. The tongue protects the bottom teeth and the contact time, if any, on the tooth surface, inter proximal and groves is too limited to have significant benefit. If the NTP Report insists topical use of water fluoridation has benefit, then the NTP Report must provide primary research which has been reviewed with the same standards as they are using to evaluate the animal studies in this Report. Research indicates fluoride concentration in saliva increases slightly after drinking fluoridated water for about an hour or two and longer in plaque. Research has not shown the slight increase to be significant.

2. Short or no contact time is one reason the NRC 2006 and many scientists do not find the argument that low concentrations of topical fluoride in water could be effective. In Dentistry we glue, bond, fluoride varnish on to the tooth at 22,600 ppm (not FDA approved); however, the FDA has found fluoride in toothpaste to be effective at 1,000 ppm, and the warning "Do Not Swallow." A few seconds of topical fluoride at 0.7 ppm is too short and too dilute to have a significant effect. The systemic increase of fluoride a couple hundredths of one part per million is minor and doubtfully reduces dental caries.

3. The FDA reported the evidence for efficacy for fluoride supplements, which are ingested, is incomplete. The FDA has not approved the ingestion of fluoride with the intent to prevent dental caries. NTP's promotion of an unapproved drug is a violation of the Food and Drug Act.

Question: What topical benefit do infants receive from fluoridated water prior to the eruption of their teeth? The un-erupted tooth receives no topical benefit. HHS and the NTP Report have attempted to "sanitize" the toxicity of fluoride by sheltering toxicity under the alleged benefit of "topical" use.

4. If “primary” potential benefit is topical, then the NTP must provide quality evidence for the degree of benefit from swallowing fluoride. The NTP report must not set the reader up with low quality research on benefit to “weigh the benefit vs risk” of ingested fluoride. Congress has charged the FDA to weigh the science on benefit vs risk, not the NTP. If topical fluoride in water has significant benefit, NTP/HHS should recommend swishing and spitting fluoride water, and like the FDA warn, “Do Not Swallow.” Dental fluorosis and neurologic harm is not due to excess topical fluoride on the teeth. NTP should ask the FDA to approve fluoride ingestion prior to promoting fluoride ingestion.

5. Effectiveness Research Limitations: The NTP Report is exacting and demanding of quality evidence for harm, yet for effectiveness the NTP Report makes no mention of the lack of quality research or limitations. Frequently, water fluoridation studies have the following flaws:

- **A. Not one Study corrects for Unknown Confounding Factors**
- **B. Not one Prospective Randomized Controlled Trial**
- **C. Socioeconomic status usually not controlled**
- **D. Inadequate size**
- **E. Difficulty in diagnosing decay**
- **F. Delay in tooth eruption not controlled**
- **G. Diet: Vitamin D, calcium, strontium, sugar, fresh and frozen year around vegetables and fruit consumption not controlled.**
- **H. Total exposure of Fluoride not determined**
- **I. Oral hygiene not determined**
- **J. Not evaluating Life time benefit**
- **K. Estimating or assuming subject actually drinks the fluoridated water.**
- **L. Dental treatment expenses not considered**
- **M. Breast feeding and infant formula excluded**
- **N. Fraud, gross errors, and bias not corrected.**
- **O. Genetics not considered**
- **P. Lack of individual measured fluoride concentrations from plasma or urine.**

However, the NTP Report has unwavering support, without any reservations, for fluoridation in spite of the lack of quality research.

6. MOTHER’S MILK: Mother’s milk has no detectible fluoride in most samples. The NTP almost completely ignores nature’s ideal dosage of fluoride for infants, while their developing brain is most vulnerable.

Question: NTP states, “*Water fluoridation represents 30% to 70% of an individual’s total exposure.*”¹ What are the sources of fluoride for an infant on formula made with fluoridated water? Formula powder has almost no fluoride. Mother’s milk has almost no fluoride. The only other common source of fluoride is water fluoridation which for an infant would represent almost 100% of their fluoride exposure, and with mother’s milk 0%. The range for infants is 0% to

¹ <http://ntp.niehs.nih.gov/pubhealth/hat/noms/fluoride/neuro-index.html>

100%, not 30% to 70%. NTP has failed to focus on the age when development of the neurological system is most vulnerable to toxic effects.

7. THE FDA CDER: The FDA has repeatedly stopped fluoride supplement manufacturers because the evidence of effectiveness is incomplete. The NTP Report fails to mention the EPA agrees with Congress that the FDA has jurisdiction over the addition of fluoride to water with the intent to prevent dental caries and that the FDA has not approved ingestion of fluoride with the intent to prevent dental caries.

8. DEVELOPED COUNTRIES: Although some countries promote fluoride ingestion, few have more than half the population fluoridated and most developed countries do not fluoridate public water. Countries with socialized dental care should be the first to embrace water fluoridation, if it were safe and effective fluoride would reduce government dental expenses. These countries pay for dental caries treatment and if ingested fluoride actually prevented caries and was safe, they would mandate water fluoridation, but they do not. The public health agencies, dental associations, courts and/or drug regulatory agencies of these countries do not support fluoride ingestion.

9. RESEARCH: A 2015 Cochrane on fluoridation reported there is very little contemporary evidence, meeting the review's inclusion criteria, that has evaluated the effectiveness of water fluoridation for the prevention of caries.

Question: What high quality research does NTP have to support the efficacy of ingested fluoride? None. So they reference HHS and HHS will soon reference NTP. Then CDC will reference HHS and NTP and NTP will reference CDC and HHS. Circular referencing will then be called proof positive the science is without question and fluoridation becomes public health tradition without quality evidence. None of the agencies actually looked at the primary research on both sides of the controversy.

10. NTP REPORT BIAS: Page 1 of the NTP Report, clearly demonstrates a fundamental material bias which compromises confidence in the entire Report. The NTP Report starts out framing the readers judgment with claims of effectiveness. The NTP Report is positioning the reader to have bias when reviewing risk and harm and wants the reader to "weigh" the benefits vs the "risks." Congress has charged the FDA CDER, not NTP with weighing the risk vs benefit of substances used with the intent to prevent, treat, cure or mitigate diseases in man and animals. The NTP Report is contaminated by raising the controversial theory of effectiveness.

Question: What Congressional authority has Congress given the NTP to assume the roll of the FDA to determine safety of any medicine? Drugs are defined as "articles intended for use in the . . . prevention of disease" [FD&C Act, sec. 201(g)(1)]

11. A survey of 55 reputable oral health specialists on the impacts of artificial water fluoridation and other preventive technologies on the decline in dental caries prevalence over the past four decades in most nations revealed that, apart from fluoridated toothpaste, there were conflicting responses on the impact of artificial water fluoridation and other fluoride-based

technologies.² However, the NTP Report is biased cherry picking research to claim benefit rather than honest scientific review.

12. The NTP Report fails to consider the disease(s) caused with fluoride deficiency. There are no diseases caused with the absence of fluoride in the diet. Fluoride is not a nutrient and is usually undetectable in Mother's Milk.

13. Awofeso argues that artificial water fluoridation is not just questionable from an ethical perspective but is, in fact, clearly unethical.³ The NTP Report fails to provide a balanced scientific statement.

14. For effectiveness, NTP must first determine the optimal therapeutic tooth fluoride concentration (if such exists), then determine the optimal plasma fluoride concentration required to achieve the optimal tooth fluoride concentration, and then determine the optimal fluoride exposure to achieve the optimal plasma and tooth concentration. Unfortunately, there are many unknowns and uncertainties, such as no optimal fluoride tooth concentration has been determined. Both teeth with caries and without caries have similar ranges of fluoride concentration. The public deserves better than the NTP Report.

15. The NTP Report states, "community water fluoridation has been identified as the most cost-effective method for delivering fluoride to all members of the community. . . ." What about those who refuse? What about Freedom of Choice? What are the references? For example, fluoride supplements are less expensive if purchased in bulk and provided to those who desire the fluoride rather than medicating everyone. Swallowing a pea size of fluoride toothpaste would be no additional cost for those on fluoride toothpaste. The NTP is repeating flawed assumptions of low cost without scientific evidence. And the costs of treating dental fluorosis and increased prevalence of fractured teeth with harder fluoridated teeth are not included and hushed up.

16. The NTP Report states, "Consuming fluoridated water and beverages and foods prepared or processed with fluoridated water throughout the day maintains a low concentration of fluoride in saliva and plaque, which enhances remineralization (US DHHS 2015)." The NTP must use primary references and not DHHS theory. What is the difference in fluoride concentration in the dentin and enamel with fluoridated water and what is the quality of that research? What concentration difference is found with fluoridated and unfluoridated water and what is the resulting enamel and dentin concentration differences?

17. The NTP Report mentions the support of PHS and HHS for fluoridation, but fails to remind the reader that PHS and HHS do not assume any liability for accuracy of policy. Actual fluoridation is left up to some of the least scientific local agencies who (like the NTP Report) blindly rely on the PHS and HHS.

² D. Bratthall, G. Hänsel-Petersson, and H. Sundberg, "Reasons for the caries decline: what do the experts believe?" *European Journal of Oral Sciences*, vol. 104, no. 4, part 2, pp. 416–422, 1996.

³ N. Awofeso, "Ethics of artificial water fluoridation in Australia," *Public Health Ethics*, vol. 5, no. 2, pp. 161–172, 2012.

19. The NTP Report asserts with confidence, “This (0.7 ppm) recommended level provides the best balance of protection from dental caries, while limiting the risk of dental fluorosis.” Months ago, 1.0 ppm was safe and effective with similar statements. What scientific evidence does the NTP Report use to suggest the 1 ppm was 30% too high? Tie that in with the research finding lower IQ in humans with increased dental fluorosis. Then tie that in with the prevalence of dental fluorosis. Will 30% provide a significant reduction in dental fluorosis protect everyone? What is the scientific evidence?

20. The NTP Report does not differentiate between naturally occurring calcium fluoride and hydrofluorosilicic acid added to public water and sodium fluoride. A strict scientific evaluation of the solubility and absorption differences must be referenced.

After 70 years of water fluoridation, we still don't know how much fluoride in the tooth or plasma is effective in reducing dental caries. . . if any. The NTP Report must be scientific and not reference policy theories and opinions. Hard data of measured evidence must be provided for claims. Well thought through evidence is essential. The NTP Report would be best to eliminate all references to benefit and stick with the title of their Report, “Systematic Literature Review on the Effects of Fluoride on Learning and Memory in Animal Studies.”

Concerns for Potential Fluoride Toxicity

1. On one hand the NTP Report accepts low quality evidence for unquestioning support of fluoride's effectiveness, while on the other hand the NTP Report requires a high level of rigor to prove harm. This double standard, accepting low quality research of efficacy yet demanding high quality proof of harm is a reason the public is not protected from excess fluoride exposure and loses confidence in government agencies. The NTP Report should determine the level of confidence it will accept for both safety and efficacy and apply the same standards to both effectiveness and safety.

For example, fluoride post-harvest fumigants raise fluoride concentrations in some foods as high as toothpaste. The EPA stopped approval of fluoride post-harvest fumigation of food with sulfural fluoride; however, Congress over-rode the EPA. Congress, like much of the public probably mistakenly thought, “fluoride is good for us, right? A little more will reduce even more dental caries, a win, win for everyone.” Even if some fluoride topically is safe and effective, when is too much too much?

2. Developmental neurotoxic effects must be inclusive of all ages, but focus on the age during the development of the neurologic system. Evading and avoiding the genetics, the fetus and infants under six months is a fatal flaw in the NTP Report.

3. 100% of the public must be protected, not just the 90th percentile of adults.

4. NTP Table 8 shows low-to-moderate level-of-evidence in development and adult animal exposure studies for a pattern of findings suggestive of an effect on learning and memory. How much more evidence does NTP need to raise a red flag? Certainly the evidence of harm is as strong as the evidence of effectiveness.

5. In toxicology, usually higher doses are used in animal studies and then the dosage is extrapolated to humans with an uncertainty factor and margin of safety.

6. Animals need 5 to 20 times the dose of fluoride to get the same plasma levels as humans. In addition, animal exposure in a controlled environment with water at 0.7 ppm fluoride is not comparable with humans drinking a range of almost no water to more than 10 liters a day of 0.7 ppm fluoride in water AND swallowing toothpaste, taking fluoride medications, eating fluoride pesticides and post-harvest fluoride fumigants, and eating fluoride foods such as tea, grapes, etc.

REMEMBER: IT TAKES MUCH MORE FLUORIDE IN ANIMALS TO ACHIEVE THE SAME PLASMA FLUORIDE CONCENTRATION OF HUMANS.

7. The NTP Report suggests none of the studies in Choi meta-analysis controlled for iodine, lead, arsenic. However, Xiang 2003 a, b did control for iodine and lead, and then arsenic in retrospect.

8. The NTP Report uses a double standard, pointing out the Choi study weaknesses but having no comment on the Broadbent study weakness. The NTP Report also References Sutton⁴ who bases their opinion on Broadbent 2015 (HHS also relies heavily on Broadbent 2015), and with bias, the NTP Report fails to note limitations to the Broadbent study which was incapable of detecting IQ loss from fluoride.⁵ Broadbent failed to consider total fluoride exposure or measured fluoride concentrations in human tissue/fluids. Most of the "controls" were taking fluoride supplements. In effect, Broadbent compared those on fluoridated water with those on fluoride supplements. Total fluoride exposure was too similar to detect an IQ loss. Broadbent criticized other studies for not controlling for 15 potential confounding factors, yet Broadbent only controlled for four of those. The controls had very corrosive water with high lead and manganese. Broadbent failed to control for mother's IQ which data was available. Of course Broadbent disputes the concerns, but does not provide data for his defense.

10. The NTP Report speaks of benefit with what seems like hugs and kisses not raising a whisper for lack of confidence in efficacy raised by many studies, nor comment on the low quality of research. And further, the report fails to mention that fluoride is considered more toxic than lead and slightly less toxic than arsenic. Is fluoride considered a poison by law? Yes. What is an estimated lethal dose for humans? Are some humans more sensitive to toxins and fluoride than others? What is the dosage required to cause an adverse reaction for the most sensitive person? What other chemicals cause a synergistic effect increasing fluoride's toxicity?

⁴ "Scientific risk assessments of toxins include individual and population exposure levels. The failure of the Health Service Executive (HSE) to perform even the most basic blood and urinary measurements essential to a safety review renders their fluoridation report nothing more than a political whitewash." - *Declan Waugh (2015)*

⁵ Osmunson B, Limeback H, Neurath C, Study Incapable of Detecting IQ Loss from Fluoride, *American Journal of Public Health*, Published online November 12, 2015

1. The NTP Report "Conclusion" again shows bias and a lack of understanding. The NTP Report states, "Very few studies assessed learning and memory effects in animals (rats and mice) at exposure levels near 0.7 parts per million...." Concentration of fluoride is not dosage. To extrapolate from animals to humans, plasma fluoride concentrations must be used. Research on fluoride at 0.7 parts per million in animals is not a reasonable evaluation of fluoride developmental toxicology for humans on 0.7 parts per million with fluoride toothpaste, fluoride pesticides, fluoride dental products, fluoride dental treatments, fluoride post-harvest fumigants, fluoride foods, fluoride medications, and fluoride industrial products.

Although NTP raises the concerns (Abstract) that some human studies have not included "co-exposures" for other toxicants, NTP has fallen into the same limitation and concern for synergistic effects of other developmental neurotoxins along with fluoride.

NTP must keep the studies going through at least the third generation of animals to evaluate generational effects. At least one study reported neurotoxicity through the third generation.

NTP must withdraw the current Report and correct fatal flaws.

Sincerely,

Bill Osmunson DDS, MPH