

WASHINGTON ACTION FOR SAFE WATER

January 1, 2010

Washington State Board of Health
Craig McLaughlin, Executive Director

PETITION FOR RULE MAKING (#8) WAC 246-290-460 THYROID RISKS FROM FLUORIDATION

OUTLINE

- I. **FLUORIDE'S DAMAGING EFFECT ON THE TYROID GLAND: STUDIES.** P 2
- II. **VIOLATION OF THE SAFE DRINKING WATER ACT.** P 23
- III. **MARKETING THE FLUORIDATED WATER DRUG** P 24
- IV. **BENEFIT RISK ASSESSMENT: "TEETH OR THYROID"** p 28
- V. **PETITION FOR WAC CHANGE: "WAC 246-290-460"** p 28

Fluoride is an enzymatic reactor affecting more than 80 enzymatic reactions.¹ The thyroid is one part of the enzymatic system which fluoride affects, disturbing thyroid homeostasis. The Board of Health is to assure the public that fluoridated water is safe for everyone and the scientific evidence for assurance is lacking.²

This petition is for safety and health with rule change under RCW 34.05.330.

RCW 43.20.50 (2) *"In order to protect public health, the state board of health shall: (a) Adopt rules for group A public water systems . . . necessary to assure safe and reliable public drinking water and to protect the public health.*

The AGO 1992 No.17,

"2. The Legislature has authorized the Board of Health to establish, and the Department of Health to enforce, a comprehensive regulatory scheme for public water systems."

*"The Board does not appear to have authority to adopt rules related to a water district deciding whether to fluoridate. **The Board's authority is to regulate allowable concentration levels and method of approval of water additives.**"*
(June 9, 2010 Board Meeting Handout, page 2, emphasis added).

¹ Garcia-Montalvo EA et al Fluoride exposure impairs glucose tolerance via decreased insulin expression and oxidative stress, *Toxicology* 2009 Sep 19;263(2-3):75-83.

² RCW 43.20.50 (2) *"In order to protect public health, the state board of health shall: (a) Adopt rules for group A public water systems . . . necessary to assure safe and reliable public drinking water and to protect the public health.*

I. FLUORIDE'S DAMAGING EFFECT ON THE THYROID GLAND: STUDIES

A. Considerations from Scientific Publications.

1. According to the US National Research Council, "several lines of information indicate an effect of fluoride exposure on thyroid function."

2. Fluoride's potential to impair thyroid function is perhaps best illustrated by the fact that -- up until the 1970s -- European doctors used fluoride as a thyroid-suppressing medication for patients with HYPER-thyroidism (over-active thyroid). Fluoride was utilized because it was found to be effective at reducing the activity of the thyroid gland - even at doses as low as 2 mg/day. Assuming no other fluoride exposure, just 8 glasses of fluoridated water alone would provide the 2 mg/day.

3. Today, many people living in fluoridated communities are ingesting doses of fluoride (1.6-6.6 mg/day) that fall within the range of doses (2 to 10 mg/day) once used by doctors to reduce thyroid activity in hyperthyroid patients.

***“Thyroid Function Suppression** Fluoride was widely used, especially in Europe, to suppress over-active thyroid function with doses in the range of 2.3-4.5 mg/day. Exposure doses in the U.S. were estimated to be 1.6-6.6 mg/day as published in 1991. Exposures are probably higher today, with increased water fluoridation since 1991, meaning the virtual epidemic of depressed thyroid function in America might be tied to excessive fluoride exposures.”*

4. While it may be that the thyroid in a patient with hyperthyroidism is particularly susceptible to the anti-thyroid actions of fluoride, there is concern that current fluoride exposures may be playing a role in the widespread incidence of HYPO-thyroidism (under-active thyroid) in the U.S.

5. Hypothyroidism, most commonly diagnosed in women over 40, is a serious condition with a diverse range of symptoms including: fatigue, depression, weight gain, hair loss, muscle pains, increased levels of "bad" cholesterol (LDL), and heart disease.. The drug (Synthroid) used to treat hypothyroidism is now one of the top five prescribed drugs in the U.S.

6. As recommended by the US National Research Council: "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."

7. Fluoride & the Thyroid - US National Research Council (2006):
"In summary, evidence of several types indicates that fluoride affects normal endocrine function or response; the effects of the fluoride-induced changes vary in degree and kind in different individuals. Fluoride is therefore an endocrine disruptor in the broad sense of altering normal endocrine function or response, although probably not in the sense of mimicking a normal hormone. The mechanisms of action remain to be worked out and appear to include both direct and indirect mechanisms, for example, direct stimulation or inhibition of hormone secretion by interference with second

messenger function, indirect stimulation or inhibition of hormone secretion by effects on things such as calcium balance, and inhibition of peripheral enzymes that are necessary for activation of the normal hormone.”

SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p 223.

8. “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.”

SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p 224.

9. “several lines of information indicate an effect of fluoride exposure on thyroid function.”

SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p 197.

10. “it is difficult to predict exactly what effects on thyroid function are likely at what concentration of fluoride exposure and under what circumstances.”

SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p 197.

11. “Fluoride exposure in humans is associated with elevated TSH concentrations, increased goiter prevalence, and altered T4 and T3 concentrations; similar effects on T4 and T3 are reported in experimental animals..”

SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p 218.

12. “In humans, effects on thyroid function were associated with fluoride exposures of 0.05-0.13 mg/kg/day when iodine intake was adequate and 0.01-0.03 mg/kg/day when iodine intake was inadequate.”

SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p 218.

13. “The recent decline in iodine intake in the United States could contribute to increased toxicity of fluoride for some individuals.”

SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p 218.

14. “Intake of nutrients such as calcium and iodine often is not reported in studies of fluoride effects. The effects of fluoride on thyroid function, for instance, might depend on whether iodine intake is low, adequate, or high, or whether dietary selenium is adequate.”

SOURCE: National Research Council. (2006). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academies Press, Washington D.C. p 222.

The History of fluoride and thyroid

15. 1854 - Maumene feeds sodium fluoride to a dog and causes a goitre to appear [also spelled goiter]. He is the first to consider fluorides as a cause of goiter. Suggests that high fluoride in water might cause endemic struma (goiter). (NOTE: The amount of fluoride given was 20 to 120 mg Na F-/day, for four months - Buergi, 1984 claims that a "cumulative dose of 10 g" was given.) Maumené E -"Expérience pour déterminer l'action des fluores sur l'economie animale" Compt Rend Acad Sci (Paris) 39:538-539 (1854)

16. 1869 - First experiments with sodium fluoride, showing inhibitory effects on glycolysis [a thyroid hormone - associated event] in isolated muscle tissue,

are published by Nasse.(see also: 1937 Litzka) Nasse O - "Beitraege zur Physiologie der contractilen Substanz" Pfluegers Archiv fuer Physiologie 2: 97-121 (1869)³

17. 1917/1918 - McKay, the dentist who investigated the cause of 'mottled teeth' - later to be renamed 'dental fluorosis', writes in the "Dental Cosmos" that enamel conditions in children with 'mottled teeth' are identical to those reported by Prof. Greves in Holland as being due to thyroid dysfunction (goitre). Greves reports that when rats were given water from the Utrecht area, goitre and mottled enamel developed.

18. 1919 -1921 - Ignorant of McKay's work, Goldemberg (Argentina) investigates the areas then commonly referred to as "goiterous waters" ('Kropfwaesser'), and reviews the work by others (Repin, Gautier, Clausmann, McCarrison, Parhou and Goldstein, Pighini, Christiani, Cahages, Houssay, Tappeiner, Schulz, Brandt and Pisotti). His findings convince him that the world-wide occurrence of goiter and cretinism is NOT due to iodine deficiency as commonly believed, but is the result of excessive fluoride intake from air, food and water. [Jod Basedow] He conducts animal experiments to test his hypothesis and reports that 2 to 3 mgs of NaF- daily for 6 to 8 months produced a 5 to 6-fold increase in the size of the thyroid gland. He calls the condition 'cretinisme fluorique'. McKay, FS - "Progress of the year in the investigation of mottled enamel with special reference to its association with artesian water" J Natl Dental Assn 5:721 (1918)

19. 1923 - Pighini causes goiters in rats, dogs and chicken by giving them fluoridated water from a goiterous area. When sodium fluoride was administered, the same histological changes in the thyroid were seen as are produced in endemic goitre. Pighini G -"Il gozzo endemico e la sua etiologia in funzioie disfunzionitiroidee" Pubblicato per cura dell'Institute Sieroterapico, Milano p.41 (1923), also cited in Roholm K - "Fluoride Intoxication, London, C.K. Clarke and Co, (1937) (F- inhibits thyroid function/cause of goiter.)

20. 1926 - Goldemberg is the first to take medical advantage of the now much-observed iodine-fluoride antagonism. He deliberates that, because fluoride was the reason behind iodine deficiency/goitre areas, it would therefore also reduce the high iodine levels in Basedow patients and begins to use fluorides to effectively cure Basedow's disease - hyperthyroidism caused by excessive iodine consumption.

21. Goldemberg publishes extensively between 1921 and 1935 on his findings of applying fluorides as anti-thyroid medication. Goldemberg L -"Action physiologique des fluorures" Compt Rend Soc Physiol (Paris) 95:1169 (1926); Goldemberg L - La Semana Med 28:628 (1921) - also cited in Wilson RH, DeEds F - "The Synergistic Action Of Thyroid On Fluoride Toxicity" Endocrinology 26:851 (1940) Goldemberg L - Compt Rend Soc Biol (Paris) 104:1031 (1930) Goldemberg L - Revista de Especialidad, T.V. No.6 (1930)

³ Additional German studies not translated during this time include:

Gautier - Bull Soc Chim 13:909 (1913), cited in: Kraft K -"Beiträge zur Biochemie des Fluors I.Über den Antagonismus zwischen Fluor und Thyroxin." Hoppe-Seglers Z.Physiol. Chem 245:58 -65 (1937), and Gautier - Bull Soc Chim 14:241 (1914); cited in: Kraft K -"Beiträge zur Biochemie des Fluors I.Über den Antagonismus zwischen Fluor und Thyroxin." Hoppe-Seglers Z.Physiol. Chem 245:58 -65 (1937)

Goldemberg L - J Physiol et Path 25:1 (1927)
 Goldemberg, Pighini, Parhou & Goldstein - La glande thyr, in: Lehrbuch der endokrin. Erkrankungen, Vol. 1, Genf, Ed. Christiani (1923)
 Goldemberg L - Prens Med Argent (Oct. 1930, Dec. 1930)
 Goldemberg L - "Traitement de la maladie de Basedow et de 'hyperthyroidisme par le fluor" Presse Méd 102:1751 (1930)
 Goldemberg L - J Physiol et Path 25:1 (1927); 26 (1928)
 Goldemberg L - "Comment agiraient-ils therapeutiquement les fluoers dans le goitre exophthalmique et dans l'hyperthyroidisme" Semana Med 39:1659 (1932)
 Goldemberg & Schraiber - Revista de la Soc Argentin de Biol: Vol. XI(1)(1935); Vol XI (2) (1935); Vol. XI (7) (1935)

22. 1927 - Gorlitzer von Mundy (Austria) reports that daily intake of 3 mgs of fluoride in rabbits and rats leads to goiter and cretinism-like conditions. Gorlitzer von Mundy V - J. Physiol.et Path gen 25:1 (1927) (3 mg NaF- fluoride intake in rabbits and rats results in goiter and cretinism-like conditions)

23. 1930 - Christiani publishes on the changes in thyroid function from fluoride injections.
 [Earlier, in 1925, Christiani and Gautier became the first to use the term 'fluorosis'. They called it "La Fluorose" and "Cachexie fluorique", using these terms to describe "fluoride intoxication" (not yet described as "dental fluorosis"...), as induced by fluoride emissions from a Swiss aluminum smelter. LINK] Cristiani H - "Alteration de la glande thyroide dans l'intoxication fluoree" Compt Rend Soc Biol 103:554-556 (1930)

24. 1932 - Gorlitzer von Mundy (Austria) publishes findings on 1500 experiments using fluoride to inhibit thyroid function in mice and metamorphosis in tadpoles.

- NOTE: As it had been shown that metamorphosis in tadpoles was regulated by thyroid hormones, one had to show inhibition of metamorphosis to satisfy claims that a medication was an "anti-thyroid". This test was known as the "Gudernatsche Tadpole Test".

Gorlitzer von Mundy V - Arch f. exper.Path 165 (1932)
 Gorlitzer von Mundy V - "Die Beinflussung des Stoffwechsels durch die Halogenwasserstoffsäuren im Tierexperiment, mit besonderer Berücksichtigung der Fluorwasserstoffsäure" Arch Exp Pathol 165:443- 461 (1932)
 (describes his 1500 investigations on fluoride use in inhibition of metamorphosis in tadpoles, mice experiments, etc., many pictures)
 Gorlitzer von Mundy V - "Ein neuer Weg zur Behandlung der Thyreotoxikose mit Fluorwasserstoffsäure" Med Klin 21:&17-719 (1932)
 (reports on the first successful use of baths containing HF in the treatment of hyperthyroidism)
 Gorlitzer von Mundy V - Wien Klin Wschr 48 (1933)
 Gorlitzer von Mundy V - Med. Klin.47:911 (1952), cited in Gorlitzer von Mundy, V - "Einfluss von Fluor und Jod auf den Stoffwechsel, insbesondere auf die Schilddrüse" Münch Med Wochenschr 105:182-186 (1963)
 Gorlitzer von Mundy, V - "Einfluss von Fluor und Jod auf den Stoffwechsel, insbesondere auf die Schilddrüse" Münch Med Wochenschr 105:182-186 (1963); also

in Gordonoff, T. - Fluor und die Schilddrüse, Toxikology des Fluors Basel/Stuttgart, pp.111-123 (1964)

25. 1932 - Machoro (Italy) uses sodium fluoride in the successful treatment of hyperthyroidism. Machioro - Riforma Med p.1436 (1932); Ref. Zbl.68, p.515 (1932); also cited in Purjesz et al, 1934

26. 1932 - Wilhelm May (Germany) also starts fluoride therapy in the treatment of hyperthyroidism, using calcium fluoride tablets, topical ointments, etc. May W - "Antagonismus zwischen Jod und Fluor im Organismus" Klin Wochenschr 14:790-792 (1935)

27. Orłowski W- "Sur la valeur therapeutique du sang animal du bore et du fluor dans la maladie de Basedow" La Presse Medicale 42:836-837 (1932)

28. Phillips PH - "The manifestations of scurvy-like symptoms induced by ingestion of sodium fluoride" J Biol Chem 100:29 (1933)

29. 1934 - Purjesz and colleagues (Poland) give chicken eggs high in fluoride to hyperthyroid patients and achieve lowering of body temperature, of pulse and BMR, as well as weight gain; report that most of the fluoride is found in liver; no fluoride is found in the blood of healthy people. Purjesz B, Berkessy L, Gönczi K, Kovacs-Oskolas M - "Über die biologische Speicherung der halogenen Elemente in Hühnereiern und im tierischen Organismus" Arch Exp Pathol Pharmacol 176:578-582 (1934)

30. 1934 - Chang, Phillips, et al. report that in the thyroid of cows fed fluoride for a long time, the fluoride content increased to 240 times as much. [Note: in the original text it states 24 times, however, Dr. Phillips later corrected the text figures in a communication with Wilson & DeEds -> see: 1940] Chang CY, Phillips PH, Hart EB, Bostedt G - J Dairy Sci 17:695 (1934)

31. Phillips PH, Lamb AR - "Histology of certain organs and teeth in chronic toxicosis due to fluorine" Arch Path 17:169 (1934)

32. 1935 - Phillips et al. (USA) report that fluoride and thyroid have synergistic effects on fluorosis in chicken.

33. 1935 - Phillips et al. conduct studies in rats and find the same results: fluoride and thyroid have synergistic toxic effects. Phillips PH, English HE, Hart EB - "The influence of sodium fluoride upon the basal metabolism of the rat under several experimental conditions" Am J Physiol 113:441-449 (1935)
[First evidence that fluoride mimicks TSH. Also, when 5.2mg of NaF (2.34 F-) was added to diet of rats fed desiccated thyroid, effects were dramatically potentiated leading to rapid weight loss and death: F- and thyroid have synergistic effects...]

34. Phillips PH, English H, Hart NB - "The augmentation of fluorosis in the chick by feeding desiccated thyroid" J Nutrition 10:399 (1935), cited in: Harris NO, Hayes RL - "A tracer study of the effects of acute and chronic exposure to sodium fluoride on the thyroid iodine metabolism of rats" J Dent Res 34:470-477 (1955)

(F- and thyroid have synergistic effects)

35. Phillips PH - "Further studies on the effects of NaF administration upon the basal metabolic rate of experimental animals" *Am J Physiol* 117:155-159(1936)
(F- and thyroid have synergistic effects)

36. 1936 - Phillips conducts further animal experiments and verifies the 1935 findings. Phillips PH, Edens RJ - "Fluorgehalt d. Schilddrüse in Fällen von Hyperthyreose" *Madison Diskussion, Biblioth.d Forsch. Knoll* (in May, 1950)

37. 1937 - Litzka (Germany) discusses the mode of action of fluorides in treating patients with hyperthyroidism: fluoride antagonizes thyroid hormone effects/glycolysis in liver and influences glycolysis in skeletal muscle. Litzka G - "Die experimentellen Grundlagen der Behandlung des Morbus Basedow und der Hyperthyreose mittels Fluortyrosin" *Med Wochenschr* 63:1037-1040 (1937)
(discusses the basis of the use of fluorides in anti-thyroid medication, documents activity on liver, skeletal muscle, inhibition of glycolysis, etc.) Litzka G - "Erfolgskontrolle bei Behandlung der Schilddrüsenüberfunktion" *Z. klin. Med.*131:791-799 (1937); Litzka G - "Die antithyreotoxische Wirkung des Fluortyrosins" *Arch. exp. Pathol. u. Pharmakol.* 183:436-458 (1936); Litzka G - "Fluortyrosine" *Klin Wochenschr.* 15:1568-1569 (1936)

1937 - Wilhelm May reports further on his fluoride therapy, including the use of sodium fluoride ointments (up to one year-therapy), and Fluorotyrosin (6 to 8 - week therapy). Also reports on findings that two other common medications given in the treatment of hyperthyroidism - Solvitren and Tyronorman - had been found to contain fluoride, in fact double the amount used in Fluorotyrosin. Further May reports that the traditional areas where people had been sent for "natural therapy" ('Kur') were found to contain higher amounts of fluoride in the water. May W - "Eine neue interne Behandlung der Hyperthyreosen einschließlic des Morbus Basedow" *Diskussionsvortrag, Verhandlungen der Deutschen Gesellschaft für innere Medizin, 49.Kongress, Wiesbaden, March 15-18, 1937, München*(1937); May W, Schwartz E - *Fortschr Med* 28:9 (1932); also cited in: Kraft K - "Beiträge zur Biochemie des Fluors I. Über den Antagonismus zwischen Fluor und Thyroxin" *Hoppe-Seglers Z.Physiol. Chem* 245:58 - 65 (1937)

38. 1937 - Kraft (Knoll AG, Germany) investigates inorganic sodium fluoride and organic fluoride compounds fluorobenzoic acid and fluorotyrosine and reports that all fluoride compounds inhibit thyroid hormones. It is a matter of amplification - the fluoride component is essential. Kraft K - "Beiträge zur Biochemie des Fluors I.Über den Antagonismus zwischen Fluor und Thyroxin." *Hoppe-Seglers Z.Physiol. Chem* 245:58 -65 (1937)⁴

⁴ Additional German studies: May W - "Behandlung the Hyperthyreosen einschliesslich des schweren genuinen Morbus Basedow mit Fluor" *Klin Wochenschr* 16:562-564 (1937)
May W - "Eine neue interne Behandlung der Hyperthyreosen einschliesslich des Morbus Basedow" *Verhandlungen der Deutschen Gesellschaft fuer Innere Medizin, 49. Kongress, Wiesbaden March 15 - 18, 1937, publ. Munich* (1937)
1939 - May H, Litzka G - "Über die Hemmung des Tumorwachstums durch Fluortyrosine" *Z. Krebsforschung* 48:376 - 382 (1939)
May R - "Untersuchungen über den Fluorgehalt des Trinkwasseres in bayerischen Kropfgebieten verschiedener Endemiestärke" *Z. Ges. Exp. Med* 107:450 (1940)

39. 1939 - Steyn (South Africa) first reports on his findings of fluoride-induced goiter. Steyn DG - "Water poisoning in man and animal, together with a discussion on urinary calculi" Onderstepoort J Vet Sci Animal Ind 12:167-230 (1939)
40. 1940 - Wilson and DeEds (USA) report dental fluorosis in rats as a result of the synergistic action of fluoride and thyroid hormones. Results are described as "strikingly clearcut". Wilson RH, DeEds F - "The Synergistic Action Of Thyroid On Fluoride Toxicity" Endocrinology 26:851 (1940).
41. 1941 - Wilson (UK) reports in the Lancet on his findings that mottling of teeth is prevalent in the same areas in the UK which had previously been prevalent with goitre. Wilson DC - "Fluorine in aetiology of endemic goitre" Lancet I:211-213 (1941)
42. 1941 - Schwarz (Germany) prepares fluoride/iodide anti-thyroid medications and combines with sedatives. Schwarz - Med. Klin. 5 (1941); cited in May, 1950
43. 1942 - Euler & Eichler (Germany) report that the chronic administration of organic fluoride compounds (fluorotyrosine) cause the same defects in bone as inorganic fluorides, although no dissociation takes place, ascribing effects to the whole molecule.
44. 1942 - Euler & Eichler further report that the chronic administration of organic fluoride compounds cause the same defects in teeth as inorganic fluorides. Identical crystal formation is seen, although no soluble (free) fluoride is observed, leading the authors to the conclusion that such crystals declared by others to contain "calcium fluoride" [see: fluoroapatite] could not be such. The organic compounds did not dissolve. Euler H, Eichler - "Ueber die Wirkung von Fluor in organischer Binding auf das Zahnsystem der Ratte" Arch exper Path 199:179-187 (1942); also Dtsch Zahn Hk 9(1) (1942)
45. 1944 - The editorial in the Journal of the American Dental Association (JADA) acknowledges that "...drinking water containing as little as 1.2 to 3ppm of fluorine will cause such developmental disturbances...as goitre".
46. Hatfield JD, Shrewsbury CL, Andrews FN, Doyle LP - "Iodine-fluorine relationship in sheep nutrition" J Anim Sci 3:71-77 (1944)
47. 1946 - The Atomic Energy Commission (Department of Pharmacology & Toxicology - headed by Harold Carpenter Hodge, incomprehensibly at the same time also head of the International Association for Dental Research (IADR) - acknowledges the German findings that all fluoride compounds - organic or inorganic - inhibit thyroid hormone activity, and declares this issue a research priority. No further research into this issue is conducted, however.

48. 1947 - Casterra uses Knoll's "K17", later to be renamed "Capacin", in the successful treatment of 500 hyperthyroid patients. Casterra H - "Erfahrungen mit einem neuen organischen Fluorpräparat bei Hyperthyreosen" Das Deutsche Gesundheitswesen 2(22):704-705 (1947)
(describes use of Knoll's "K 17" - later named Capacin - in successful treatment of over 500 hyperthyroid patients. K 17 => 3-fluoro-4-hydroxyphenylacetic acid)
49. 1948 - Steyn (Africa) finds that fluoride has definite anti-thyroid effects. He investigates the incidence of endemic goiter in the North Western Cape Province in South Africa and reports that his findings "closely agree with the ... 1944 JADA editorial", and that goiters are actually 'fluoride-induced'. Steyn DG - "Fluoride and endemic goitre" S Afr Med J 22:525-526 (1948)
50. 1949 - Richard May reports on the highly successful use of the organic fluoride compounds Pardinon (IG Farben) and Capacin (Knoll AG) in the treatment of hyperthyroidism. Up until 1943, 10,000 patients had been cured. May Richard - "Erfahrungen in der Behandlung von Hyperthyreose- und Basedow-Kranken mit einer organischen Fluorverbindung (Fluoroxyphenylelessigsäure, 'Capacin')" Deutsche Med. Wochenschr.74(12):374-375 (1949)
51. 1949 - Euler et al. test various organic fluoride compounds and find again that all organic fluoride compounds inhibit thyroid hormone activity. Euler H, Eichler O, Hindemith H - "Über die Wirkung einiger organischer Fluoride bei chronischer Darreichung" Arch exp. Path u Pharmakol. Bd.206:75-82 (1949), also cited in: Steyn DG - The problem of dental caries and the fluoridation of public water supplies - Johannesburg (1958)
(All organic fluoride compounds inhibit thyroid function, all compounds act on glycogen/liver - activity only differentiated by amplitude)
52. 1950 - Wilhelm May publishes monograph on the fluoride-iodine antagonism, including over 300 references, detailing the known biochemical findings. [Originally slated for publication in 1944, the lack of paper in Germany prohibits publication until 6 years later.] May W - "Die Basedowsche Krankheit" Aulendorf (1950)
53. 1950 - Richard May reports that between 1935 and 1947 over 5000 hyperthyroid patients had been treated successfully with Pardinon and Capacin in the May clinic alone. May R - "Therapie mit organischen Fluorverbindungen" Med Wochenschr 4:489-490 (1950)
54. 1951 - Kraft K - "Über die Synthese einiger aromatischer Fluorverbindungen" Knoll Research, Chem Ber. 84(2):150-156 (1951)
(describes manufacturing processes of numerous organic fluorides, after it was shown that all organic fluoride compounds displayed stronger anti-thyroid activity than the fluoride ion)
55. May Wilhelm - "Fluor als Therapeuticum" Arzneimittel Forschung 1:33-37 (1951) (Review on fluoride as a therapeutic agent...discusses fluoride Goldemberg's 1926 use in treatment of whooping cough (-> Pertussin - G(i) proteins), Goldemberg's pioneering work in 1928 in the treatment of hyperthyroidism, etc..., as well as his son's - Richard May - decision in 1949 to recommend use of fluoride compounds as an anti-caries prophylaxis...discusses fluoroform as whooping cough

(pertussis) medication, difluorophenyl compounds as wound-disinfectants such as "Epidermin", another fluorophenyl compound called "Fluor-rheumin" against rheumatism, etc.)

56. 1952 - Kraft and Dengel (Germany) investigate yet more fluorophenyl-derived fluoride compounds, all of which lower BMR. Kraft K, Dengel F - "Über die Synthese einiger aromatischer Fluorverbindungen, II. Mitteilung" Chem Ber 85(6):577-582 (1952) (more reports on fluorophenyl/organic fluoride investigations..."in regards to their characteristics in lowering BMR...")

57. 1952 - Reynolds Metals Corp vs Paul Martin hypothyroidism caused by fluoride is documented. Reynolds Metals Corp vs. Paul Martin et al - Transcript of Record. US Court of Appeals, Ninth District, Nos.14990-14992 (1952) (Court case: Family of three residing near aluminum smelter in Troutdale, Oregon. Litigation of this case revealed muscular pains, general fatigue, arthritis in conjunction with liver and kidney damage, and hypothyroidism.)

58. Gordonoff T, Minder W - "Caries prophylaxis with fluorine as a physiological problem" Schweiz Med Wochenschr. 82:972-973 (1952)

59. 1953 - Wadhwani (India) reports that fluoride concentrated in thyroid gland of rats consuming 0.9mg F- per day. Wadhvani TK -"Metabolism of Fluoride. Absorption, retention, distribution and elimination of fluorine and its effect on the Vitamin C content of different tissues, and on the iodine content of thyroids of rats and monkeys" J Indian Inst Sci (35)354-362 (1953)
Fluoride concentrated in thyroid gland of rats consuming 0.9mg F- per day.

60. 1954 - Wespi (Italy) reports mottled teeth ('dental fluorosis') together with goitre in Italy. Wespi HJ - "Besteht ein Antagonismus zwischen Fluor und Jod?" Praxis 43:616-623 (1954)
(Wespi reports both dental fluorosis and goitre in the same patients in Campagnano di Roma and Casamicciola...)

61. 1954 - Jentzer (Switzerland) reports that less than normal amounts of thyroid hormone are deposited in the pituitary gland when rabbits are given fluoride in water - at levels corresponding to that of artificially fluoridated water. Jentzer A -"Action du fluor sur le relais thyroïdohypophysaire demontree par l'iode 131" Bull Schweiz Akad Med Wiss 10:211-220 (1954)
(Less than normal amounts of thyroid hormone are deposited in the pituitary gland when rabbits are given fluoride in water at levels corresponding to that of artificially fluoridated water)

62. 1955 - Benagiano & Fiorentini (Italy) describe the effects of fluoride on thyroid function. They find that the farther away from the toxic dose, the longer it takes for fluoride to cause thyroid changes. (This in accord with May (1950), who found that although it might take months - "sometimes even a year" - even low fluoride amounts would always be successful in lowering iodine levels...May urged the practitioner to be patient...) Benagiano A, Fiorentini S -"Ricerche sperimentali e cliniche sui rapporti tra fluore e tirodi" Annali di Stomatol 4:3-16(1955)

63. 1955 - Korrodi, Wegmann, Galetti and Held also verify a fluoride - iodine antagonism, presuming that the fluoride ion pushes out the iodine in the thyroid gland.

64. Steyn DG, Kieser J, Odendaal WA, Malherbe MA, Synan HW, Sunkel W, Naude CP, Klintworth H, Fisher E - "Endemic goitre in the Union of South Africa and some neighbouring territories" Pretoria:Union of South Africa, Department of Nutrition (March 1955)

65. 1957 - Galetti et al. treat hyperthyroid patients with fluoride at daily doses lower than those estimated being the current average intake in the US, and document a significant reduction in protein-bound iodine, as well as an overall reduction of iodine and a reduction of iodine uptake by the thyroid gland. Galletti PM, Joyet G - "Effect of fluoride on thyroidal iodine metabolism in hyperthyroidism" J Clin Endocrinol 18:1102-1110 (1958)

66. 1959 - Jentzer again shows reduced iodine levels in the pituitary gland under the influence of fluorides. Jentzer, A - "Effet du fluor et du fluor-iod sur la teneur en iode de la thyroide de lapin" Bull Schweiz Akad Med Wiss 15:412-422 (1959). (In rabbits fed 0.05mg F- per day [!] iodine content in thyroid was reduced by 25%. Also showed that the iodine uptake in the pituitary gland was greatly reduced under the influence of fluoride)

67. Steyn DG - "The problem of dental caries and the fluoridation of public water supplies" Johannesburg (1958)

68. 1960 - Gordinoff and Minder describe the results of experiments with radioactive iodine (I131) which show that fluorides remove an iodine atom during the conversion process (T4 to T3). Effects are dose-responsive, meaning the higher the fluoride intake the lower the iodine measurements. Gordonoff T, Minder W - "Fluoride and the thyroid gland" in "World Review of Nutrition and Dietetics" Pitman Medical Co, Vol 2:234-247 (1960)

69. 1959/1960 - Anbar et al (Israel) report in Nature and other journals that fluoroborates and other fluoride compounds inhibit thyroid hormone transport and concentrate in the thyroid gland. [BTW: The first fluoroborate 'safety document' appeared in 1932!] Anbar M, Guttman S, Lewitus Z - "Effect of monofluorosulphanate, difluorophosphate, and F borate ions on the iodine uptake of the thyroid gland" Nature 183:1517 (1959); Anbar M, Guttman S, Lewitus Z- "The accumulation of fluoroborate ions in thyroid glands of rats" Endocrinology 66:888 (1960) (-> fluoroborate concentrates in thyroid gland, inhibits iodide transport.

70. 1962 - Steyn (Africa) reports that drinking water containing "as little as 1 to 2 ppm of fluorine can cause serious disturbances of general health and especially in normal thyroid gland function and in the normal processes of calcium-phosphate metabolism (parathyroid function)."

71. 1962 - Spira reports on the fluorine-induced endocrine disturbances in mental illness. Spira L - "Fluorine-induced endocrine disturbances in mental illness" Folia Psychiat Neurol Jap 16:4-14 (1962) NLM CIT. ID: 62182027

72. 1963 - Gorlitzer von Mundy reports on the [then] current knowledge gained from experiments by Gordonoff with I131 as to how the effects of the enzyme responsible for the T4 to T3 conversion were inhibited if a fluorine ion was absorbed before the conversion from T4 to T3 occurs.

73. Gedalia I, Brand N - "The relationship of fluoride and iodine in drinking water in the occurrence of goiter" Arch Int Pharmacodyn 142:312-5 (1963)

74. 1964 - Ritzel reports on disturbances in T4 metabolism in areas with fluoridated drinking water. Ritzel G - "Thyroxinstoffwechsel und Trinkwasser-fluoridierung" Int Z Vitaminforsch 34:422-426 (1964)⁵

75. 1964 - Steyn (Africa) - again - reviews the "overwhelming evidence" on the fluoride-iodine antagonism. (Steyn, Maumene, Euler et al., Wadwhani, Wadwhani and Ramaswamy, Chang et al., Littich, Benagiano and Fiorentini, Fiorentini, Feltman, De Eds, Baume and Becks, Orban, Spira, Galetti et al., Gordonoff and Minder, Wilson, Wespi, Goldemberg, Todd, Coton, Gorlitzer, May, Hodenberg, Korrodi et al., Christiani, Jentzer, Grab and Overdisse) Steyn DG - "Chronic fluorine poisoning caused by the drinking of subterranean waters containing excessive quantities of fluorine" in: Gordonoff, T. - Fluor und die Schilddrüse, Toxikology des Fluors Basel/Stuttgart (1964) Steyn DG - "Once More - Fluoridation" Review
Chief Research Officer, Division of Life Sciences, Atomic Energy Board, Pretoria, Republic of South Africa, (Emeritus Professor of Pharmacology, University of Pretoria) University of Pretoria NUWE REEKS No.24 (1964)

76. 1964 - Steyn reports on his detailed 1949-1950 experiments on young rats, conducted to determine if there was in fact a fluoride-iodine antagonism. The experiment, which ran for 12 months, showed that the more severe the teeth were mottled, the more severe the thyroid dysfunction. It further showed that iodine supplementation was not likely to prevent the endemic goiter caused by excessive fluoride in drinking water, and that fluoride intake needed to be reduced.

77. Pastan I, Macchia V, Katzen R - "Effect of fluoride on metabolic activity of thyroid slices" Endocrinology 83(1):157-60 (1968)

78. 1969 - Rodesch et al. and Zor et al. independently report that fluoride mimicks TSH. Rodesch F, Neve, P, Willems C, Dumont JE - "Stimulation of thyroid metabolism by thyrotropin, cyclic 3',5'-AMP, dibutyryl cyclic 3',5'-AMP and prostaglandin E1" Eur J Biochem 8(1):26-32 (1969)

79. 1969 - Siddiqui show small visible goiters in persons 14 to 17 years of age in India to be connected directly to high fluoride concentrations in drinking water. Siddiqui AH - "Incidence of Simple Goiter in Areas of Endemic Fluorosis in Nalgonda District, Andhra Pradesh, India" Fluoride 2 (4):Pages 192 - 249 (1969)

⁵ Gordonoff T - "Zum Fluorproblem" Osterr Z Stomatol 54:561:571 (1957)

Gordonoff T (Ed) - "Fluor und die Schilddrüse", Toxikology des Fluors (Toxicology of fluorine) Symposium, Ber, Oct.15-17 1962, Schwabe Verlag, Basel/Stuttgart, pp.111-123 (1964)

80. Zor U, Kaneko T, Lowe IP, Bloom G, Field JB - "Effect of thyroid-stimulating hormone and prostaglandins on thyroid adenyl cyclase activation and cyclic adenosin 3'-5'-monophosphate." *J Biol Chem* 244(19):5189-95. (1969)
81. 1970 - Ahn and Rosenberg confirm that fluoride mimicks TSH. Ahn CS, Rosenberg IN - "Iodine metabolism in thyroid slices - effects of TSH, dibutyryl cyclic 3',5'-AMP, NaF and prostaglandin E1" *Endocrinology* 86(2):396-405 (1970)
82. 1970 - Burke documents that TSH and fluoride have additive effects. Burke G - "Comparison of thyrotropin and sodium fluoride effects on thyroid adenyl cyclase" *Endocrinology* 86(2):346-52 (1970)
83. 1971 - Narbutt et al. show that in rats fed sodium fluoride at 0.1 and 1 mg/day there is an increase in the thyroid weights after 4 weeks, irrespective of dosage. Narbutt recommends iodine administration during fluoride prophylaxis. Narbutt B, Romer TE, Grabski J, Szymik N - "Influence of natrium fluoride on the structure of the rat thyroid" *Endocrinol Pol* 22 (5):445-451 (1971)
84. 1972 - Willems et al. document that sodium fluoride blocks thyroid hormone secretion. Willems C, Van Sande J, Dumont JE - "Inhibition Of Thyroid Secretion By Sodium Fluoride (In Vitro)" *Biochimica Et Biophysica Acta* 264:197-204 (1972)
85. 1972 - Day and Powell-Jackson study 648 people in 13 mountainous regions in Nepal where the iodine content in the water is low and find a close relationship between fluoride intake and the incidence of goiter. Day TK, Powell-Jackson PR - "Fluoride, Water Hardness, and Endemic Goitre" *Lancet* 1:1135-1138 (1972)
86. 1976 - Polish researchers Bobek and Kahl document that rats consuming fluoride in water at 0.1 to 1 mg/day have significantly lowered T4, T3, and free thyroxine index in plasma. They ascribe this to an inhibition of thyroid hormone transport by fluoride. Bobek S, Kahl S, Ewy Z - "Effect Of Long Term Fluoride Administration on Thyroid Hormone Levels In Rats" *Endocrinol Exp (Bratisl)* 10:289-295 (1976)
87. 1976 - Aliev finds that goiter, caries and fluorosis are correlated in Azerbaijan. Aliev Yu M - "Some biogeochemical characteristics of the environment in Azerbaijan, USSR" *Gig Sanit* (8):103-104 (1976)
88. 1976 - Orgiazzi et al. use fluoride as TSH analogue in assessing "cold nodules". Orgiazzi J, Chopra IJ, Solomon DH, Williams DE - "Comparison of the effect of TSH and fluoride on the adenylate cyclase activity of cold thyroid nodules" *Ann Endocrinol (Paris)* 37(2):107-8 (1976)
89. Tokar' VI, Savchenko ON - "Effect of inorganic fluorine compounds on the functional state of the pituitary-testis system" *Probl Endokrinol (Mosk)* 23(4):104-7 (1977)

90. 1978 - In German thyroid medications like "Druesensalbe Fides", "Strumadragees Fides" and "Strumetten" still list calcium fluoride and hydrogen fluoride as active ingredients, and are listed in the 1978 index of the German Federal Association of the Pharmaceutical Industry. ("Schilddruesentherapeutika" in "Rote Liste", Bundesverband der Pharmazeutischen Industrie, e.V., Frankfurt, Germany)

91. 1978 - Maccia et al. use fluoride as TSH analogue (hyperplastic thyroid, hyperfunctioning follicular carcinoma, "cold" nodules). Macchia V, Mandato E, Carella C, Pisano G, Biscaglia G - "The adenylate cyclase-cyclic cAMP-phosphodiesterase system in pathological human thyroid" J Endocrinol Invest 1(4):337-45 (1978)

92. 1978 - Kalderon & Sheth use fluoride as TSH analogue ("cold" nodules). Kalderon AE, Sheth V - "Secretion and adenylate cyclase in thyroid nodules" Arch Pathol Lab Med 102(7):381-86 (1978)

93. 1978 - George Waldbott writes that in most cases of poisoning from fluoridated water in which he had occasion to study the action of the thyroid gland, its function was low. He cites a case of a 33-year-old male who exhibited typical manifestations of pre-skeletal fluorosis and a basal metabolism rate of -22, indicative of hypothyroidism. Within three months after the man ceased consuming fluoridated water, the thyroid function had returned to normal (BMR=0). In addition, Waldbott writes that "simultaneously, other symptoms associated with low grade fluoride poisoning - including excessive thirst, headaches, blurred vision, arthritis in shoulders, elbows, knees, and gastrointestinal disturbances - also disappeared." [He did not know that the symptoms he ascribed to "low-grade fluoride poisoning" would likewise be considered symptoms of hypothyroidism some 20 years later.] Waldbott, GL; Burgstahler, AW; McKinney, HL - "Fluoridation: The Great Dilemma" Coronado Press (1978)

94. 1979 - Toccafondi et al. use fluoride as TSH analogue in assessing hyperfunctioning nodules (thyroid toxic adenoma). Toccafondi RS, Rotella CM, Tanini A, Fani P, Arcangeli P - "Thyrotrophin-responsive adenylate cyclase activity in thyroid toxic adenoma" Acta Endocrinol (Copenh) 92(4):658-68 (1979)

95. 1979 - Walinder et al. use fluoride as TSH analogue to activate human thyroid tumors (nodules). Walinder O, Karlsson FA, Dahlberg PA - "Adenyl cyclase activity in human thyroid plasma membranes from normal human thyroid tissue and thyroid adenomas" Acta Endocrinol (Copenh) 92(1):95-104 (1979)

96. 1979 - Hillman et al. find that cattle afflicted with fluorosis develop hypothyroidism. (Fluorosis here caused by mineral supplements.) Hillman D, Bolenbaugh DL, Convey EM - "Hypothyroidism and anemia related to fluoride in dairy cattle" J Dairy Sci 62(3):416-23 (1979)

97. 1982 - Mizukami et al. use fluoride as TSH analogue (adenomatous goiter). Mizukami Y, Matsubara F, Matsukawa S - "Localization of adenylate cyclase and 5'-nucleotidase activities in human thyroid follicular cells" Histochemistry 74(1):9-19(1982)

98. 1983 - Sidora et al. find iodine deficiency and "adaptive amplification of the hypophyseal-thyroid system, not ensuring an absolute compensation in the citizens using drinking water with an 'enhanced' fluorine content as compared to a

'decreased' one, accompanied by an augmented incidence of functional disturbance". Sidora VD, Shliakhta AI, Iugov VK, Kas'ianenko AS, Piatenko VG - "Indices of the pituitary-thyroid system in residents of cities with various fluorine concentrations in drinking water" *Probl Endokrinol (Mosk)* 29(4):32-5 (1983)

99. Jonderko G, Kita K, Pietrzak J, Primus-Slowinska B, Ruranska B, Zylka-Wloszczyk M, Straszeczka J - "Effect of subchronic sodium fluoride poisoning on the thyroid gland of rabbits with normal and increased supply of iodine" *Endokrynol Pol* 34(3):195-203 (1983)

100. 1983 - Desai et al.(India) report increased incidence of goiter in endemic fluorosis areas. Desai VK, Saxena DK, Bharsar BS, Kantharia SL - "Health survey of residents of villages surrounding fluoride mines in relation to their drinking water fluoride level" Abstracts, 13th Conference ISFR, New Delhi (1983)

101. 1985 - Bachinskii et al.(See Appendix G) document how fluorides at 2.3 ppm in water cause tension of function of the pituitary-thyroid system that is expressed in TSH-elevated production, a decrease in the T3 concentration [both sure-tell diagnostic signs of hypothyroidism] and more intense absorption of radioactive iodine by the thyroid [as in iodine deficiency]. The results lead to a conclusion that excess of fluorine in drinking water was a risk factor of more rapid development of thyroid pathology. Bachinskii PP, et al. (1985) Action of the body fluorine of healthy persons and thyroidopathy patients on the function of hypophyseal-thyroid the system. *Probl Endokrinol (Mosk)* 31(6):25-9. (The English translation is attached. Let me know if you want the Russian published version.) Also note the serum fluoride level for the control was 0.21 mg/L to 0.22 mg/L which is higher than considered "normal" 0.15 mg/L and higher than Xiang found with an 8 mg/L 8 IQ point drop. Also note that these remote areas do not have fluoridated toothpaste, post-harvest fumigants, and as many other sources of fluoride. A 2.3 ppm fluoride in water is similar total exposure or "dosage" as those in the USA on 1 ppm fluoride and fluoridated toothpaste. Bachinskii PP, Gutsalenko OA, Naryzhniuk ND, Sidora VD, Shliakhta AI - "Action of the body fluorine of healthy persons and thyroidopathy patients on the function of hypophyseal-thyroid the system" *Probl Endokrinol (Mosk)* 31(6):25-9 (1985) (-> reduced T3, increased TSH and I131 uptake)

102. Yu YN. (1985). [Effects of chronic fluorosis on the thyroid gland]. *Zhonghua Yi Xue Za Zhi*. 65(12):747-9.

103. 1985 - Clark and Gerend use fluoride as TSH analogue in human thyroid cancers. Clark OH, Gerend PL - "Thyrotropin regulation of adenylate cyclase activity in human thyroid neoplasms" *Surgery* 97(5):539-46 (1985)

104. Monti M, Hedner P, Ikomi-Kumm J, Valdemarsson S - "Erythrocyte metabolism in hyperthyroidism: a microcalorimetric study on changes in the Embden-Meyerhof and the hexose monophosphate pathways" *Acta Endocrinol (Copenh)* 115(1):87-90(1987)

105. Shashi A. (1988). Biochemical effects of fluoride on thyroid gland during experimental fluorosis. *Fluoride* 21: 127-130. (See abstract)

106. 1988 - Zhao publishes first results of investigations into mutual interactive effects of fluoride and iodine in goitre and dental fluorosis. Zhao WY - "A preliminary study of the interaction of iodide and fluoride in experimental iodide-goiter and fluorosis" *Chung Hua Yu Fang I Hsueh Tsa Chih* 22(3):146-8 (1988)
107. 1988 - Guan et al. report on synergistic effects of iodine deficiency and fluoride excess in rat thyroid. Guan ZZ, Zhuang ZJ, Yang PS, Pan S - "Synergistic action of iodine-deficiency and fluorine-intoxication on rat thyroid" *Chin Med J (Engl)* 101(9):679-84 (1988)
108. 1989 - Tokar' and others in a study on workers exposed to fluorides write that "changes in the pituitary-thyroid axis are caused by disorders of the regulatory chain and fluorine impact on thyroid hormones' metabolism at the level of target cells". (-> G-proteins) Tokar VI, et al. (1989). [Chronic effects of fluorides on the pituitary-thyroid system in industrial workers]. *Gig Tr Prof Zabol* (9):19-22. (See abstract) Tokar' VI, Voroshnin VV, Sherbakov SV - "Chronic effects of fluorides on the pituitary-thyroid system in industrial workers" *Gig Tr Prof Zabol* (9):19-22 (1989)
109. 1989 - Ren et al. report more findings on the devastating effects on IQ of fluoride in low iodine areas. Ren DL, Liu Y, An Q - "An investigation of intelligence development of children aged 8-14 years in high-fluoride and low-iodine areas." *Chinese J of Control of Endemic Diseases* 4:251-254 (1989)
110. 1991 - Lin Fa-Fu et al. report that a low iodine intake coupled with "high" (0.88ppm) fluoride intake exacerbates the central nervous lesions and the somatic developmental disturbance of iodine deficiency. The authors considered the possibility that "excess" fluoride ion affected normal de-iodination. Fluorides caused increase of reverse T3 (rT3) and elevated TSH levels, as well as increased I131 uptake (see: Bachinskii et al, 1985). Lin Fa-Fu, Aihaiti, Zhao Hong-Xin, Lin Jin, Jiang Ji-Yong, Maimaiti, and Aiken - "The Relationship of a Low-Iodine and High-Fluoride Environment to Subclinical Cretinism in Xinjiang" *ICCIDD Newsletter, Volume 7 Number 3 August* (1991)
http://64.177.90.157/science/html/lin_fa-fu.html
111. 1991 - Delemer et al. show that fluoroaluminate (AlF₄⁻) and TSH have additive effects. Delemer B, Dib K, Saunier B, Haye B, Jacquemin C, Correze C - "Alteration of the functional activity of Gs protein in thyrotropin-desensitized pig thyroid cells" *Mol Cell Endocrinol* 75(2):123-31 (1991)
112. 1993 - Brtko et al. find that fluoride inhibits binding of ¹²⁵I-T₃ to its receptor in rat liver nuclei. Brtko J, Knopp J, Baker ME - "Inhibition of 3,5,3'-triiodothyronine binding to its receptor in rat liver by protease inhibitors and substrates" *Mol Cell Endocrinol* 93(1):81-6 (1993)
113. 1993 - Desai et al. investigate 22,276 people in India and find dental fluorosis and goitre significantly and positively correlated. Desai VK, Solanki DM, Bansal RK "Epidemiological study of goitre in endemic fluorosis district of Gujarat" *Fluoride* 26(3):187-190 (1993)
114. 1993 - Trivedi reported serum fluoride levels significantly higher in endemic fluorosis patients with impaired glucose tolerance (0.08 mg/l) and endemic

fluorosis patients without glucose tolerance (0.02 mg/l) and controls at 0.01 mg/l. Trivedi N, et al Reversible impairment of glucose tolerance in patients with endemic fluorosis, *Diabetologia*, 36:826-828. See Appendix E. Note: Xiang 2010 found an 8 IQ point decrease at 0.08 mg/l compared to 0.04 mg/l fluoride serum level.

115. 1994 - Tezelmann et al. report that fluoride, by increasing the intracellular cAMP concentration, causes desensitization of the thyroid stimulating hormone receptor (TSHr). No specific thyroid factor(s) other than increased levels of cAMP are required for TSHr desensitization. Tezelman S, Shaver JK, Grossman RF, Liang W, Siperstein AE, Duh QY, Clark OH - "Desensitization of adenylate cyclase in Chinese hamster ovary cells transfected with human thyroid-stimulating hormone receptor" *Endocrinology* 134(3):1561-9 (1994)
(Fluorides cause insensitization (decreased response) of the TSH receptor).

116. 1994 - Yang et al. investigate intelligence in children and report that high iodine and high fluoride exert "severe damage to the human body". Yang Y, Wang X, Guo X - "Effects of high iodine and high fluorine on children's intelligence and the metabolism of iodine and fluorine" *Chung Hua Liu Hsing Ping Hsueh Tsa Chih* 15(5):296-8 (1994)

117. 1995 - Balabolkin et al. study the thyroid and immune statuses in workers continuously exposed to fluorine. "...T3 is seen reduced in 51% of the workers. The examinees with 'euthyroid condition' had immune disorders with an allergic tendency (increased number of B-lymphocytes, immunoglobulins A). In workers with subclinical hypothyroidism, the immune alterations were more evident, T-lymphocytes count rose, but their functional activity declined, indicating impaired cooperation of immunocytes as a result of imperfect control under low concentrations of T3." (aberrant G protein activation). Bylgly A, et al. (2004). The effects of fluoride on thyroid hormones in rabbits. *Indian Veterinary Journal* 81:986-988. Balabolkin MI, Mikhailets ND, Lobovskaia RN, Chernousova NV - "The interrelationship of the thyroid and immune statuses of workers with long-term fluorine exposure" *Ter Arkh* 67(1):41-2(1995)

118. 1996 - Mikhailets et al. again report on the low T3 levels in same workers exposed to fluorides. Suggests that the "low T3" syndrome could be used as a diagnostic tool in assessment of "fluorosis". Mikhailets ND, Balabolkin MI, Rakitin VA, Danilov IP - "Thyroid function during prolonged exposure to fluorides." *Problemy Endokrinologii* 42 (1):6-9 (1996)

- "Thyroid function was examined in 165 workers of electrolysis shops of aluminum production with more or less expressed signs of chronic fluoride intoxication (fluorosis) by radioimmunoassay of hormones and the test of ¹³¹I absorption by the thyroid. The detected thyroid abnormalities were characterized by a moderate reduction of iodine-absorbing function of the thyroid, low T3 with normal T4 level, and a slight increase of TTH concentration. These changes augmented with longer service and fluorosis progress. Hence, the syndrome of low T3 and reduced absorption of ¹³¹I may be considered as diagnostic signs of fluorosis. In case of toxic involvement of the liver in fluorosis patients, low T3 syndrome is observed much more frequently: in 75.6% cases. Liver abnormalities evidently lead to disorders in the peripheral conversion of T4 in T3, occurring primarily in liver parenchyma. Indirect effect of fluorine on the enzymatic system of deiodination cannot be ruled out as well."

119. 1996 - Mahmood investigates the effects of low doses of sodium fluoride on the thyroid glands of guinea pigs. Findings are:

1. Depletion of colloid from the follicles.
2. Shrinkage of follicles.
3. Disruption of follicular basement membrane associated with oedema and degeneration of the follicular epithelial cells.
4. Increased follicular vascularity.
5. Fatty degeneration in the inter-follicular connective tissue. Mahmood Bhat GH - "Effect of fluoride ions on the thyroid glands of guinea pigs" *JK Practitioner International* 3(2): 94-6 (1996)

120. Paloyan Walker R, Kazuko E, Gopalsami C, Bassali J, Lawrence AM, Paloyan E - "Hyperparathyroidism associated with a chronic hypothyroid state" *Laryngoscope* 110(7):903-9 (1997)

121. 1998 - Zhao et al. conduct an extensive study on mice receiving several fluoride-iodine combinations in addition to basal diet. The authors find that iodine and fluorine have "mutually interacting" effects on both goiter and fluorosis in the experimental mice. Zhao W, et al. (1998). Long-term Effects of Various Iodine and Fluorine Doses on the Thyroid and Fluorosis in Mice. *Endocrine Regulations* 32(2):63-70. ([See abstract](#) | [See study](#))

122. "Long-term Effects of Various Iodine and Fluorine Doses on the Thyroid and Fluorosis in Mice" Zhao W, Zhu H, Yu Z, Aoki K, Misumi J, Zhang X - *Endocr Regul* 32(2):63-70 (1998)

123. 1998 - Swarup et al., investigating fluoride-intoxicated cattle near an aluminum smelter in India, find decreased levels of triiodothyronine (T3) in the affected animals when compared to normal animals. Swarup D, Dwivedi SK, Dey S, Ray SK - "Fluoride intoxication in bovines due to industrial pollution" *Indian Journal of Animal Sciences* 68 (7):605-608 (1998), also in *Fluoride* 31(4):225(1998)

124. 1999 - Data by Jooste et al shows that goitre occurrence in iodine-sufficient areas in Africa is due to fluoride. In 5 out of 6 villages goitre prevalence directly corresponds to fluoride in water, observable at concentrations even lower than deemed "optimal" for "caries prevention". Jooste PL, Weight MJ, Kriek JA, Louw AJ - "Endemic goitre in the absence of iodine deficiency in schoolchildren of the Northern Cape Province of South Africa" *Eur J Clin Nutr* 53(1):8-12 (1999)

125. 2001 - Negoita et al. report the increase of acquired hypothyroidism in the St. Regis Akwesasne Mohawks, a population long known to be poisoned by fluoride emissions from a Reynolds aluminum smelter. Negoita S, Swamp L, Kelley B, Carpenter DO - "Chronic diseases surveillance of St. Regis Mohawk Health Service patients" *J Public Health Manag Pract* 7(1):84-91 (2001)

126. 2001 - Trabelsi M, et al. Effect of fluoride on thyroid function and cerebellar development in mice. *Fluoride* 34: 165-173. ([See study](#)) Travbesli M, Guermazi F, Zeghal N - "Effect of fluoride on thyroid function and cerebellar development in mice" *Fluoride* 34(3):165-173 (2001)

127. 2001 - 2002 - Gupta et al. (India) and Suketa (Japan) show that in cases of fluorosis there is hyperparathyroidism, as seen in elevated parathyroid hormone (PTH) levels. Gupta SK, Khan TI, Gupta RC, Gupta AB, Gupta KC, Jain P, Gupta A - "Compensatory hyperparathyroidism following high fluoride ingestion - a clinico - biochemical correlation" *Indian Pediatr* 38(2):139-46 (2001)
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11224578&dopt=Abstract

128. Liu G, et al. (2002). Effect of sodium fluoride upon activity of peroxidase in the thyroid gland of chickens. *Chinese Journal of Veterinary Science and Technology* 32:32-33.

129. 2002 - As a result of research into molecular biology there are hundreds upon hundreds of studies available documenting the actions of fluorides upon G proteins, the "On" and "Off" switches involved in cellular signal transmission.

130. Suketa Y - "Fundamental and applied studies on transport and metabolism of electrolytes and glucose--aim to contact with molecular biology" *Yakugaku Zasshi* 122(8):507-25 (2002)
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12187767

131. During the 1980s and 1990s fluorides become known as the universal G-protein activator. Although there have been numerous studies before showing that fluorides act like TSH, the thyroid-stimulating-hormone - as seen above -, it can now be documented in deep detail, for it is known that G proteins in thyroid physiology are normally absolutely dependent on TSH and are inactive without it. TSH is the master, sometimes also referred to as the "first violinist in the orchestra".

132. The TSH receptor is the only receptor known able to activate all G protein families, an activity directly imitated by fluoride.

133. Liu G, et al. (2003). Effects of adding selenium to diets on the function of thyroid of fluorositic chicks. *Journal of Shanghai Jiaotong University - Agricultural Science* 21: 177-180.

134. 2004 - Shen et al. show both an antagonistic as well as synergistic relationship of iodine and fluoride on phospholipid and fatty acid composition in brain cells of rats, depending on the amount of iodine. Shen X, Zhang Z, Xu X - "Influence of combined iodine and fluoride on phospholipid and fatty acid composition in brain cells of rats" *Wei Sheng Yan Jiu* 33(2):158-61 (2004)
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15208994
(re:antagonistic relationship of iodine and fluoride on phospholipid and fatty acid composition in brain cells of rats)

135. 2004 - Wang et al. investigate the effects of fluoride and low iodine on biochemical indexes in the brain and learning/memory in offspring rats.

"In comparison with control rats, the learning and memory ability of the offspring rats was depressed by high fluoride, low iodine, or the combination of high fluoride and low iodine. Brain protein was decreased by low iodine and even more by the combined interaction of high fluoride and low iodine. The activity of cholinesterase (ChE) in the brain was affected to some extent by high fluoride and low iodine but was especially affected by high fluoride and low iodine together." Wang J, Yaming G, Ning H, Wang S - "Effects of high fluoride and low iodine on biochemical indexes of the brain and learning-memory of offspring rats" *Fluoride* 37(3):201-8 (2004)

136. 2004 - Bouaziz et al. investigate the effects of fluoride on thyroid hormones and bone in suckling mice and find a reduction of plasma free T4 and T3 levels in the offspring, as well as accelerated bone resorption activity. (Bone formation is regulated by the endocrine system.) Bouaziz H, Ammar E, Ghorbel H, Ketata S, Jamoussi K, Ayadi F, Guermazi F, Zeghal N - "Effect of fluoride ingested by lactating mice on thyroid function and bone maturation of their suckling pups" *Fluoride* 37(2):133-142 (2004)

137. Bylgyly A, et al. (2004). The effects of fluoride on thyroid hormones in rabbits. *Indian Veterinary Journal* 81:986-988.

138. 2005 - Dr. Susheela and co-workers present not only the first reports on TSH and free TH levels in children and adolescents with DF but, in addition, show that even in children without DF - but elevated fluoride serum levels - abnormal TH metabolism is present, as previously observed in workers exposed to fluoride, as well as children and adults with various amounts of fluoride in the water supply. Susheela AK, et al. (2005). Excess fluoride ingestion and thyroid hormone derangements in children living in Delhi, India. *Fluoride* 38: 98-108. Susheela AK, Bhatnagar M, Vig K, Mondal NK - "Excess fluoride ingestion and thyroid hormone derangements in children living in Delhi, India" *Fluoride* 38(2):98-108 (2005)

139. Anon - "The specific features of the development of iodine deficiencies in children living under environmental pollution with fluorine compounds" *Gig Sanit* (6):53-5 (2005) MEDLINE

140. 2005 - Ruiz-Payan et al. show that even at 1 ppm (fluoride in water) T3 levels are reduced in adolescents living in Northern Mexico. Ruiz-Payan A, Duarte-Gardea M, Ortiz M, Hurtado R - "Chronic effects of fluoride on growth, blood chemistry, and thyroid hormones in adolescents residing in three communities in Northern Mexico" Abstracts, XXVIth ISFR Conference, Wiesbaden, Germany, September 26-29, 2005

141. Schuld A. (2005). Is dental fluorosis caused by thyroid hormone disturbances? *Fluoride* 38: 91-94

142. 2005 - Russian researchers investigate iodine deficiency in areas polluted with fluoride from air: The excess intake of fluorine was shown to increase the incidence of thyroid diseases and to lower anthropometric indices in children. The preventive measures performed to eliminate iodine-deficiency disorders under intensive ambient air pollution with fluorine compounds were found to be insufficiently effective."

143. Fluorine could affect hormone levels of each layer of the Hypothalamus-Hypophysis-Testis axis, and show the male reproductive endocrine disturbing effects. Ma X, Cheng X, Li F, Guo J. Experimental research on endocrine disturbing effect of fluorine on hypothalamus-hypophysis-testis axis in male rats, Wei Sheng Yan Jiu, 2008 Nov;37(6):733-5.

144. "Thus, excessive F administration induces thyroid dysfunction in rats; dietary Pr and Ca level play key roles in F-induced thyroid dysfunction." Source: Wang H, Yang Z, Zhou B, Gao H, Yan X, Wang J. Fluoride-induced thyroid dysfunction in rats: roles of dietary protein and calcium level. Toxicol Ind Health. 2009 Feb;25(1):49-57.

145. "The consumption of drinking water rich in fluoride has toxic effects on the central nervous system. . . Our results show that biologically relevant concentrations of fluoride are capable of increasing cell migration in tumour cells, suggesting that exposure to fluoride could stimulate tumour infasion." Source Mendoza-Schulz A, et al The effects of fluoride on cell migration, cell proliferation, and cell metabolism in GH4C1 pituitary tumour cells, Toxicol Lett. 2009 Oct 28;190(2):179-86.

146. F(-) is an oxidizing agent and a well-known reversible enzymatic inhibitor that interferes with the enzyme activity of at least 80 proteins. . . Exposure to high levels of F(-) in drinking water may decrease insulin mRNA and its secretion from beta-cells, and might therefore affect the OGTT (oral glucose tolerance test). Source Garcia-Montalvo EA et al Fluoride exposure impairs glucose tolerance via decreased insulin expression and oxidative stress, Toxicology 2009 Sep 19;263(2-3):75-83.

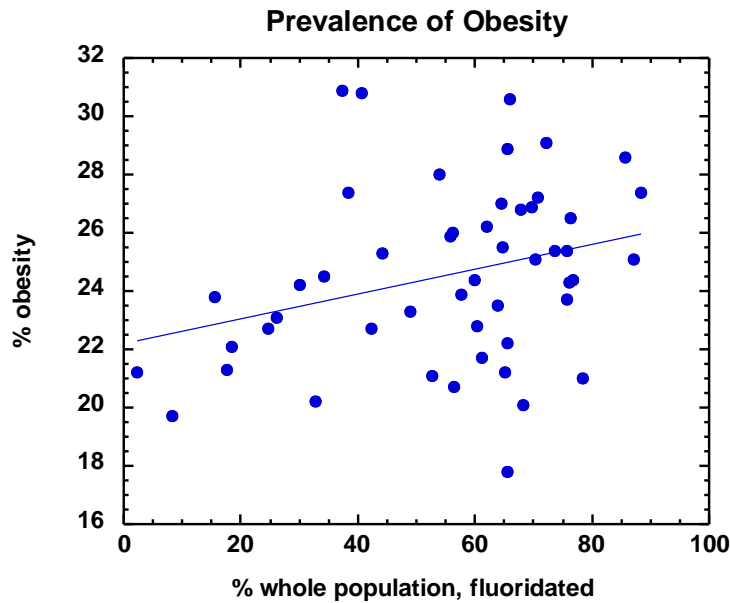
147. "Thus, excessive F administration induces thyroid dysfunction in rats; dietary PRr and Ca level play key roles in F-induced thyroid dysfunction." Wang H, Yang Z, et al, Fluoride-induced thyroid dysfunction in rats: roles of dietary protein and calcium level, Toxicol Ind Health 2009 Feb; 25(1):49-57

148. "Otosclerosis is a common form of hearing loss characterized by abnormal bone remodeling in the otic capsule. . . Environmental factors include fluoride and viral factors, particularly measles . . ." Source Schrauwen I, Van Camp G., The etiology of otosclerosis: a combination of genes and environment. Laryngoscope 2010 Jun;120(6):1195-202. Department of Medical Genetics, University of Antwerp.

149. "Fluoride could effect hormone levels of each layer of the hypothalamus-hypophysis-testis axis, and show the reproductive endocrine disturbing effects. The reproductive endocrine disturbing effects of male maybe more severe than those of female." Hao P, MaX et al Effects of fluoride on human hypothalamus-hypophysis-testis axis hormones, Wei Sheng Yan Jiu 2010 Jan;39(1):53-5.

B. Epidemiological Considerations of Fluoride Damage in the USA at Fluoridation Concentrations of 1ppm.

. “The implication of endocrine disruptors in the etiology of obesity and diabetes”⁶ is of growing concern. The Graphs below rank the 50 US states on percentage of the whole population fluoridated and plotting obesity or diabetes. Graph A⁷ and B next page. These graphs raise further concern that increased fluoride exposure is increasing diabetes and obesity in the public at large.



GRAPH A⁸

⁶ Diamanti-Kandarakis E, et al The impact of endocrine disruptors on endocrine targets, Horm Metab Res July, 2010, 42(8):543-52.

⁷ % of whole population fluoridated =% of public water users fluoridated X % of residents on Public Water 2004 data, Behavioral Risk Factor Surveillance System, CDC

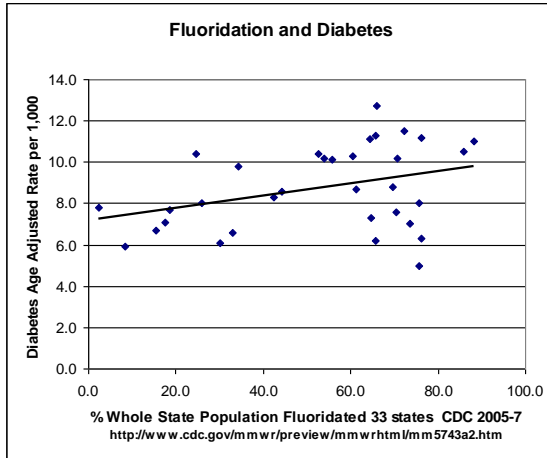
<http://apps.nccd.cdc.gov/nohss/FluoridationV.asp>

<http://pubs.usgs.gov/circ/2004/circ1268/htdocs/table05.html>

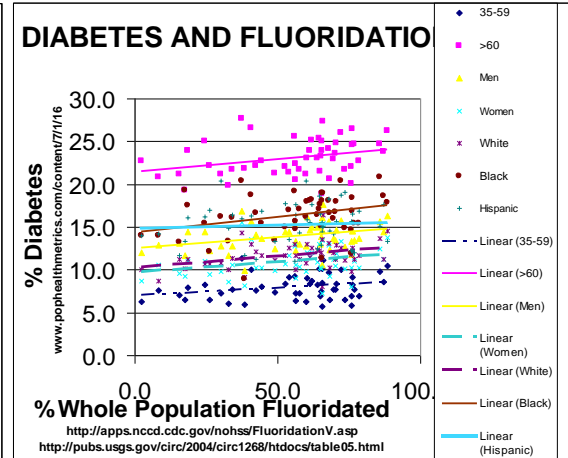
<http://www.unitedhealthfoundation.com/shr2005/components/obesity.html>

<http://apps.nccd.cdc.gov/giscvh/map.aspx>

⁸ Kathleen Thiessen PhD, member of the NRC 2006 review of fluoride in drinking water for the EPA, made this scatter graph of the 50 USA states ranked in order of their whole population fluoridated and reported obesity for each state.



Graph B⁹



Graph C

The epidemiological evidence comparing states in the USA supports the studies presented above.

II. VIOLETION OF THE SAFE DRINKING WATER ACT

This petition is made in the interest of the health and safety of the people of Washington. The intent of this petition is for public health education, within the jurisdiction of the Board of Health.

A. The MOU (Appendix A) between the EPA and the FDA is an agreement as to how the “food” regulation authority of the FDA will be harmonized with the “water” regulation authority of the EPA.

The MOU (Appendix A) between the EPA and the FDA is an agreement as to how the “food” regulation authority of the FDA will be harmonized with the “water” regulation authority of the EPA (because water is considered a food) and it does not give up any FDA authority to EPA regarding regulation of drugs.¹⁰ The FDA has stated to Congress¹¹ that fluoride when used in the mitigation or prevention of disease is a drug subject to FDA regulation. When bulk fluoride is added to drinking water to create a “fluoride and water” drug with intent to prevent or mitigate dental disease (tooth decay or dental caries), it is a drug subject to FDA regulation. Fluoride is recommended by the CDC and others to prevent and control dental caries (i.e. tooth decay) which the CDC calls an “infectious, multifactorial disease.” (Appendix B CDC 8-17-01)

MOU 225-79-2001 (Appendix A) is an agreement to resolve conflicting legal authorities granted to the EPA and FDA. The conflicting EPA and FDA legal authorities

⁹ See Graph A footnotes for Graphs B

¹⁰ Appendix C FOI response from FDA.

¹¹ Appendix D

are described in this MOU at 2-3. This MOU only seeks to resolve FDA authority over food in (FFDCA 201(f) (21 U.S.C. 321(f))), FFDCA 402 (21 U.S.C. 341)), FFDCA 406 (21 U.S.C. 346)), FFDCA 409 (21 U.S.C. 348)), and FFDCA 410 (21 U.S.C. 349)). MOU at 2.

However, the FDA has separate authority over drugs. FFDCA 201(g)(1) (21 U.S.C. 321(g)(1) and FFDCA 501 et seq. (21 U.S.C. 351 et seq.) The term “drug” is defined both in 21 U.S.C. 321(g)(1) and in RCW 69.04.009 as including

“(1) articles recognized in the official United States pharmacopoeia, official homeopathic pharmacopoeia of the United States, or official national formulary, or any supplement to any of them; and (2) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in human beings or other animals;”

If an entity wants to add a drug substance, active ingredient, as defined in RCW 69.04.009 to public drinking water, it could be adding or manufacturing a drug as defined in FFDCA 201(g)(1) (21 U.S.C. 321(g)(1)). Such drugs would be subject to FDA approval despite the existence of the MOU.

B. The United States Environmental Protection Agency Scientists are Opposed to Fluoridation:

1. *“In summary, we hold that fluoridation is an unreasonable risk. That is, the toxicity of fluoride is so great and the purported benefits associated with it are so small - if there are any at all – that requiring every man, woman and child in America to ingest it borders on criminal behavior on the part of governments.”¹²*

2. EPA scientists (NFFE) to the Court regarding the scientific basis for the authorized Recommended Maximum Contaminant Level (RMCL) for fluoride in drinking water.

“. . . NFFE believes that serious errors were made by the Agency in setting the fluoride RMCL . . . the Agency deliberately chose not to base its decision on relevant expertise. . . . The process by which EPA arrived at the RMCL for fluoride is scientifically irrational and displays an unprofessional review of relevant scientific data.”¹³

The Board of Health does not protect the safety of the public when relying on the EPA Maximum Contaminant Level for fluoride. The EPA does not determine the safety of drugs and the RCML is irrational and not protective of health.

C. The Federal Safe Drinking Water Act.

*“The Safe Drinking Water Act **prohibits** the deliberate addition of any substance to drinking water for health-related purposes other than disinfection of the water.*

¹² Dr. J. William Hirzy, Senior Vice-President, Headquarters Union, US Environmental Protection Agency, March 26, 2001. This letter describes some of the harms of water fluoridation as seen by water fluoridation opponents. See also Appendix B.

¹³ Amicus to the US Court of Appeals, DC Circuit, Natural Resources Defense Council, Inc., v EPA Civ. No. 85-1839 <http://www.fluoridealert.org/health/epa/nrdc/union-brief1986.pdf>

*Decisions on whether or not to fluoridate drinking water are made at a state or local level*¹⁴(emphasis added)

The Safe Drinking Water Act 42 USC 300g-1(b)(11)

“No national primary drinking water regulation may require the addition of any substance for preventive health care purposes unrelated to contamination of drinking water.”

*“Washington has a formal agreement with the Environmental Protection Agency (EPA) (PDF 99 KB) for meeting the requirements of the federal Safe Drinking Water Act (SDWA).*¹⁵

The formal agreement includes being prohibited from adding substances to water for the prevention of disease. At a minimum, health education is a critical first step in complying with the SDWA.

III. VIOLATION OF FEDERAL AND STATE DRUG LAWS MARKETING THE FLUORIDATED WATER DRUG.

For the protection of the public, the Food Drug and Cosmetic Act requires manufacturers to gain FDA CDER approval before marketing drugs. The Board’s refusal to gain FDA CDER approval for the fluoridated water drug, suggesting such requirement “would effectively rule out water fluoridation in Washington”¹⁶ is clear evidence the Board has ample evidence fluoridation is not safe at current concentrations. On the one hand the Board is assuring the public of fluoridation’s safety and on the other hand the Board is so unsure of the safety that the Board has refused to ask the FDA CDER for approval.

If fluoridation were in fact safe and effective, FDA approval would have already been achieved and following federal laws would not rule out fluoridation.

“Laws, Regulations, Policies and Procedures

*The mission of the FDA is to enforce laws enacted by the U.S. Congress and regulations established by the Agency to protect the consumer's health, safety, and pocketbook. The Federal Food, Drug, and Cosmetic Act is the basic food and drug law of the U.S. With numerous amendments, it is the most extensive law of its kind in the world. The law is intended to assure consumers that foods are pure and wholesome, safe to eat, and produced under sanitary conditions; that drugs and devices are safe and effective for their intended uses; that cosmetics are safe and made from appropriate ingredients; and that all labeling and packaging is truthful, informative, and not deceptive.*¹⁷

¹⁴ Appendix C FOI response from EPA

¹⁵ http://www.doh.wa.gov/ehp/dw/our_main_pages/dwover.htm accessed 10/20/10

¹⁶ See BOH denial for first petition, FDA Approval.

¹⁷ <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/Approvals/Default.aspx?Menu=Applications/NewDrugApplicationNDA/default.htm> Accessed 10/29/10

A. “21 U.S.C. 321 CHAPTER II—DEFINITIONS (g)(1) The term "drug" means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them;”

Sodium Fluoride is listed in the 2007 US Pharmacopoeia pages 3194-3196.¹⁸
Congress and the President have clearly defined drugs and fluoride is listed.

B. “21 U.S.C. 321 CHAPTER II—DEFINITIONS (g)(1) The term "drug" means . . . (B) articles intended for use in the . . . prevention of disease in man or other animals;”

C. Under an FOI request, the FDA responded,

“A search of the Drugs@FDA database . . . of approved drug products and the Electronic Orange Book . . . does not indicate that sodium fluoride, silicofluoride, or hydrofluorosilicic acid has been approved under a New Drug Application (NDA) or Abbreviated New Drug Application (ANDA) for ingestion for the prevention or mitigation of dental decay. . . . At the present time, the FDA is deferring any regulatory action on sodium fluoride products. . . .”¹⁹

D. The FDA responded to Representative Ken Calvert that Fluoride is a Drug.

“Fluoride, when used in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or animal, is a drug that is subject to Food and Drug Administration (FDA) regulation.”²⁰

E. Fluoride toothpaste labels state, “Drug Facts” and “Do Not Swallow.”

”Upon review of the Food and Drug Administration's (FDA) drugs@fda site (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm> <<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>>), it identifies one approved NDA fluoride product. Therefore, all other marketed fluoride products without an application are not approved FDA drugs.”

F. The Washington State Board of Pharmacy has confirmed fluoride is a prescription drug under state and federal law.

“Fluoride is a legend drug regulated under chapter 69.41 RCW. RCW 69.41.010 defines a ‘legend drug’ as drugs ‘which are required by state law or regulation of

¹⁸ Appendix E 2007 USP NF

¹⁹ Email from the FDA (7-22-09) .

²⁰ Appendix F FDA Calvert 2000

the state board of pharmacy to be dispensed on prescription only or are restricted to use by practitioners only."²¹

G. The IOM is clear that the role of drug approval is with the FDA. When cautioning about identifying and preventing medical errors, the IOM stated,

*"As used in this study, the phrase "drug safety and quality" did not include known risks associated with the medication itself, product purity, or integrity, that are the subject of extensive FDA oversight and regulation through the drug approval process and good manufacturing practice (GMP) regulations and guidance."*²²

F. The Surgeon General's office also relies on the FDA for Drug Approval.

"The level of evidence, for example, to justify the entry of a new drug into the marketplace has to be substantial enough to meet with approval by the U.S. Food and Drug Administration (FDA). According to U.S. drug law, a new drug's safety and efficacy must be established through controlled clinical trials conducted by the drug's manufacturer or sponsor (FDA, 1998). The FDA's decision to approve a drug represents the culmination of a lengthy, research-intensive process of drug development, which often consumes years of animal testing followed by human clinical trials (DiMasi & Lasagna, 1995). The FDA requires three phases of clinical trials before a new drug can be approved for marketing (FDA, 1998)."²³

A Surgeon General's support does not exempt fluoridation from FDA approval.

G. The FDA has no records of Congressional Approval for FDA to Relinquish Drug Regulatory Approval for Fluoride in Drinking Water or Congressional Approval for EPA to Assume Jurisdiction as Related to Public Water Systems.²⁴ See Appendix C

H. Fluoride is Exempt from Poison Laws when Used as a Drug.

Fluoridation products such as sodium fluoride are considered lethal at about 5 mg/Kg BW. In contrast, naturally occurring calcium fluoride found naturally in water is considered lethal at about 5,000 mg/Kg BW.²⁵ The EPA regulates safety guidelines of maximum contaminant levels based on the safer calcium fluoride. The Board of health should consider safety factors perhaps 5,000 times greater for the addition of fluoride to public water systems.

²¹ State of Washington Department of Health Board of Pharmacy June 4, 2009 letter to Bill Osmunson DDS; RCW 69.41.010(12) defines legend drugs; WAC 246-883-020(2) states legend drugs are listed in 2002 *Drug Topics Red Book*. See Appendix A WA Bd of Pharmacy 6 09.

²² <http://iom.edu/Activities/Quality/MedicationErrors.aspx> Accessed 10/16/10

²³ <http://www.surgeongeneral.gov/library/mentalhealth/chapter1/sec2.html>

²⁴ Appendix D

²⁵ Merck Index, 9th Edition, Merck and Co., Inc., Rahway, N.J. 1976, p 1663.

I. For the Safety of the Public, the FDA Drug Approval Process Guidance.

Without FDA CDER Drug Approval Process to ensure safety, efficacy, label and good manufacturing practices (GMP) and as the Washington State consumer watchdog for public water safety, the Board must provide equivalent or better safety, efficacy, label and GMP oversight. The Board must provide the same protection as the FDA, which **Includes:**

“American consumers benefit from having access to the safest and most advanced pharmaceutical system in the world.

The main consumer watchdog in this system is the U.S. Food and Drug Administration's Center for Drug Evaluation and Research (CDER). The center's best-known job is to evaluate new drugs before they can be sold. The center's evaluation not only prevents quackery, but also provides doctors and patients the information they need to use medicines wisely. CDER ensures that drugs, both brand-name and generic, work correctly and that their health benefits outweigh their known risks.

Drug companies seeking to sell a drug in the United States must first test it. The company then sends CDER the evidence from these tests to prove the drug is safe and effective for its intended use. A team of CDER physicians, statisticians, chemists, pharmacologists, and other scientists reviews the company's data and proposed labeling. If this independent and unbiased review establishes that a drug's health benefits outweigh its known risks, the drug is approved for sale. The center doesn't actually test drugs itself, although it does conduct limited research in the areas of drug quality, safety, and effectiveness standards.

Before a drug can be tested in people, the drug company or sponsor performs laboratory and animal tests to discover how the drug works and whether it's likely to be safe and work well in humans. Next, a series of tests in people is begun to determine whether the drug is safe when used to treat a disease and whether it provides a real health benefit.”²⁶

The above process of safety efficacy testing of fluoridation compounds by the Board, water systems or any other organization does not appear to have been done. Application to the FDA CDER for their evaluation that the benefit outweighs the risk is legally essential. The Board has refused FDA CDER evaluation, taking the responsibility to assure the benefits do in fact outweigh the risks. The wise use of drugs by doctors, patients, and the Board of Health includes an approved drug label and the Board must provide a label for fluoridation. Our petitions are part of the label.

For decades, the regulation and control of new drugs in the United States has been based on the New Drug Application (NDA). Since 1938, every new drug has been the subject of an approved NDA before U.S. commercialization. The NDA application is

²⁶ <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm> Accessed 10/26/10

the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the U.S.

“Title 21: Food and Drugs§ 314.50 Content and format of an application. (d)(1)(i) *Drug substance* . A full description of the drug substance including its physical and chemical characteristics and stability; the name and address of its manufacturer; the method of synthesis (or isolation) and purification of the drug substance; the process controls used during manufacture and packaging; and the specifications necessary to ensure the identity, strength, quality, and purity of the drug substance and the bioavailability of the drug products made from the substance, including, for example, tests, analytical procedures, and acceptance criteria relating to stability, sterility, particle size, and crystalline form. The application may provide additionally for the use of alternatives to meet any of these requirements, including alternative sources, process controls, and analytical procedures. Reference to the current edition of the U.S. Pharmacopeia and the National Formulary may satisfy relevant requirements in this paragraph.²⁷”

IV. BENEFIT RISK ASSESSMENT: TEETH OR THYROID

In simple terms, the Board needs judgment to weigh the difficulty of fixing teeth vs. protecting the thyroid and reducing the incidence of obesity and diabetes. We can fix teeth. Fixing a damaged thyroid is less successful. Which is worse “a cavity or thyroid damage?”

Of particular note is the study above by Trivedi (1993) (See citation 114 above and Appendix E). Trivedi reported serum fluoride levels significantly higher in endemic fluorosis patients with impaired glucose tolerance (**0.08 mg/l**) and endemic fluorosis patients without glucose tolerance (0.02 mg/l) and controls at 0.01 mg/l. Xiang (2010) found an 8 IQ point drop compared when comparing fluoride serum levels of **0.08 mg/l** and 0.04 mg/l. Both thyroid damage and brain damage are occurring at 0.08 mg/l serum fluoride. Mean serum fluoride for healthy controls was 0.01 mg/l serum fluoride. The historical "normal" of 0.15 mg/l serum fluoride is almost twice as high as levels with known brain and impaired glucose tolerance.

Bachinskii (1985 - see Appendix F) reported the controls had 0.21mg/l to 0.22 mg/l serum fluoride, significantly higher than 0.08 mg/l with known risks. What is the serum fluoride level of people in Washington State? What measured evidence does the Board have that residents have lower serum fluoride than 0.01mg/l which maybe protective?

V. PETITION FOR WAC CHANGE: “WAC 246-290-460”

A. Mother’s milk averaging 4 ppb (parts per billion or 0.004 ppm) of fluoride and a high of about 10 ppb is the highest concentration of fluoride in water which should be considered safe for infant formula.

B. Research appears consistent and strong enough to consider high fluoride intake, even at 1 ppm, may be the most common cause of mental retardation, in some

²⁷ <http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=2a88f275a8609a20ed3f25adbeb7205f&rgn=div5&view=text&node=21:5.0.1.1.4&idno=21#21:5.0.1.1.4.1.1.1> accessed 10/30/10

communities. More mental retardation in some communities may be caused from fluoride than all other causes combined.

C. EPA September 5, 2000: said many could be adversely affected by fluoridated drinking water. Providing caution and public health education is a critical component for the Board of Health.

"EPA is in the process of developing medical fact sheets to provide medical practitioners (doctors, nurses, dieticians, etc.) with health data relative to drinking water contaminants that can be then used in counseling patients. This work has just begun, and will initially focus on the elderly, children and pregnant women. It will later be expanded to cover other at-risk populations. In addition, EPA has made it a requirement for public water systems to provide their clients with health effects information on contaminants in their water supply, including fluoride [Consumer Confidence Rule FR 63(160): 44512-44536]."*

"POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE. Existing data indicate that subsets of the population may be unusually susceptible to the effects of fluoride and its compounds. These populations include the elderly, people with deficiencies of calcium, magnesium and vitamin C, and people with cardiovascular and kidney problems . . . Poor nutrition increases the incidence and severity of dental fluorosis and skeletal fluorosis."²⁸

The consumer confidence rule was mostly shoveled under the carpet and fluoridation is still a protected pollutant.

WASW requests the following rule change:

PETITION FOR WAC CHANGE: "WAC 246-290-460

"Where fluoride concentrations in group A water systems average above 10 ppb (parts per billion) of fluoride or if the system is without the ability to measure low concentrations of fluoride, water suppliers shall include the following notice with each customer's water bill, "The Washington State Board of Health finds the fluoride level in this water may contribute to thyroid damage, diabetes and/or obesity. Pregnant mothers, infants and those at risk of thyroid damage are advised to drink water containing less fluoride."

The Board has denied previous petitions six and seven for rule change relying, in part, on the "majority" of scientific opinion. If the Board denies this opinion, please provide who the "majority" the Board is relying on, the studies, surveys, national drug regulatory agencies, countries and names which represent the "majority." Because the FDA CDER is the legal authority to provide an opinion on safety and efficacy of fluoridation drugs, any other source of "majority" opinion or consensus must be to the level of confidence required by the FDA CDER.

²⁸ Charles Fox acknowledges the Toxicological Profile for Fluorides (US Agency for Toxic Substances and Disease Registry, 1993) page 112 statement:

WASW relies on the FDA CDER to evaluate the safety and efficacy of the fluoridated water drug and the "majority," hundreds, of scientific peer reviewed studies, the majority of developed nations of the world (see Appendix F), and the majority of professionals, over 3,200, willing to put their signatures to a petition calling for an end to fluoridation (Appendix F). We are willing to list the studies and the scientists who have found fluoridation to be an unacceptable risk. WASW has provided clear Federal and Washington state laws which regulate the fluoridated water drug. We support and uphold these laws and request the Board to support these laws and protect the public as charged by the Legislature. The Board is requested to list the names of those scientists and studies they are relying on to deny our petitions.

History is replete with scientific and political errors and errors of entering wars, medical errors of blood letting, thalidomide and mercury treatments, when the evidence is cherry picked and one side of the evidence is provided a stronger forum for expression. The Board of Health is to provide safe water, not simply defend tradition, listen to one side of the evidence or cherry pick those opinions. Repeatedly we have asked to provide a presentation to the Board and been ignored. Repeatedly we have provided evidence to the Board of lack of legal footing for fluoridation. Repeatedly we have provided evidence of lack of efficacy or safety from hundreds of scientific studies. Who is holding the reigns of the Board of Health?

Respectfully submitted,

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