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Before the
ENVIRONMENTAL PROTECTION AGENCY

In Re Final Rules on Sulfuryl Fluoride)
Pesticide Residue Tolerances)
_____)

Docket Nos. OPP-2005-0174;
OPP-2003-0373

To:

Public Information and Records Integrity Branch
Information Resources and Services Division
Room 7502C
Office of Pesticide Programs
U.S. EPA
1200 Pennsylvania Ave. N.W.
0001 Washington, D.C. 20460-0001

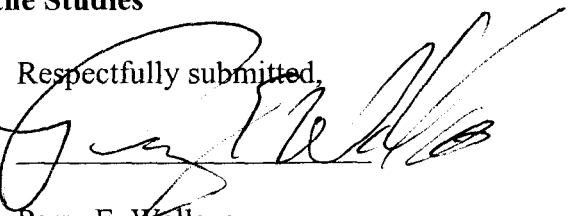
Jonathan Fleuchaus
Office of General Counsel
Room 2333A
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1200 Pennsylvania Ave. NW
Washington, D.C. 20460-

Objectors' Submission to Docket

18 IQ Studies

Objectors Fluoride Action Network, Beyond Pesticides and Environmental Working Group, through counsel, hereby submit to the Docket 18 IQ studies. These materials are presented as follows:

- **Part I: Listing of Studies**
(with descriptions of publication and translation)
- **Part II: Studies**
- **Part III: Two Overview Papers on the Studies**

Respectfully submitted,


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Part I
Listing of Studies

Papers attached:

- 18 IQ studies
- 2 overview papers of the IQ studies

(1) Chen Y, Han F, Zhou Z, Zhang H, Jiao X, Zhang S, Huang M, Chang T, Dong Y. (1991)
Research on the intellectual development of children in high fluoride areas.
Chinese Journal of Control of Endemic Diseases 1991;6 Suppl:99-100. 1991.
English version published in Fluoride 41(2):120–124. April-June 2008.
Translated by Julian Brooke and published with the concurrence of the Chinese Journal of Control of Endemic Diseases.

(2) Guo X, Wang R, Cheng C, Wei W, Tang L, Wang Q, Tang D, Liu G, He G, Li S. (1991)
A preliminary investigation of the IQs of 7-13 year old children from an area with coal burning-related fluoride poisoning.
Chinese Journal of Endemiology 1991;10(2):98-100. 1991.
English version published in Fluoride 41(2):125–128. April-June 2008.
Translated by Julian Brooke and published with the concurrence of the Chinese Journal of Endemiology.

(3) Hong F, Cao Y, Yang D, Wang H. (2001)
Research on the effects of fluoride on child intellectual development under different environments.
Chinese Primary Health Care 2001;15(3):56-7. 2001.
Translated by Julian Brooke and published with the concurrence of Chinese Primary Health Care.
English version published in Fluoride 41(2):156–160. April-June 2008.

(4) Li Y, Li X, Wei S. (1994)
The effects of high fluoride intake on child mental work capacity and preliminary investigation into mechanisms involved.
The Journal of West China University of Medical Sciences 1994; 25(2): 188-191. 1994.
• Translation into English by Julian Brooke. (English translation not yet published)

(5) Li Y, Jing X, Chen D, Lin L, Wang Z. (2003)
The effects of endemic fluoride poisoning on the intellectual development of children in Baotou.
Chinese Journal of Public Health Management 2003;19(4):337-8. 2003.
Translated by Julian Brooke and published with the concurrence of the Chinese Journal of Public Health Management.
English version published in Fluoride 41(2):161–164. April-June 2008.

(6) Qin L, Huo S, Chen R, Chang Y, Zhao M. (1990)
Using the Raven's standard progressive matrices to determine the effects of the level of fluoride in drinking water on the intellectual ability of school-age children.
Chinese Journal of the Control of Endemic Diseases 5:203-204.
Translated by Julian Brooke and published with the concurrence of the Chinese Journal of Control of Endemic Diseases.
English version published by Fluoride 41(2):115–119. April-June 2008.

(7) Ren D, Li K, Liu D. (1989)

A study of the intellectual ability of 8-14 year-old children in high fluoride, low iodine areas.

Chinese Journal of Control of Endemic Diseases Vol. 4, No. 4, p 251. 1989.

• Translation into English by Julian Brooke. (English translation not yet published)

(8) Wang G, Yang D, Jia, Wang H. (1996)

A study of the IQ levels of four- to seven-year-old children in high fluoride areas.

Endemic Diseases Bulletin, Vol. 11, No. 1, 60-6. February 1996.

• Translation into English by Julian Brooke. (English translation not yet published)

(9) Wang S, Zhang H, Fan W, Fang S, Kang P, Chen X, Yu M. (2005)

The effects of endemic fluoride poisoning caused by coal burning on the physical development and intelligence of children.

Journal of Applied Clinical Pediatrics 20(9): 897-898. September 2005.

• Translation into English by Julian Brooke. (English translation not yet published)

(10) Li XS, Zhi JL, Gao RO. (1995)

Effect of fluoride exposure on intelligence in children.

Fluoride 28(4): 189-192. 1995.

(11) Lin FF, Aihaiti, Zhao HX, Lin J, Jiang JY, Maimaiti, and Aiken (1991)

The relationship of a low-iodine and high-fluoride environment to subclinical cretinism in Xinjiang.

Xinjiang Institute for Endemic Disease Control and Research;

Office of Leading Group for Endemic Disease Control of Hetian Prefectural Committee of the Communist Party of China; and County Health and Epidemic Prevention Station, Yutian, Xinjiang.

(12) Lu Y, Sun ZR, Wu LN, Wang X, Lu W, Liu SS. (2000)

Effect of high-fluoride water on intelligence in children.

Fluoride 33(2): 74-78. 2000.

(13) Rocha-Amador D, Navarro ME, Carrizales L, Morales R, Calderón J. (2007)

Decreased intelligence in children and exposure to fluoride and arsenic in drinking water.

Cad. Saúde Pública, Rio de Janeiro, 23 Sup 4:S579-S587. 2007.

(14) Trivedi MH, Verma RJ, Chinoy NJ, Patel RS, Sathawara NG . (2007)

Effect of high fluoride water on intelligence of school children in India.

Fluoride 40(3):178-183. July-September. 2007.

(15) Wang SX, Wang ZH, Cheng XT, Li J, Sang Z-P, Zhang X-D, Han L-L, Qiao X-Y, Wu Z-M, Wang Z-Q. (2007)

Arsenic and fluoride exposure in drinking water: children's IQ and growth in Shanyin County, Shanxi Province, China.

Environmental Health Perspectives 115(4):643-647. April 2007.

(16) Xiang Q, Liang Y, Chen L, Wang C, Chen B, Chen X, Zhou M. (2003)

Effect of fluoride in drinking water on children's intelligence.

Fluoride 36(2): 84-94. 2003.

(17) Zhao LB, Liang GH, Zhang DN, Wu XR. (1996)

Effect of high-fluoride water supply on children's intelligence.

Fluoride 29(4): 190-192. 1996.

(18) Seraj B*, Shahrabi M, Falahzade M, Falahzade F, Akhondi N. (2007)

Effect of high fluoride concentration in drinking water on children's intelligence.

• English translation forwarded by lead author: (B. Seraj, Department of Pediatric Dentistry, Faculty of Dentistry, Tehran University of Medical Sciences)
Journal of Dental Medicine 19(2):80-86. 2007.

2 Overview Papers:

Connett M, Limeback H.

Fluoride and its effect on human intelligence. A systematic review.

International Association for Dental Research 83rd General Session and Exhibition. Toronto, Canada.

Poster 2205. July 4, 2008.

Tang Q-Q, Du J, Ma H-H, Jiang S-J, Zhou X-J.

Fluoride and Children's Intelligence: A Meta-analysis.

Biol Trace Elem Res. 2008 Aug 10. 2008.

Part II

Studies

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Part III

Two Overview Papers on the Studies

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Over view Paper I

Fluoride and its Effect on Human Intelligence. A Systematic Review

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IADR 83rd General Session and Exhibition, July 4, 2008

(International Association for Dental Research)

2:00 PM-3:15 PM, Friday

Metro Toronto Convention Centre Exhibit Hall D-E (Ontario, Canada)

Poster 2205 - PTT Poster Session #2

http://iadr.confex.com/iadr/2008Toronto/techprogram/abstract_105335.htm

Title: Fluoride and its effect on human intelligence. A systematic review.

Authors: Michael Connett and Hardy Limeback

Objectives: A systematic review was undertaken to examine if fluoride (F⁻) exposure is associated with a decline in human intelligence (IQ).

Materials and Methods: Ovid MEDLINE and its allied versions, CINAHL, AMED, EMBASE, Cochrane DSR, ACP Journal Club, DARE, CCTR, CMR, HTA, and NHSEED, Health and Psychosocial Instruments, HealthSTAR, International Pharmaceutical Abstracts were searched from the earliest record until January 2008. Only original human studies examining the effect of F⁻ on IQ were selected. Elevated F⁻ in drinking water was the primary variable but studies where F⁻ was elevated in the urine as a result of pollution were also included. Hand-searching of the bibliographies of the selected studies, as well as a separate search strategy in Cab Direct and online Chinese databases (Chinese version of Google Scholar and several others) were performed and the relevant Chinese studies were translated into English.

Results: Of a total of 224 papers searched for relevancy from their titles, abstracts, and full copy, 20 original studies met our inclusion criteria, were read in full and critiqued by the authors. Only 6 of the studies were reviewed by the 2006 US NRC Subcommittee on Fluoride in Drinking Water and 4 studies were published after 2006. The extent of F⁻ exposure was reported in all but one study and 9 studies reported urinary F⁻. Most papers omitted important details (e.g. blinding, managing confounders). All but 2 reported statistically significant (t-tests) declines in IQ in children exposed to elevated levels of F⁻. One study reported a bivariate analysis and another did multiregression analysis. Three studies were conducted outside of China, suggesting that this is not just a relationship that is limited to one country.

Conclusions: While the evidence is not conclusive, we identified 18 ecological studies that purport an association between high fluoride exposure and decreased human intelligence.

Author (yr.)	Group compared	Water [F-] ppm	n	Urine [F-]	IQ test	IQ Results	S.D. +/-	p	conclusion	Method Search
Hu ('89)	Low F High F	<0.70 >7.0	181 198	ND ND		84.9 85.15	NR NR	>0.05	"the effect of fluoride poisoning on intellectual ability is negligible"	Manual Manual (translate)
Ren ('89)	Low I High F, low I	Not reported	169 160	ND	Wechsler	85 64.8	22.3 20.4	<0.01	"Disrupted child intellectual development" is "clearly much more serious" from a "harmful environment containing both high fluoride and low iodine... than the effects of iodine deficiency alone"	Manual (translate)
Qin ('90)	Low F Normal F High F	0.1-0.2 0.5-1.0 2.1-4.0	147 59 141	ND ND ND	Raven	23.03 28.14 21.17	NR NR NR	>0.05 <0.01	"A child whose drinking water is above 2.0 mg/L or below 0.2 mg/L manifest intellectual deficits as compared to 'normal' control group."	Manual (translate)
Guo ('91)	Control Endemic Fluorosis	Serum F 0.10 0.15	61 60	ND ND	Chinese Binet	83.95 77.30	8.93 8.52	(7-9 yr.) <0.05	"children living in high fluoride areas have lower IQs"	Manual (translate)
Lin ('91)	Low F ₁ (Low D) High F ₁ (High D)	0.34 (0.96 ppb) 0.88 (5.21 ppb)	256 250	1.52 2.56		78 71	NR NR	<0.01	"Low iodine intake coupled with high fluoride intake exacerbates the central nervous lesions and the somatic developmental disturbance of iodine deficiency."	Universi of Toron
Chen ('91)	Low F High F	0.89 4.55	320 320	ND ND	Raven	104.03 100.24	14.96 14.52	<0.01	"fluoride has a direct connection with intellectual development of children"	Manual (translate)
Yang ('94)	Low F ₁ (Low D) High F ₁ (High D)	0.5 (0.13 mg/L) 2.97 (0.1 mg/L)	416 1102	0.82 2.03	Chinese Compara- five Scales of Intelle- gence Test	81.97 76.67	11.97 7.75	>0.05	"O somewhat lower but not significant"	Universi of Toron
Li ('94)	Low F	0.3 in all water 0.5 ppm (grain)	51	ND ND	Work capacity	Two com- ponents of		<0.05 and	"early prolonged high fluoride intake causes a decrease an a	Universi of Toron

	HF I no fluorosis HF II fluorosis HF III fluorosis	4.7 ppm (grain) 5.3 ppm (grain) 31.6 ppm (grain)	33 37 36	ND ND ND	(reaction time, short-term memory, etc.	mental capacity decreased		<0.01	child's mental work capacity"	
Li ('95)	Low F High F	fluorosis low-mild severe	226 230	1.02 2.69	Rui Wen	89.9 80.3	10.4 12.9	<0.01	High fluoride environment can adversely affect the development of intelligence in children	University of Toronto
Wang ('96)	Low F High F	<1.0 >1.0 – 8.6	83 147	ND ND	Wechsler	101.23 95.64	15.84 14.34	<0.05	"high fluoride intake has a clear influence on the IQ of preschool children"	Manual (translate)
Zhao ('96)	Low F High F	0.91 4.12	160 160	ND ND	Pau Wan	105.21 97.69	14.99 13.00	<0.01	"The intake of high fluoride drinking water before birth had a significant deleterious influence on children's IQ."	University of Toronto
Lu ('00)	Low F High F	0.37 3.15	58 60	1.43 4.99	Raven	103.5 92.2	13.86 20.45	<0.005	"exposure of children to high levels of fluoride may therefore carry the risk of impaired development of intelligence"	University of Toronto
Hong ('01)	Low F High F High F, low I	0.75 2.90 2.94	32 85 28	ND ND ND	Raven	82.79 80.58 68.38	8.98 2.28 19.12	>0.05 <0.01	F makes I-deficiency worse, lowering IQ more than just with low I	Manual (translate)
Li ('03)	Non-fluorosis fluorosis	ND ND	301 419	ND ND	Raven	96.97 88.67	18.43 15.26	<0.01	Fluoride disrupts intellectual development	Manual (translate)
Xiang ('03)	Low F High F	0.36 2.47	135 155	1.11 3.47	Combined raven	100.41 92.02		0.003	"drinking water fluoride levels greater than 1.0 mg/L may adversely affect the development of children's intelligence"	University of Toronto
Wang ('05)	Control dental fluorosis skeletal fluorosis		49 97 57	1.61 1.35	Raven	percentiles 5-25 >75 4 14 24 8 12 2		<0.01	"..Negative correlation between urine fluoride and intelligence"	Manual (translate)
Seraj ('07)	Low F High F	0.4 2.5	85 41	ND ND	Raven	98.9 87.9	12.9 11.0	0.000	"High F may be associated with impaired development of intelligence"	Manual (translate)

Rocha-Amador ('07)	Low F Mod F High F	0.8 5.3 9.4	52 20 60	1.5 6.0 5.5	Wechsler	β values -6.7 -11.2 -10.2		<0.001 <0.001 <0.001	"Children exposed to either F or As have increased risks of reduced IQ scores"	Manual
Trivedi ('07)	Low F High F	2.01 5.55	101 89	2.30 6.13	Stanford-Binet	100.04 91.72	1.23 1.13	<0.001	"..the mean IQ level of students exposed to high F drinking water was significantly lower than that of the students to a lower F level drinking water"	Universit of Toron
Wang ('07)	Low F High F	0.5 8.3	110 106	1.5 5.1	Raven	105 101	15 16	<0.05	"Children's intelligence and growth can be affected by high concentrations of As or fluoride."	Universit of Toron

Grey= reviewed by the NRC

Yellow = not found in the U of T search