While the dose of 50 mg Al/kg bw/d is an estimation of the lower end of a broad range of LOELs observed under different experimental conditions, it is not considered to be an overly conservative estimate of the effect level of concern. As previously discussed, there are two sources of bias against consideration of lower values of LOEL in the above characterization: (a) low-dose studies were not considered if the administered dose was less than the probable base diet dose; and (b) LOELs from single-dose studies may be overestimates of the actual effect levels. The dose of 50 mg Al/kg bw/d has, however, produced neurotoxic, reproductive and developmental effects in laboratory animals more consistently under a wide range of experimental conditions, as compared to lower doses. This exposure level is therefore retained for the purpose of the characterization of human health risks as the level of concern for neurotoxic, neurodevelopmental and reproductive effects.

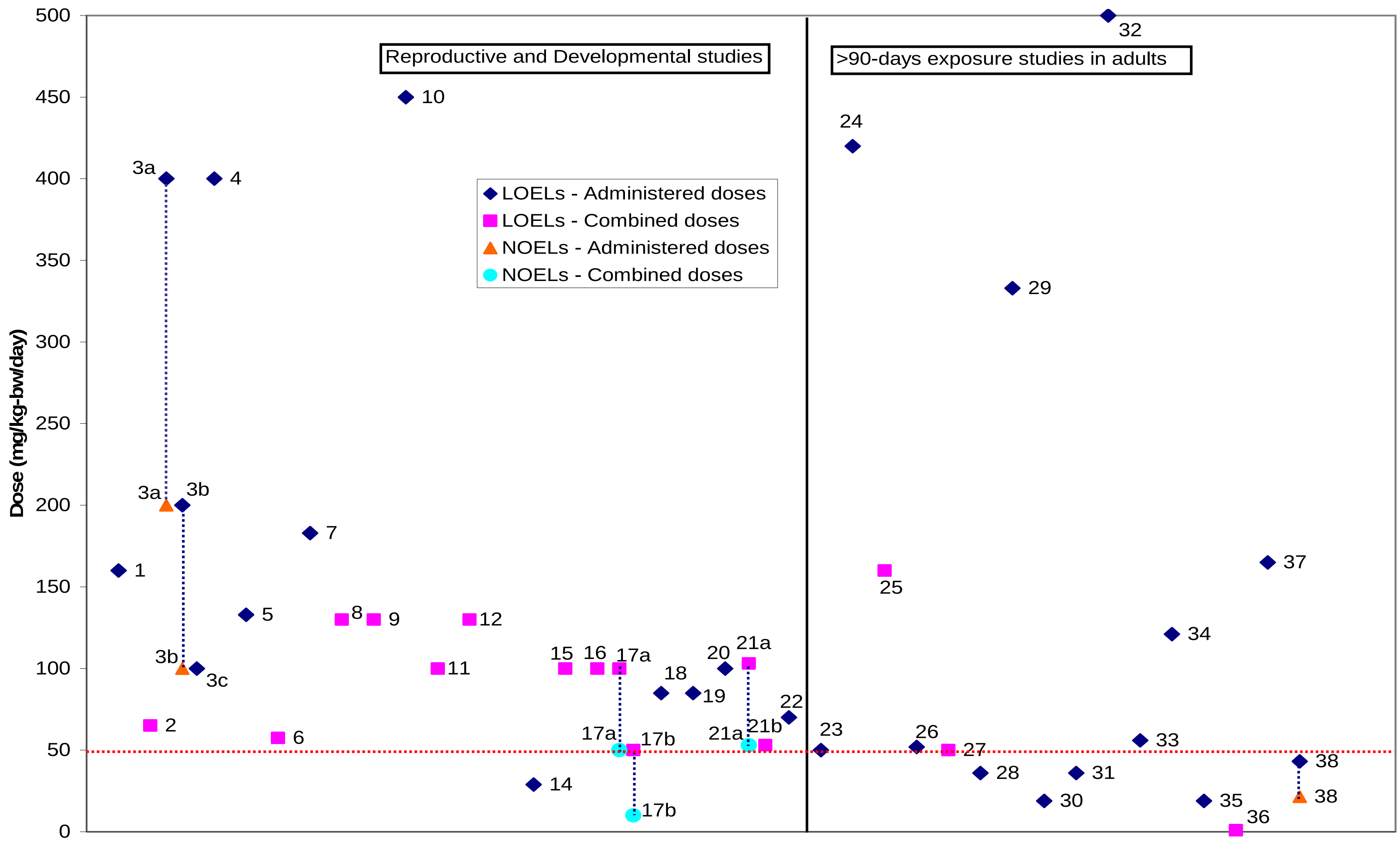

Figure 3.1 Compilation of the LOEL values from the two major subsets of studies (Adult exposure > 90 days and Reproductive/developmental) considered in the exposure-response analysis.

The numbers represent the 38 studies in which LOELs were observed, as summarized in Tables C1 and C2, and listed below. Where the base diet aluminum level is quantified, the LOEL is expressed as combined dose. NOELs associated with LOELs are indicated when observed.

Study references and endpoints:

Reproductive and developmental studies:

1. **Bernuzzi et al. 1986**: Reduced body weight of pups, impaired negative geotaxis.
2. **Golub et al. 1987**: Reduced birthweight, decreased body weight gain in pups.
3. **Bernuzzi et al. 1989**:
   a. Impaired locomotor coordination;
   b. Impaired righting reflex;
   c. Impaired grasping reflex.
4. **Muller et al. 1990**: Impaired negative geotaxis, impaired performance in suspension and locomotor coordination tests.
5. **Gomez et al. 1991**: Reduced fetal body weight, increase in skeletal variations.
6. **Colomina et al. 1992**: Maternal toxicity, reduced fetal body weight (aluminum lactate), increased incidence of morphological effects (aluminum lactate).
7. **Misawa and Shigeta 1993**: Maternal toxicity, decreased pup weight, delay in pinna detachment and eye opening in females, delayed development of auditory startle in males.
8. **Golub et al. 1993**: Effects on Mn metabolism.
9. **Golub et al. 1994**: Reduced auditory startle response.
10. **Poulos et al. 1996**: Delayed expression of phosphorylated high molecular weight neurofilament protein in tracts in diencephalon, maternal toxicity.
11. **Golub et al. 1996**: Lower retention of both Mn and Fe.
12. **Verstraeten et al. 1998**: Increased phospholipid and galactolipid contents in brain myelin, increased lipid peroxidation.
13. **Llansola et al. 1999**: Decrease in pup body weight, decreased number of cells in cerebellum, disaggregation of microtubules and neuronal death in cerebellar neuron cultures.
14. **Belles et al. 1999**: Increased mortality of dams and increased early deliveries, reduced fetal body weight.
15. **Golub and Tarara 1999**: Decreased myelin sheath width.
16. **Golub et al. 2000**: Reduced forelimb and hindlimb grip strength, decreased thermal sensitivity.
17. **Golub and Germann (2001b)**:
    a. Impaired performance in rotarod test (males);
    b. Decreased weight gain in pups, impaired learning of maze with respect to cue utilization (females).
18. **Wang et al. 2002a**: Reduced body weight, deficits in synaptic plasticity in dentate gyrus of hippocampus.
19. **Chen et al. 2002**: Deficits in synaptic plasticity in dentate gyrus of hippocampus.
20. **Nehru and Anand 2005**: Increased lipid peroxidation, decreased superoxide dismutase and catalase activity in cerebrum and cerebellum.
21. **Colomina et al. 2005**:
    a. Reduced forelimb strength in males;
    b. Increased number of days to sexual maturation.
22. **Sharma and Mishra 2006**: Decreased number of corpora lutea, number of implantation sites, placental and fetal weight, increased skeletal malformations, increased oxidative stress in brains of mothers/fetuses and sucklings.

> 90 days exposure studies in adults:

23. **Commissaris et al. 1982**: Reduced motor activity, impaired learning (shuttle box).
24. **Johnson et al. 1992**: Decreased levels of microtubule associated protein-2 and spectrin in hippocampus.
25. **Golub et al. 1992**: Decreased motor activity, hindlimb grip strength and auditory and air puff startle responsiveness.
26. **Lal et al. 1993**: Reduced spontaneous motor activity; impaired learning (shuttle box, maze), increased brain lipid peroxidation, reduced Mg^{2+}- and $Na^{+}K^{+}$-ATPase activities.
27. **Florence et al. 1994**: Cytoplasmic vacuolization in astrocytes and neurons.
28. **Gupta and Shukla 1995**: Increased lipid peroxidation in brain.
29. **Zatta et al. 2002**: Increased acetylcholinesterase activity.
30. **Silva et al. 2002**: Increased synaptosomal membrane fluidity, decreased cholesterol/phospholipid ratio in synaptosomes.
31. **Flora et al. 2003**: Evidence of increased lipid peroxidation in brain.
32. **Jing et al. 2004**: Impaired performance in Morris water maze, altered synapses in hippocampus and frontal cortex.
33. **Gong et al. 2005**: Impaired performance in Morris water maze.
34. **Shi-Lei et al. 2005**: Impaired performance in Morris water maze, decrease in long-term potentiation in hippocampal slices.
35. **Silva et al. 2005**: Decreased Na+/K+-ATPase activity in brain cortex synaptosomes.
36. **Huh et al. 2005**: Induced apoptosis in brain, increased efficiency of monoamine oxidases and increased level of caspase 3 and 12 in brain.
37. **Rodella et al. 2006**: Decreased nitrergic neurons in the somatosensory cortex.
38. **Mameli et al. 2006**: Impaired vestibulo-ocular reflex.

3.2.4 Human health risk characterization for aluminum sulphate, aluminum chloride, and aluminum nitrate

As noted in the Introduction (section 1) three aluminum salts are specifically named for assessment on the PSL2: chloride, nitrate and sulphate. Although the data available for the assessment do not allow for accurate quantification of exposure associated with specific salts, it is possible to qualitatively estimate their relative contribution to different environmental media (see Table 3.2).

Based on the use pattern of these three salts, described in section 2.2.1, the major use of sulphate and chloride salts is in water treatment, therefore exposure to these particular salts would be expected via drinking water. Aluminum sulphate has a minor use as a food additive; other aluminum-containing additives are much more widely used. Aluminum nitrate use is limited in comparison to the sulphate and chloride salts. It is used in fertilizers and as a chemical reagent in various industries and is not expected to contribute significantly to aluminum in food and soil, the principal media of total aluminum exposure.

Based on these use patterns, the only media in which the mean concentration is significantly affected by the use of these salts is drinking water. Although the contribution of aluminum via these salts cannot be accurately quantified, in order to quantitatively compare the exposure level of concern with potential exposure to aluminum from the three salts, as a surrogate for exposure it is assumed that all aluminum in drinking water is derived from aluminum chloride and aluminum sulphate.

Therefore, the human health risk characterization for the three salts is based on the comparison of the exposure level of concern of 50 mg/kg bw/d, identified in the exposure-response analysis of section 3.2.3, and the age-group with the highest average daily intake of total aluminum from drinking water (10.8 μg/kg bw/d in non-breastfed infants, see Table 3.1). The ratio of these two levels, generally referred to as the margin of exposure (MOE), is greater than 4000. This margin of exposure is considered adequate, taking into account the fact that aluminum exposure from the three salts is overestimated in this calculation, and the following considerations.

To account for toxicokinetic and toxicodynamic variability and uncertainty, a factor of at least 100 within the MOE is considered appropriate. As there is little consensus as to the mode of action, and multiple mechanisms are likely involved, the delineation of chemical-specific adjustment factors is not possible here. Effects at the lower-bound were generally small changes in performance in motor activity and learning tests identified across a range of studies, and the MOE is considered adequate to account for uncertainties in the identification of this lower-bound.

The adequacy of the collective database for the neurotoxicity and reproductive/developmental toxicity of orally-administered aluminum was reviewed in section 3.2.2.2. As discussed, there is a clear need for further investigation in experimental animals, in which studies are designed to provide a basis for determining a critical dose for risk assessment. The existing database is nonetheless extensive, providing a basis for the determination of the lower range of LOELs observed in the different studies, carried out under different experimental conditions and for an array of aluminum salts. The neurobehavioural and neurodevelopmental effects most frequently associated with the range of LOELs may be characterized as small but statistically significant changes in performance in motor activity and learning tests.

Collectively the limited aluminum bioavailability data do not indicate that the relative bioavailabilities of aluminum in drinking water, soil and different types of food are significantly different (see section 2.3.3.1). Therefore, it is not anticipated that aluminum from drinking water would contribute relatively more bioavailable aluminum, in proportion to its external dose, as compared with other sources. In addition there is no evidence to suggest that there are differences in relative bioavailability between humans and experimental animals.

3.2.5 Uncertainties and degree of confidence in human health risk characterization

There is a moderately high degree of confidence in the deterministic exposure assessment for aluminum, as it relates to the average external dose associated with food, drinking water, soil and air, due to a large database of experimental information for most media. There is more uncertainty with respect to the maximum or high-end exposures in the population for the different media due to the variability in measured levels.

For total aluminum, food is the principal source of exposure, followed by soil, while exposure via drinking water and air combined is less than 2 % of total aluminum intake. Based on their use pattern, the three aluminum salts on the PSL2 are not significant contributors to the principal media of total aluminum exposure. Given the importance of food in the total exposure to aluminum, a probabilistic analysis of the exposure to aluminum from foods accounting for intakes by different subsets of the Canadian population is warranted. In addition, such an analysis should distinguish aluminum originating from food additives from natural aluminum sources in foods.

The greatest uncertainty with respect to the exposure assessment is the uncertainty and variability relating to the extent to which different aluminum salts are absorbed from the different media. Although some experimental bioavailability data are available for food and water, collectively the limited aluminum bioavailability data do not indicate that the relative bioavailabilities of aluminum in drinking water, soil and different types of food are significantly different. However, further research in this area, particularly in regard to soil, could provide evidence for significant differences that would in turn influence the human health risk characterization.

3.2.6 Recommendations for research

Areas for further research are described briefly below, in order to identify the main avenues for reducing the uncertainties associated with the human health database for aluminum.

3.2.6.1 Exposure assessment

Consideration of bioavailability is important to the characterization of human health risks of aluminum if relative bioavailabilities for different exposure media and different species (i.e., humans and experimental animals) differ from unity. This hypothesis could be explored through the determination of bioaccessibilities of aluminum in aluminum-treated drinking water, different soil and dust samples, in selected food items (e.g., processed cheese and packaged bakery items), and in laboratory animal chow, followed by the comparison of these in vitro bioaccessibilities with the in vivo bioavailability of aluminum determined in experimental studies for a given media.

In light of the wide use of aluminum-containing products applied to the skin, the dermal absorption of aluminum in humans should be more adequately characterized.

3.2.6.2 Exposure-response assessment

Further epidemiological study of aluminum exposure in the Canadian population is called for, to the extent that such research addresses the limitations of previous studies, including the characterization of aluminum exposure by dietary and other sources.

Additional experimental animal studies on toxicokinetics of different salts, including aluminum fluoride as well as the neurological and neurodevelopmental effects of aluminum, is necessary to provide information for better characterizing the exposure-response relationship. Following OECD guidelines for neurotoxicity and neurodevelopmental toxicity, these studies would include adequate numbers of animals, multiple doses, and examination of a standard array of neurological and neurodevelopmental endpoints. Note that one such study is currently underway in Canada.

3.3 Conclusion

CEPA 1999 64(a) and 64 (b): Based on the available data, it is proposed that the three aluminum salts, aluminum chloride, aluminum nitrate and aluminum sulphate, are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

CEPA 1999 64(c): Based on available data concerning the exposure of the Canadian population to aluminum chloride, aluminum nitrate and aluminum sulphate, and in consideration of the health effects observed in humans and in experimental animals, it is proposed that these aluminum salts are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore proposed that the three aluminum salts, aluminum chloride, aluminum nitrate and aluminum sulphate, do not meet the definition of “toxic” as set out in section 64 of CEPA 1999.

REFERENCES

Abd el-Fattah AA, al-Yousef HM, al-Bekairi AM, al-Sawaf HA. 1998. Vitamin E protects the brain against oxidative injury stimulated by excessive aluminum intake. Biochem Mol Biol Int 46(6): 1175-1180.

Abd-Elghaffar S, El-Sokkary GH, Sharkawy AA. 2005. Aluminum-induced neurotoxicity and oxidative damage in rabbits: protective effect of melatonin. Neuro Endocrinol Lett 26(5): 609-616.

Abercrombie DE, Fowler RC. 1997. Possible aluminum content of canned drinks. Toxicol Ind Health 13(5): 649-654.

Adams WJ, Conard B, Ethier G, Brix KV, Paquin PR, DiToro D. 2000. The challenges of hazard identification and classification of insoluble metals and metal substances for the aquatic environment. HERA 6: 1019-1038.

Adler AJ, Berlyne GM. 1985. Duodenal aluminum absorption in the rat: effect of vitamin D. Am J Physiol 249(2 Pt 1): G209-213.

[ATSDR] Agency for Toxic Substances and Disease Registry. 2006. Draft toxicological profile for aluminum. September 2006 draft for public comments. Washington (DC): U.S. Department of Health and Human Services, Public Health Service. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp22.html

Akila R, Stollery BT, Riihimaki V. 1999. Decrements in cognitive performance in metal inert gas welders exposed to aluminium. Occup Environ Med 56(9): 632-639.

Al Moutaery K, Al Deeb S, Biary N, Morais C, Ahmad Khan H, Tariq M. 2000. Effect of aluminum on neurological recovery in rats following spinal cord injury. J Neurosurg 93(2 Suppl): 276-282.

[AEC] Alberta Environmental Centre. 1984. Alum sludge treatment and disposal. Edmonton (AB): Underwood McLellan Ltd. for Alberta Environment.

[AEC] Alberta Environmental Centre. 1987. Binding, uptake and toxicity of alum sludge. Edmonton (AB): Alberta Environment, Standards and Approvals Division. 117 p.

Alexopoulos E, McCrohan CR, Powell JJ, Jugdaohsingh R, White, KN. 2003. Bioavailability and toxicity of freshly neutralized aluminium to the freshwater crayfish *Pacifastacus leniusculus*. Arch Environ Contam Toxicol 45: 509-514.

Alfrey AC. 1993. Aluminum and renal disease. Contrib Nephrol 102: 110-124.

Allen DD, Orvig C, Yokel RA. 1995. Evidence for energy-dependent transport of aluminum out of brain extracellular fluid. Toxicology 98: 31-39.

Allen DD, Yokel RA. 1992. Dissimilar aluminum and gallium permeation of the blood-barrier demonstrated by in vivo microdialysis. J Neurochem 58: 903-908.

Almer B, Dickson W, Ekstrom C, Homstrom E, Miller, U. 1974. Effects of acidification on Swedish lakes. Ambio 3: 30-36 [cited in Driscoll CT, Schecher WD. 1990].

Alstad NEW, Kjelsberg BM, Vøllestad LA, Lydersen E, Poléo ABS. 2005. The significance of water ionic strength on aluminium toxicity in brown trout (*Salmo trutta* L.). Environ Pollut 133: 333-342.

Alva AK, Edwards DG, Blamey FPC. 1986. Relationships between root length of soybean and calculated activities of aluminium monomers in nutrient solution. Soil Sci Soc Am J 50: 959–962.

Alvarez-Hernandez X, Adigosky SR, Stewart B, Glass J. 1994. Iron status affects aluminum uptake and transport by caco-2 Cells. J Nutr 124: 1574-1580.

Amador FC, Santos MS, Oliveira CR. 1999. Lipid peroxidation facilitates aluminum accumulation in rat brain synaptosomes. J Environ Health A 58: 427-435.

Appelberg M. 1985. Changes in haemolymph ion concentration of *Astacus astacus* L. and *Pacifastacus leniusculus* (DANA) after exposure to low pH and aluminium. Hydrobiologia 121: 19-25.

Aremu DA, Meshitsuka S. 2005. Accumulation of aluminum by primary culturel astrocytes from aluminum amino acid complex and its apoptotic effect. Brain Res 1031(2): 284–296.

Ares J. 1986. Identification of aluminum species in acid rain forest soil solutions on the basis of Al:F reaction kinetics. II. An example at the Solling area. Soil Sci 142: 13.

Ascherio A, Zhang S, Hernan M, Olek M, Coplan P, Brodovicz K. 2001. Hepatitis B vaccination and the risk of multiple sclerosis: case-control studies. Gastroenterol Clin Biol 25(10): 927-929.

Baker JP. 1982. Effects on fish of metals associated with acidification. In: Johnston J, editor. Acid rain/fisheries. Proceedings of an International Symposium on Acidic Precipitation and Fisheries Impact. American Fisheries Society, Bethesda, Maryland.

Baker JP, Bernard DP, Christensen SW, Sale MJ, Freda J, Heltcher K, Marmorek D, Rowe L, Scanlon P, Suter G, Warren-Hicks W, Welbourn P. 1990. Biological effects of changes in surface water acid–base chemistry. NAPAP Report 13. In: National Acid Precipitation Assessment Program, Acidic deposition: state of science and technology. Vol. II. Oak Ridge (TN): Oak Ridge National Laboratory, Environmental Sciences Division. p. 13.47–13.61 (Publication No. 3609).

Barcelo J, Guevara P, Poschenrieder C. 1993. Silicon amelioration of aluminum toxicity in teosinte (*Zea mays* L. ssp. *mexicana*). Plant Soil 154: 249–255.

Barnes LM. 1985. Some characteristics of primary sludges derived from physico-chemically treated sewage. Water Pollut 84: 502-514.

Bast-Pettersen R, Drablos PA, Goffeng LO, Thomassen Y, Torres CG. 1994. Neuropsychological deficit among elderly workers in aluminum production. Am J Ind Med 25(5): 649-662.

Basu S, Das Gupta R, Chaudhuri AN. 2000. Aluminium related changes in brain histology: protection by calcium and nifedipine. Indian J Exp Biol 38(9): 948-950.

Bataineh H, Al-Hamood M, Elbetieha A. 1998. Assessment of aggression, sexual behavior and fertility in adult male rat following long-term ingestion of four industrial metal salts. Hum Exp Toxicol 17: 570-576.

Baydar T, Nagymajtenyi L, Isimer A, Sahin G. 2005. Effect of folic acid supplementation on aluminum accumulation in rats. Nutrition 21(3): 406-410.

Baydar T, Papp A, Aydin A, Nagymajtenyi L, Schulz H, Isimer A, Sahin G. 2003. Accumulation of aluminum in rat brain: does it lead to behavioral and electrophysiological changes? Biol Trace Elem Res 92(3): 231-244.

Becaria A, Lahiri DK, Bondy SC, Chen D, Hamadeh A, Li H, Taylor R, Campbell A. 2006. Aluminum and copper in drinking water enhance inflammatory or oxidative events specifically in the brain. J Neuroimmunol 176(1): 16-23.

Becking G, Priest N, D. 1997. Is aluminium in drinking water a neurotoxic risk to humans? In: Press MU. Managing Health int Aluminium Industry. London. p. 300-307.

Beisinger KE, Christensen GM. 1972. Effects of various metals on survival, growth, reproduction and metabolism of *Daphnia magna*. J Fish Res Bd Canada 29: 1691-1700.

Bélanger N, Fyles H, Hendershot W. 1999. Chemistry, bioaccumulation and toxicity in the terrestrial environment — PSL2 assessment of aluminum salts. Montreal (QC): Environment Canada. Unpublished report.

Belles M, Albina ML, Sanchez DJ, Domingo JL. 1999. Lack of protective effects of dietary silicon on aluminium-induced maternal and developmental toxicity in mice. Pharmacol Toxicol 85(1): 1-6.

Bellia JP, Birchall JD, Roberts NB. 1996. The role of silicic acid in the renal excretion of aluminium. Ann Clin Lab Sci 26(3).

Bendell-Young L, Chouinard J, Pick FR. 1994. Metal concentrations in chironomids in relation to peatland geochemistry. Arch Environ Contam Toxicol 27: 186–194.

Bendell-Young L, Pick FR. 1995. Contrasting the geochemistry of aluminum among peatlands. Water Air Soil Pollut 81: 219–240.

Benson WH, Alberts JJ, Allen HE, Hunt CD, Newman MC. 1994. Synopsis of discussion Session on the bioavailability of inorganic contaminants. In: Hamelink JL, Landrum PF, Bergman HL, Benson WH, editors, Bioavailability: Physical, chemical and biological interactions. Proceedings of the 13th Pellston workshop, Michigan, August 17-22, 1992, Boca Raton (FL): Lewis Publishers. p. 63-72.

Bergerioux C, Boisvert J. 1979. Rapid neutron activation method for the determination of minerals in milk. Int J Nucl Med Biol 6(2): 128-131.

Bergman JJ, Boots BF. 1997. Alum sludge management at Buffalo Pound WTP. Report prepared by Buffalo Pound Water Treatment Plant for Environment Canada. Gatineau (QC): Environment Canada. Unpublished report.

Berkowitz J, Anderson MA, Graham RC. 2005. Laboratory investigation of aluminum solubility and solid-phase properties following alum treatment of lake waters. Water Res 39: 3918-3928.

Bernuzzi V, Desor D, Lehr PR. 1986. Effects of prenatal aluminum exposure on neuromotor maturation in the rat. Neurobehav Toxicol Teratol 8(2): 115-119.

Bernuzzi V, Desor D, Lehr PR. 1989a. Effects of postnatal aluminum lactate exposure on neuromotor maturation in the rat. Bull Environ Contam Toxicol 42(3): 451-455.

Bernuzzi V, Desor D, Lehr PR. 1989b. Developmental alternations in offspring of female rats orally intoxicated by aluminum chloride or lactate during gestation. Teratology 40(1): 21-27.

Bertrand A, Robitaille G, Boutin R, Nadeau P. 1995. Growth and ABA responses of maple seedlings to aluminum. Tree Physiol 15: 775–782.

Bertsch PM. 1990. The hydrolytic products of aluminum and their biological significance. Environ Geochem Health 12: 7–14.

Bertsch PM, Parker DR. 1996. Aqueous polynuclear aluminum species. In: Sposito G, editor, The environmental chemistry of aluminum. 2nd edition. Boca Raton, Florida: CRC Press p. 117–168.

Besser JM, Brumbaugh WG, May TW, Church SE, Kimball BA. 2001. Bioavailability of metals in stream food webs and hazards to brook trout (*Salvelinus fontinalis*) in the Upper Animas River watershed, Colorado. Arch Environ Contam Toxicol 40: 48-59.

Bia MJ, Cooper K, Schnall S, Duffy T, Hendler E, Malluche H, Solomon L. 1989. Aluminum induced anemia: pathogenesis and treatment in patients on chronic hemodialysis. Kidney Int 36(5): 852-858.

Bilkei-Gorzo A. 1993. Neurotoxic effect of enteral aluminium. Food Chem Toxicol 31(5): 357-361.

Birchall JD, Bellia JP, Roberts NB. 1996. On the mechanisms underlying the essentiality of silicon- interactions with aluminium and copper. Coord. Chem. Rev. 149: 231-240.

Birkeland PW. 1984. Soils and geomorphology. New York (NY): Oxford University Press. 372 p.

Bishop NJ, Morley R, Day JP, Lucas A. 1997. Aluminum neurotoxicity in preterm infants receiving intravenous-feeding solutions. N Engl J Med 336(22): 1557-1561.

Booth CE, McDonald DG, Simons BP, Wood CM. 1988. Effects of aluminum and low pH on net ion fluxes and ion balance in brook trout (*Salvelinus fontinalis*). Can. J. Fish. Aquat. Sci. 45: 1563–1574.

Bowdler NC, Beasley DS, Fritze EC, Goulette AM, Hatton JD, Hession J, Ostman DL, Rugg DJ, Schmittdiel CJ. 1979. Behavioral effects of aluminum ingestion on animal and human subjects. Pharmacol Biochem Behav 10(4): 505-512.

Boyce BF, Eider HY, Fell SG, Nicholson WA, Smith GD, Dempster DW, Gray CC, Boyle IT. 1981. Quantitation and localisation of aluminum in human cancellous bone in renal osteodystrophy. Scan Electron Microsc 3: 329-337.

Braul L, Viraraghavan T, Corkal D. 2001. Cold water effects on enhanced coagulation of high DOC, low turbidity water. Water Quality Research Journal of Canada 36(4): 701-717.

Brezonik PL, Mach CE, Downing G, Richardson N, Brigham M. 1990. Effects of acidification on minor and trace metal chemistry in Little Rock Lake, Wisconsin. Environ Toxicol Chem 9: 871–885.

Brown DJA. 1981. The effects of various cations on the survival of brown trout, *Salmo trutta*, at low pHs. J. Fish Biol 18: 31–40.

Brown BA, Driscoll CT. 1992. Soluble aluminum silicates: stoichiometry, stability and implications for environmental geochemistry. Science 256: 1667-1670.

Budaveri S, O'Neil MJ, Smith A, Heckelman PE, editors. 1989. The Merck index: An encyclopedia of chemicals, drugs, and biologicals. Rahway (NJ): Merck & Co.

Cameron RS, Ritchie GSP, Robson AD. 1986. Relative toxicities of inorganic aluminium complexes to barley. Soil Sci Soc Am J 50: 1231-1236.

Campbell A, Becaria A, Lahiri DK, Sharman K, Bondy SC. 2004. Chronic exposure to aluminum in drinking water increases inflammatory parameters selectively in the brain. J Neurosci Res 75(4): 565-572.

Campbell PGC. 1995. Interactions between trace metals and organisms: a critique of the free-ion activity model. In: Tessier A, Turner DR, editors, Metal speciation and bioavailability. Chichester: J. Wiley & Sons. p. 45–102.

Campbell PGC, Hansen HJ, Dubreuil B, Nelson WO. 1992. Geochemistry of Quebec North Shore salmon rivers during snowmelt: organic acid pulse and aluminum mobilization. Can. J. Fish. Aquat. Sci. 49: 1938-1952.

Campbell PGC, Lewis AG, Chapman PM, Crowder AA, Fletcher WK, Imber B, Luoma SN, Stokes PM, Winfrey M. 1988. Biologically available metals in sediments. NRCC 27694. Ottawa: National Research Council of Canada. 298 p.

Campbell PGC, Stokes PM. 1985. Acidification and toxicity of metals to aquatic biota. Can. J. Fish. Aquat. Sci. 42: 2034–2049.

Canada. 2000. *Canadian Environmental Protection Act: Persistence and Bioaccumulation Regulations,* P.C. 2000-348, 23 March, 2000, SOR/2000-107, Canada Gazette. Part II, vol. 134, no. 7, p. 607−612. Available from: http://canadagazette.gc.ca/partII/2000/20000329/pdf/g2-13407.pdf

[CCME] Canadian Council of Ministers of the Environment. 1998. Protocol for the derivation of Canadian tissue residue guidelines for the protection of wildlife that consume aquatic biota. Winnipeg (MB): Canadian Council of Ministers of the Environment.

[CCME] Canadian Council of Ministers of the Environment. 2003. Canadian water quality guidelines for the protection of aquatic life. Aluminium. In: Canadian environmental quality guidelines. Winnipeg (MB): Canadian Council of Ministers of the Environment.

[CCME] Canadian Council of Ministers of the Environment. 2008. Canada-wide strategy for the management of municipal wastewater effluent. Available at: www.ccme.ca/ourwork/water.html?category_id=81.

[CSHA] Canadian Study of Health and Aging. 1994. The Canadian Study of Health and Aging: Risk factors for Alzheimer's disease in Canada. Neurology 44: 2073–2080.

Caramelo CA, Cannata JB, Rodeles MR, Fernandez Martin JL, Mosquera JR, Monzu B, Outeirino J, Blum G, Andrea C, Lopez Farre AJ and others. 1995. Mechanisms of aluminum-induced microcytosis: lessons from accidental aluminum intoxication. Kidney Int 47(1): 164-168.

Cheminfo Services Inc. 2008. Characterization and analysis of aluminum salts and releases to the environment in Canada. Final report. Vancouver (BC): Prepared for Environment Canada, Environmental Stewardship Branch.

Chen J, Wang M, Ruan D, She J. 2002. Early chronic aluminium exposure impairs long-term potentiation and depression to the rat dentate gyrus in vivo. Neuroscience 112(4): 879-887.

Cherroret G, Bernuzzi V, Desor D, Hutin MF, Burnel D, Lehr PR. 1992. Effects of postnatal aluminum exposure on choline acetyltransferase activity and learning abilities in the rat. Neurotoxicol Teratol 14(4): 259-264.

Cherroret G, Capolaghi B, Hutin M-F, Burnel D, Desor D, Lehr PR. 1995. Effects of postnatal aluminum exposure on biological parameters in the rat plasma. Toxicol Lett 78: 119-125.

Chiba J, Kusumoto M, Shirai S, Ikawa K, Sakamoto S. 2002. The influence of fluoride ingestion on urinary aluminum excretion in humans. Tohoku J Exp Med 196(3): 139-19.

Choinière J, Beaumier M. 1997. Bruits de fond géochimiques pour différents environnements géologiques au Québec.

Church SE, Kimball BA, Frey DL, Ferderer DA, Yager TJ, Vaughn RB. 1997. Source, transport, and partitioning of metals between water, colloids, and bed sediments of the Animas River, Colorado. U.S. Geological Survey Open-File Report 97-151 [cited in Farag et al. 2007].

City of Ottawa. 2002. City Facilities Environmental Effects Monitoring Project, Summary Report: Study of Ottawa's Water Purification and Wastewater Treatment Plants. Prepared by the Water Environment Protection Program, Utilities Services, Transportation and Public Works.

Clark KL, Hall RJ. 1985. The effects of elevated hydrogen ion and aluminum concentrations on the survival of amphibian embryos and larvae. Can J Zool. 63: 116-123.

Clayton CA, Perritt RL, Pellizzari ED, Thomas KW, Whitmore RW, Wallace LA, Ozkaynak H, Spengler JD. 1993. Particle Total Exposure Assessment Methodology (PTEAM) study: distributions of aerosol and elemental concentrations in personal, indoor, and outdoor air samples in a southern California community. J Expo Anal Environ Epidemiol 3(2): 227-250.

Clayton RM, Sedowofia SK, Rankin JM, Manning A. 1992. Long-term effects of aluminium on the fetal mouse brain. Life Sci 51(25): 1921-1928.

Cochran M, Chawtur V, Phillips J, Dilena B. 1994. Effect of citrate infusion on urinary aluminium excretion in the rat. Clin Sci 86: 223-226.

Colomina MT, Gomez M, Domingo JL, Corbella J. 1994. Lack of maternal and developmental toxicity in mice given high doses of aluminium hydroxide and ascorbic acid during gestation. Pharmacol Toxicol 74(4-5): 236-239.

Colomina MT, Gomez M, Domingo JL, Llobet JM, Corbella J. 1992. Concurrent ingestion of lactate and aluminum can result in developmental toxicity in mice. Res Commun Chem Pathol Pharmacol 77(1): 95-106.

Colomina MT, Roig JL, Sanchez DJ, Domingo JL. 2002. Influence of age on aluminum-induced neurobehavioral effects and morphological changes in rat brain. Neurotoxicology 23(6): 775-781.

Colomina MT, Roig JL, Torrente M, Vicens P, Domingo JL. 2005. Concurrent exposure to aluminum and stress during pregnancy in rats: Effects on postnatal development and behavior of the offspring. Neurotoxicol Teratol 27(4): 565-574.

Colomina MT, Sanchez DJ, Sanchez-Turet M, Domingo JL. 1999. Behavioral effects of aluminum in mice: influence of restraint stress. Neuropsychobiology 40(3): 142-149.

Commissaris RL, Cordon JJ, Sprague S, Keiser J, Mayor GH, Rech RH. 1982. Behavioral changes in rats after chronic aluminum and parathyroid hormone administration. Neurobehav Toxicol Teratol 4(3): 403-410.

Confavreux C, Suissa S, Saddier P, Bourdes V, Vukusic S. 2001. Vaccinations and the risk of relapse in multiple sclerosis. Vaccines in Multiple Sclerosis Study Group. N Engl J Med 344(5): 319-326.

Connor DJ, Harrell LE, Jope RS. 1989. Reversal of an aluminum-induced behavioral deficit by administration of deferoxamine. Behav Neurosci 103(4): 779-783.

Connor DJ, Jope RS, Harrell LE. 1988. Chronic, oral aluminum administration to rats: cognition and cholinergic parameters. Pharmacol Biochem Behav 31(2): 467-474.

Connor JN, Martin MR. 1989. An assessment of sediment phosphorus inactivation, Kezar Lake, New Hampshire. Water Resources Bulletin 25(4): 845–853.

Cornwell DA, Burmaster JW, Francis JL, Friedline JCJ, Houck C, King PH, Knocke WR, Novak JT, Rolan AT, San Giacomo R. 1987. Committee report: research needs for alum sludge discharge. Sludge Disposal Committee. J Am Water Works Assoc 79: 99–104.

Corrales I, Poschenrieder C, Barcelo J. 1997. Influence of silicon pretreatment on aluminium toxicity in maize roots. Plant Soil 190: 203–209.

Courchesne F, Hendershot WH. 1997. *La genèse des podzols*. Géographie physique et quaternaire 51: 235–250.

Cournot-Witmer G, Zinngraff J, Plachot JJ, Escaig F, Lefevre R, Boumati P, Bourdeau A, Garadedian M, Galle P, Bourdon R and others. 1981. Aluminium localization in bone from hemodialyzed patients: Relationship to matrix mineralization. Kidney Int 20: 375–378.

Cox AE, Camberato JJ, Smith BR. 1997. Phosphate availability and inorganic transformation in an alum sludge-affected soil. J Environ Qual 26: 1393–1398.

Crane M, Whitehouse P, Comber S, Ellis J, Wilby R. 2005. Climate change influences on environmental and human health chemical standards. Human and Ecological Risk Assessment 11: 289-318.

Cranmer JM, Wilkins JD, Cannon DJ, Smith L. 1986. Fetal-placental-maternal uptake of aluminum in mice following gestational exposure: effect of dose and route of administration. Neurotoxicology 7(2): 601-608.

Cronan CS, Driscoll CT, Newton RM, Kelly JM, Schofield CL, Bartlett RJ, April R. 1990. A comparative analysis of aluminum biogeochemistry in a northeastern and a southeastern forested watershed. Water Resour Res 26: 1413–1430.

Cronan CS, Schofield CL. 1990. Relationships between aqueous aluminum and acidic deposition in forested watersheds of North America and Europe. Environ Sci Technol 24: 1100–1105.

Cronan CS, Walker WJ, Bloom PR. 1986. Predicting aqueous aluminum concentrations in natural waters. Nature (London) 324: 140–143.

Cumming JR, Weinstein LH. 1990. Al mycorrhizal interactions in physiology of pitch pine seedling. Plant Soil 125: 7–18.

Cunat L, Lanhers MC, Joyeux M, Burnel D. 2000. Bioavailability and intestinal absorption of aluminum in rats: effects of aluminum compounds and some dietary constituents. Biol Trace Elem Res 76(1): 31-55.

Dabeka B. 2007. Draft - Résultats préliminaires des données brutes de l'étude de la diète totale - 2000 à 2002. Ottawa.

Dann T. 2007. Output for PM2.5 and PM10 Al for 1986-2006. Personal communication with Tom Dann. In: Analysis and Air Quality, Environment Canada. Ottawa.

Dave G. 1985. The influence of pH on the toxicity of aluminum, cadmium, and iron to eggs and larvae of the zebrafish, *Brachydanio rerio.* Ecotoxicol Environ Saf 10: 253–267.

Dave G. 1992. Sediment toxicity and heavy metals in 11 lime reference lakes of Sweden. Water Air Soil Pollut 63: 187–200.

Dave KR, Syal AR, Katyare SS. 2002. Effect of long-term aluminum feeding on kinetics attributes of tissue cholinesterases. Brain Res Bull 58(2): 225-233.

David MB, Driscoll CT. 1984. Aluminum speciation and equilibria in soil solutions of a haplorthod in the Adirondack Mountains (New York, U.S.A.). Geoderma 33: 297–318.

Day JP, Barker J, King SJ, Miller RV, Templar J. 1994. Biological chemistry of aluminium studied using 26Al and accelerator mass spectrometry. Nucl Instrum Methods Phys Res 92: 463-468.

DeWald LE, Sucoff E, Ohno T, Buschena C. 1990. Response of northern red oak (*Quercus rubra*) seedlings to soil solution aluminium. Can J For Res. 20: 331–336.

Dillon PJ, Evans HE, Scholer PJ. 1988. The effects of acidification on metal budgets of lakes and catchments. Biogeochemistry 3: 201–220.

Divine KK, Lewis JL, Grant PG, Bench G. 1999. Quantitative particle-induced X-ray emission imaging of rat olfactory epithelium applied to the permeability of rat epithelium to inhaled aluminum. Chem Res Toxicol (7): 575–581.

Do P. 1999. Personal communication with Environment Canada. Engineering and Environmental Services, City of Calgary, Alberta.

Domingo JL, Gomez M, Sanchez DJ, Llobet JM, Corbella J. 1993. Effect of various dietary constituents on gastrointestinal absorption of aluminum from drinking water and diet. Res Commun Chem Pathol Pharmacol 79(3): 377-380.

Domingo JL, Llorens J, Sanchez DJ, Gomez M, Llobet JM, Corbella J. 1996. Age-related effects of aluminum ingestion on brain aluminum accumulation and behavior in rats. Life Sci 58(17): 1387-1395.

Domingo JL, Paternain JL, Llobet JM, Corbella J. 1987a. Effects of oral aluminum administration on perinatal and postnatal development in rats. Res Commun Chem Pathol Pharmacol 57(1): 129-132.

Donald JM, Golub MS, Gershwin ME, Keen CL. 1989. Neurobehavioral effects in offspring of mice given excess aluminum in diet during gestation and lactation. Neurotoxicol Teratol 11(4): 345-351.

Driscoll CT, Baker JP, Bisogni JJ, Schofield CL. 1980. Effect of aluminum speciation on fish in dilute acidified waters. Nature 284: 161-164.

Driscoll CT, Bisogni JJ. 1984. Weak acid/base systems in dilute acidified lakes and streams in the Adirondack region of New York State. In: Schnoor JL, editor, Modeling of total acid precipitation impacts. Boston: Butterworth. p. 53-72.

Driscoll CT, Postek KM. 1996. The chemistry of aluminum in surface waters. In: Sposito G, editor, The environmental chemistry of aluminum. 2nd edition. Boca Raton (FL): CRC Press. p. 363–418.

Driscoll CT, Schecher WD. 1988. Aluminum in the environment. In: Sigel H, Sigel A, editors, Metal ions in biological systems. Aluminum and its role in biology. Vol. 24. New York (NY): Marcel Dekker. p. 59–122.

Driscoll CT, Schecher WD. 1990. The chemistry of aluminum in the environment. J. Environ Perspect Health 12: 28–49.

Driscoll CT, Otton JK, Inverfeldt A. 1994. Trace metals speciation and cycling. In: Moldan B, Cerny J, editors, Biogeochemistry of small catchments: a tool for environmental research. New York (NY): Wiley and Sons. pp. 299–322.

Driscoll CT, van Breemen N, Mulder J. 1985. Aluminum chemistry in a forested spodosol. Soil Sci Soc Am J. 49: 437–444.

Drueke TB, Jouhanneau P, Banide H, Lacour B, Yiou F, Raisbeck G. 1997. Effects of silicon, citrate and the fasting state on the intestinal absorption of aluminium in rats. Clin Sci (Lond) 92(1): 63-67.

Duan J, Wang J, Graham N, Wilson F. 2002. Coagulation of humic acid by aluminium sulphate in saline water conditions. Desalination 150: 1-14.

Dudka S, Ponce-Hernandez R, Hutchinson TC. 1995. Current level of total element concentrations in the surface layer of SUdbury's soils. Sci Total Environ 162: 161-171.

Duis K, Oberemm A. 2001. Aluminium and calcium – key factors determining the survival of vendace embryos and larvae in post-mining lakes? Limnologica 31: 3-10.

Dunn CE. 1990. Lithogeochemistry study of the Cretaceous in Central Saskatchewan - Preliminary Report. Saskatchewan Geological Survey 90-4: 193-197.

Durand I, Keller JM, Cherroret G, Colins S, Dauca M, Lehr PR. 1993. Impact d'une intoxication aluminique postnatale précoce sur l'épithélium dodénal de rat: Etudes en microscopie électronique à transmission et en microanalyse de rayons X. Bulletin de l'Académie et de la Société lorraines des sciences 65(1): 3-19.

Dussault EB, Playle RC, Dixon DG, McKinley RS. 2001. Effects of sublethal, acidic aluminum exposure on blood ions and metabolites, cardiac output, heart rate, and stroke volume of rainbow trout, *Oncorhynchus mykiss*. Fish Physiol Biochem 25: 347-357.

DuVal G, Brubb B, Bentley P. 1986. Aluminum accumulation in the crystalline lens of humans and domestic animals. Trace Elem Med 3: 100-104.

Edwardson JA, Moore PB, Ferrier IN, Lilley JS, Newton GW, Barker J, Templar J, Day JP. 1993. Effect of silicon on gastrointestinal absorption of aluminium. Lancet 342(8865): 211-212.

Eickhoff TC, Myers M. 2002. Workshop summary. Aluminum in vaccines. Vaccine 20 Suppl 3: S1-4.

El-Demerdash FM. 2004. Antioxidant effect of vitamin E and selenium on lipid peroxidation, enzyme activities and biochemical parameters in rats exposed to aluminium. J Trace Elem Med Biol 18(1): 113-121.

El-Rahman SS. 2003. Neuropathology of aluminum toxicity in rats (glutamate and GABA impairment). Pharmacol Res 47(3): 189-194.

Environment Canada. 1995. National Analysis of Trends in Emergencies System (NATES) database output.

Environment Canada. 1996. Ecological risk assessments of Priority substances under the Canadian Environmental Protection Act. Resource document. Gatineau (QC): Environment Canada, Commerical Chemicals Branch. Available on request.

Environment Canada. 1997. Notice respecting the second Priority Substances List and di(2-ethylhexyl) phthalate. *Canada Gazette*, Part I, February 15, 1997. p. 366–368.

Environment Canada. 2008a. Summary of Provincial and Territorial Management Activities Pertaining to Drinking Water Treatment Plant Waste Discharge to Surface Waters in Canada. Unpublished table. Existing Substances Division, September 2008. Available on request.

Environment Canada. 2008b. National Enforcement Management Information System and Intelligence System (NEMISIS) database output.

Environment Canada 2008c. Personal communication Director of Water and Wastewater Services, City of Ottawa.

Environment Canada and Health Canada. 2000. State of the science report for aluminum chloride, aluminum nitrate and aluminum sulphate. Ottawa (ON): Environment Canada, Health Canada.

Environmental & OHP. 2005. Étude sur la santé dans la région de Belledune. Area Health study - Appendix A - Human Health RIsk assessment. Department of Health and Wellness, Government of New Brunswick.

European Commission. 2000a. IUCLID (International Uniform Chemical Information Database) Dataset. Existing Chemical Substance ID: 7446-70-0. Aluminium chloride. European Chemicals Bureau. Accessed July 26, 2007. http://ecb.jrc.it/documents/Existing_Chemicals/IUCLID/DATA_SHEETS/7446700.pdf.

European Commission. 2000b. IUCLID Dataset. Existing Chemical Substance ID: 10043-01-3. Aluminium sulphate. European Chemicals Bureau. Accessed July 26, 2007. http://ecb.jrc.it/documents/Existing_Chemicals/IUCLID/DATA_SHEETS/7446700.pdf.

[EFSA] European Food Safety Authority. 2008. Safety of aluminium from dietary intake. Scientific Opinion of the Panel on Food Additives, Flavourings, Processing Aids and Food Contact Materials (AFC). The EFSA Journal 754: 1-4.

Exley C. 2006. Aluminium-adsorbed vaccines. Lancet Infect Dis 6(4): 189.

Exley C, Burgess E, Day JP, Jeffery EH, Melethil S, Yokel RA. 1996. Aluminum toxicokinetics. J Toxicol Environ Health 48(6): 569-584.

Farag AM, Nimick DA, Kimball BA, Church SE, Harper DD, Brumbaugh WG. 2007. Concentrations of metals in water, sediment, biofilm, benthic macroinvertebrates, and fish in the Boulder River watershed, Montana, and the role of colloids in metal uptake. Arch Environ Contam Toxicol 52: 397-409.

Farag AM, Woodward DF, Little EE, Steadman B, Vertucci FA. 1993. The effects of low pH and elevated aluminum on Yellowstone cutthroat trout (*Oncorhynchus clarki bouvieri*). Environ Toxicol Chem 12: 719–731.

Fattoretti P, Bertoni-Freddari C, Balietti M, Giorgetti B, Solazzi M, Zatta P. 2004. Chronic aluminum administration to old rats results in increased levels of brain metal ions and enlarged hippocampal mossy fibers. Ann N Y Acad Sci 1019: 44-47.

Fattoretti P, Bertoni-Freddari C, Balietti M, Mocchegiani E, Scancar J, Zambenedetti P, Zatta P. 2003. The effect of chronic aluminum(III) administration on the nervous system of aged rats: clues to understand its suggested role in Alzheimer's disease. J Alzheimers Dis 5(6): 437-444.

Fiejka MA, Fiejka E, Dlugaszek M. 1996. Effect of aluminum hydroxide administration on normal mice: tissue distribution and ultrastructural localization of aluminum in liver. Pharmacol Toxicol 78: 123-128.

Findlow JA, Duffield JR, Williamns DR. 1990. The chemical speciation of aluminum in milk. Chem Spec Bioavail 2: 3-32.

Flarend R, Bin T, Elmore D, Hem SL. 2001. A preliminary study of the dermal absorption of aluminium from antiperspirants using aluminium-26. Food Chem Toxicol 39(2): 163-168.

Flaten TP. 1990. Geographical associations between aluminium in drinking water and death rates with dementia (including Alzheimer's disease), Parkinson's disease and amyotrophic lateral sclerosis in Norway. Aluminium and disease. Norway. p 152-167.

Flaten TP, Glattre E, Viste A, Sooreide O. 1991. Mortality from dementia among gastroduodenal ulcer patients. J Epidemiol Community Health 45(3): 203-206.

Fleming J, Joshi JG. 1987. Ferritin: isolation of aluminum-ferritin complex from brain. Proc Natl Acad Sci U S A 84(22): 7866-7870.

Flora SJ, Dhawan M, Tandon SK. 1991. Effects of combined exposure to aluminium and ethanol on aluminium body burden and some neuronal, hepatic and haematopoietic biochemical variables in the rat. Hum Exp Toxicol 10(1): 45-48.

Flora SJ, Mehta A, Satsangi K, Kannan GM, Gupta M. 2003. Aluminum-induced oxidative stress in rat brain: response to combined administration of citric acid and HEDTA. Comp Biochem Physiol C Toxicol Pharmacol 134(3): 319-328.

Florence AL, Gauthier A, Ponsar C, Van den Bosch de Aguilar P, Crichton RR. 1994. An experimental animal model of aluminium overload. Neurodegeneration 3(4): 315-323.

Foley CM, Polinsky MS, Gruskin AB, Baluarte HJ, Grover WD. 1981. Encephalopathy in infants and children with chronic renal disease. Arc Neurol 38: 656-658.

Forbes WF, Agwani N. 1994. Geochemical Risk factors for mental functioning, based on the Ontario Longitudinal study of aging (LSA) III. The effects of different aluminum-containing compounds. La revue canadienne du vieillissement. Can J Aging 13(4): 488-498.

Forbes WF, Agwani N, Lachmaniuk P. 1995a. Geochemical Risk factors for mental functioning, based on the Ontario Longitudinal study of aging (LSA) IV. The role of silicone-containing compounds. La revue canadienne du vieillissement. Can J Aging 14(4): 630-641.

Forbes WF, Gentleman JF, Lessard S. 1995b. Geochemical Risk factors for mental functioning, based on the Ontario Longitudinal study of aging (LSA) V. Comparisons of the results, relevant to aluminum water concentrations, obtained from the LSA and from Death Certificates mentioning Dementia. La revue canadienne du vieillissement. Can J Aging 14(4): 642-656.

Forbes WF, Hayward LM, Agwani N. 1992. Geochemical Risk factors for mental functioning, based on the Ontario Longitudinal study of aging (LSA) I. Results from a preliminary investigation. Can J Aging II(3): 269-280.

Forbes WF, Hayward LM, Agwani N, McAiney CA. 1994. Geochemical Risk factors for mental functioning, based on the Ontario Longitudinal study of aging (LSA) II. The role of pH. Can J Aging 13(3): 249-267.

Forbes WF, McLachlan DR. 1996. Further thoughts on the aluminum-Alzheimer's disease link. J Epidemiol Community Health 50(4): 401-403.

Forster DP, Newens AJ, Kay DW, Edwardson JA. 1995. Risk factors in clinically diagnosed presenile dementia of the Alzheimer type: a case-control study in northern England. J Epidemiol Community Health 49(3): 253-258.

Fortin C, Campbell PGC. 1999. Calculs de spéciation pour l'aluminium rejeté en eaux courantes. Montréal (QC) : Environment Canada, Environmental Protection Service.

Fraga CG, Oteiza PI, Golub MS, Gershwin ME, Keen CL. 1990. Effects of aluminum on brain lipid peroxidation. Toxicol Lett 51(2): 213-219.

France RL, Stokes PM. 1987. Influence of Mn, Ca and Al on hydrogen ion toxicity to the amphipod *Hyalella azteca.* Can J Zool. 65: 3071–3078.

Frecker MF. 1991. Dementia in Newfoundland: identification of a geographical isolate? J Epidemiol Community Health 45(4): 307-311.

Freda J. 1991. The effects of aluminum and other metals on amphibians. Environ Pollut 71: 305–328.

Freeman RA, Everhart WH. 1971. Toxicity of aluminum hydroxide complexes in neutral and basic media to rainbow trout. Trans. Am. Fish. Soc. 4: 644–658.

Frick KG, Herrmann J. 1990. Aluminum accumulation in a lotic mayfly at low pH — a laboratory study. Ecotoxicol Environ Saf 19: 81–88.

Froment DH, Buddington B, Miller NL, Alfrey AC. 1989. Effect of solubility on the gastrointestinal absorption of aluminum from various aluminum compounds in the rat. J Lab Clin Med 114(3): 237-242.

Gagnon C, Turcotte P. 2007. Role of colloids in the physical speciation of metals in the dispersion plume of a major municipal effluent. J Water Sci 20(3): 275-285.

Ganrot PO. 1986. Metabolism and possible health effects of aluminum. Environ Health Perspect 65: 363-441.

Garbossa G, Galvez G, Castro ME, Nesse A. 1998. Oral aluminum administration to rats wih normal renal function. 1. Impairment of erythropoiesis. Hum Exp Toxicol 17(6): 312-317.

Garrels RM, Mackenzie FT, Hunt C. 1975. Chemical cycles and the global environment. Los Altos (CA): William Kaufmann Inc.206 p. [cited in Driscoll and Postek 1996].

Garrett RG. 1998. Aluminium levels in Canadian soils and glacial tills from the Prairies and Southern Ontario. Geological Survey of Canada. p 5.

Gauthier E, Fortier I, Courchesne F, Pepin P, Mortimer J, Gauvreau D. 2000. Aluminum forms in drinking water and risk of Alzheimer's disease. Environ Res 84(3): 234-246.

Gensemer RW, Playle RC. 1999. The bioavailability and toxicity of aluminum in aquatic environments. Critical Reviews in Environmental Science and Technology 29(4): 315-450.

George DB, Berk SG, Adams VD, Morgan EL, Roberts RO, Holloway CA, Lott RC, Holt LK, Ting RS, Welch AW. 1991. Alum sludge in the aquatic environment. Denver (CO): American Water Works Association Research Foundation. 224 p.

George DB, Berk SG, Adams VD, Ting RS, Roberts RO, Parks LH, Lott RC. 1995. Toxicity of alum sludge extracts to a freshwater alga, protozoan, fish, and marine bacterium. Arch Environ Contam Toxicol 29: 149–158.

Germain A, Gagnon C, Lind CB. 2000. Entry and exposure characterization for aluminum chloride, aluminum nitrate and aluminum sulfate. Supporting document for *Canadian Environmental Protection Act* Priority Substances List Assessment Program.Unpublished report. Montreal (PQ): Environment Canada. 111 p.

Giroux M, Rompré M, Carrier D, Audesse P, Lemieux M. 1992. Caractérisation de la teneur en métaux lourds totaux et disponibles des sols du Québec. agrosol V (2): 46-55.

Golub MS, Donald JM, Gershwin ME, Keen CL. 1989. Effects of aluminum ingestion on spontaneous motor activity of mice. Neurotoxicol Teratol 11(3): 231-235.

Golub MS, Germann SL. 1998. Aluminum effects on operant performance and food motivation of mice. Neurotoxicol Teratol 20(4): 421-427.

Golub MS, Germann SL. 2000. Long-term consequences of developmental aluminum (Al) in mice. Neurotoxicol Teratol 22(3): 460.

Golub MS, Germann SL. 2001a. Spatial learning strategies in aged mice exposed to aluminum (Al). Neurotoxicol Teratol 23(3): 293.

Golub MS, Germann SL. 2001b. Long-term consequences of developmental exposure to aluminum in a suboptimal diet for growth and behavior of Swiss Webster mice. Neurotoxicol Teratol 23(4): 365-372.

Golub MS, Germann SL, Han B, Keen CL. 2000. Lifelong feeding of a high aluminum diet to mice. Toxicology 150(1-3): 107-117.

Golub MS, Germann SL, Torrente M. 2002. In utero aluminum exposure affects myelination in the guinea pig. Neurotoxicol Teratol 24(3): 423.

Golub MS, Gershwin ME, Donald JM, Negri S, Keen CL. 1987. Maternal and developmental toxicity of chronic aluminum exposure in mice. Fundam Appl Toxicol 8(3): 346-357.

Golub MS, Han B, Keen CL. 1996a. Iron and manganese uptake by offspring of lactating mice fed a high aluminum diet. Toxicology 109: 111-118.

Golub MS, Han B, Keen CL. 1996b. Developmental patterns of aluminum and five essential mineral elements in the central nervous system of the fetal and infant guinea pig. Biol Trace Elem Res 55(3): 241-251.

Golub MS, Han B, Keen CL, Gershwin ME. 1992a. Effects of dietary aluminum excess and manganese deficiency on neurobehavioral endpoints in adult mice. Toxicol Appl Pharmacol 112(1): 154-160.

Golub MS, Han B, Keen CL, Gershwin ME. 1993. Developmental patterns of aluminum in mouse brain and effects of dietary aluminum excess on manganese deficiency. Toxicology 81(1): 33-47.

Golub MS, Han B, Keen CL, Gershwin ME. 1994. Auditory startle in Swiss Webster mice fed excess aluminum in diet. Neurotoxicol Teratol 16(4): 423-425.

Golub MS, Han B, Keen CL, Gershwin ME, Tarara RP. 1995. Behavioral performance of Swiss Webster mice exposed to excess dietary aluminum during development or during development and as adults. Toxicol Appl Pharmacol 133(1): 64-72.

Golub MS, Keen CL, Gershwin ME. 1992b. Neurodevelopmental effect of aluminum in mice: fostering studies. Neurotoxicol Teratol 14(3): 177-82.

Golub MS, Tarara RP. 1999. Morphometric studies of myelination in the spinal cord of mice exposed developmentally to aluminum. Neurotoxicology 20(6): 953-959.

Gomez M, Bosque MA, Domingo JL, Llobet JM, Corbella J. 1990. Evaluation of the maternal and developmental toxicity of aluminum from high doses of aluminum hydroxide in rats. Vet Hum Toxicol 32(6): 545-548.

Gomez M, Domingo JL, Llobet JM. 1991. Developmental toxicity evaluation of oral aluminum in rats: influence of citrate. Neurotoxicol Teratol 13(3): 323-328.

Goncalves PP, Silva VS. 2007. Does neurotransmission impairment accompany aluminum neurotoxicity? J Inorg Biochem (101): 1291-1338.

Gong QH, Wu Q, Huang XN, Sun AS, Nie J, Shi JS. 2006. Protective effect of Ginkgo biloba leaf extract on learning and memory deficit induced by aluminum in model rats. Chin J Integr Med 12(1): 37-41.

Gong QH, Wu Q, Huang XN, Sun AS, Shi JS. 2005. Protective effects of Ginkgo biloba leaf extract on aluminum-induced brain dysfunction in rats. Life Sci 77(2): 140-148.

Gonzalez-Munoz MJ, Pena A, Meseguer I. 2008. Role of beer as a possible protective factor in preventing Alzheimer's disease. Food Chem Toxicol 46: 49–56.

Gopalakrishnan S, Thilagam H, Raja PV. 2007. Toxicity of heavy metals on embryogenesis and larvae of the marine sedentary polychaete *Hydroides elegans*. Arch Environ Contam Toxicol 52: 171-178.

Gourrier-Fréry C, Fréry N. 2004. Aluminium. EMC- Toxicologie Pathologie 1: 79-95.

Gramiccioni L, Ingrao G, Milana MR, Santaroni P, Tomassi G. 1996. Aluminium levels in Italian diets and in selected foods from aluminium utensils. Food Addit Contam 13(7): 767-774.

Graves AB, Rosner D, Echeverria D, Mortimer JA, Larson EB. 1998. Occupational exposures to solvents and aluminium and estimated risk of Alzheimer's disease. Occup Environ Med 55(9): 627-633.

Graves AB, White E, Koepsell TD, Reifler BV, Van Belle G, Larson EB. 1990. The association between aluminum-containing products and Alzheimer's disease. J Clin Epidemiol 43 (1): 35-44.

[GVRD] Greater Vancouver Regional District. 2006. Wastewater. The Greater Vancouver Sewerage & Drainage District quality control annual report 2006. 131 p + Appendices. Available at: http://www.gvrd.bc.ca/sewerage/pdf/QualityControlAnnualReport2006forGVS&DD.pdf.

Greger JL, Baier MJ. 1983. Excretion and retention of low or moderate levels of aluminium by human subjects. Food Chem Toxicol 21(4): 473-477.

Greger JL, Chang MM, MacNeil GG. 1994. Tissue turnover of aluminum and Ga-67: effect of iron status. Proceedings of the Society for Experimental Biology and Medicine 207(89-96).

Greger JL, Radzanowski GM. 1995. Tissue aluminium distribution in growing, mature and ageing rats: relationship to changes in gut, kidney and bone metabolism. Food Chem Toxicol 33(10): 867-875.

Guillard O, Fauconneau B, Olichon D, Dedieu G, Deloncle R. 2004. Hyperaluminemia in a woman using an aluminum-containing antiperspirant for 4 years. Am J Med 117(12): 956-959.

Gun RT, Korten AE, Jorm AF, Henderson AS, Broe GA, Creasey H. 1997. Occupational risk factors for alzheimer disease: A case-control Study. Alzheimer Dis Assoc Disord 11(1): 21-27.

Gundersen DT, Bustaman S, Seim WK, Curtis LR. 1994. pH, hardness, and humic acid influence aluminum toxicity to rainbow trout (*Oncorhynchus mykiss*) in weakly alkaline waters. Can. J. Fish. Aquat. Sci. 51: 1345–1355.

Guo T, Chen Y, Zhang Y, Jin Y. 2006. Alleviation of Al toxicity in barley by addition of calcium. Agric. Sci. China 5(11): 828-833.

Gupta A, Shukla GS. 1995. Effect of chronic aluminum exposure on the levels of conjugated dienes and enzymatic antioxidants in hippocampus and whole brain of rat. Bull Environ Contam Toxicol 55(5): 716-722.

Gupta VB, Anitha S, Hegde ML, Zecca L, Garruto RM, Ravid R, Shankar SK, Stein R, Shanmugavelu P, Jagannatha Rao KS. 2005. Aluminium in Alzheimer's disease: are we still at a crossroad? Cell Mol Life Sci. 62(2): 143-158.

Guyton AC. 1991. Textbook of Medical Physiology. Philadelphia: WB Saunders Co. 1014 p.

Guzyn W. 2003. Phytotoxicology 2001 and 2002. Investigations: Algoma Ore Division, Twp. of Michipicoten (Wawa). Ministry of Environment. Ontario.

Hackenberg U. 1972. Chronic ingestion by rats of standard diet treated with aluminum phosphide. Toxicol Appl Pharmacol 23(1): 147-158.

Hall WS, Hall LW, Jr. 1989. Toxicity of alum sludge to *Ceriodaphnia dubia* and *Pimephales promelas*. Bull Environ Contam Toxicol 42: 791-798.

Hall RJ, Driscoll CT, Likens GE, Pratt JM. 1985. Physical, chemical, and biological consequences of episodic aluminum additions to a stream. Limnol Oceanogr 30: 212-220.

Haluschak PW, Mills GF, Eilers RG, Grift S. 1998. Status of selected Trace elements in Agricultural Soils of Southern Manitoba. Agriculture and Agri-food Canada. Soil Resource section. Soils and Crops Branch, Manitoba Agriculture. 46 p.

Hammond KE, Evans DE, Hodson MJ. 1995. Aluminium–silicon interactions in barley (*Hordeum vulgare* L.) seedlings. Plant Soil 173: 89–95.

Hanninen H, Matikainen E, Kovala T, Valkonen S, Riihimaki V. 1994. Internal load of aluminum and the central nervous system function of aluminum welders. Scand J Work Environ Health 20(4): 279-285.

Haram EM, Weberg R, Berstad A. 1987. Urinary excretion of aluminium after ingestion of sucralfate and an aluminium-containing antacid in man. Scand J Gastroenterol 22(5): 615-618.

Harris WR, Berthon G, Day JP, Exley C, Flaten TP, Forbes WF, Kiss T, Orvig C, Zatta PF. 1996. Speciation of aluminum in biological systems. J Toxicol Environ Health 48(6): 543-568.

Havas M. 1985. Aluminum bioaccumulation and toxicity to *Daphnia magna* in soft water at low pH. Can. J. Fish. Aquat. Sci. 42: 1741–1748.

Havas M. 1986. A hematoxylin staining technique to locate sites of aluminum binding in aquatic plants and animals. Water, Air, Soil Pollut. 30: 735-741.

Havas M, Likens GE. 1985. Changes in ^{22}Na influx and outflux in *Daphnia magna* (Straus) as a function of elevated Al concentrations in soft water at low pH. Proc Natl Acad Sci U S A 82: 7345-7349 [cited in Rosseland et al. 1990].

Havens KE. 1990. Aluminum binding to ion exchange sites in acid-sensitive versus acid-tolerant cladocerans. Environ Pollut 64: 133–141.

Health Canada. 1994. Human Health Risk Assessment for Priority Substances.

Health Canada. 1998a. Exposure Factors for Assessing total daily intake of Priority substances by the General Population of Canada - Draft report. Ottawa (ON): Health Canada, Environmental Health Directorate, Priority Substances Section.

Health Canada. 1998b. Guidelines for Canadian Drinking Water Quality - Technical Documents: Aluminum. Ottawa. 22 p.

Health Canada. 1999. CEPA Supporting Documentation - Human Exposure Assessment of aluminium chloride, aluminium nitrate, and aluminium sulfate. Canada: Health Canada. 1-21 p.

Health Canada. 2003. Trace Metal Analysis – Infant Formula [Internet]. Available from: http://www.hc-sc.gc.ca/fn-an/surveill/other-autre/infant-nourisson/index-eng.php.

Health Canada. 2004. Consolidation of the Food and Drugs Act and the Food and Drug Regulations. Division 16. Food Additives and tables, Part B. July 2004, Ottawa. Available at: http://www.hc-sc.gc.ca/fn-an/legislation/acts-lois/fda-lad/index-eng.php.

Health Canada. 2007a. Guidelines for Canadian Drinking Water Quality Summary Table. Prepared by the Federal-Provincial-Territorial Committee on Drinking Water of the Federal-Provincial-Territorial Committee on Health and the Environment. March 2007. Available from: (www.healthcanada.gc.ca/waterquality).

Health Canada. 2007b. Total water systems in Canada. Personal communication with members of the Federal/Provincial/Territorial Committee on Drinking Water and personnal communications with some municipalities in Quebec and Alberta. Ottawa.

Health Canada. 2007c. Personal communication with the McLaughlin Centre of Population Health Risk Assessment, Institute of Population Health, University of Ottawa. Ottawa.

Health Canada. 2008a. Supporting Document for the Second Priority Substances List Draft Assessment for Aluminum Salts.

Health Canada. 2008b. Personal communication with the Food Packaging Materials and Incidental Additives Section, Chemical Health Hazard Assessment Division, Food Directorate, Health Canada.

Hem JD, Robertson CE. 1967. Form and stability of aluminum hydroxide complexes in dilute solution. U.S. Geological Survey. 55 p. Water Supply Paper No. 1827-A.

Hendershot WH, Courchesne F. 1991. Comparison of soil solution chemistry in zero tension and ceramic-cup tension lysimeters. European Journal of Soil Science 42: 577-583.

Hendershot WH, Courchesne F, Jeffries DS. 1995. Aluminum geochemistry at the catchment scale in watersheds influenced by acidic precipitation. In: Sposito G, editor, The environmental chemistry of aluminum. 2nd edition. Boca Raton (FL): CRC Press. p. 419–449.

Henry DA, Goodman WG, Nudelman RK, DiDomenico NC, Alfrey AC, Slatopolsky E, Stanley TM, Coburn JW. 1984. Parenteral aluminum administration in the dog: I. Plasma kinetics, tissue levels, calcium metabolism, and parathyroid hormone. Kidney Int 25(2): 362-369.

Hernan MA, Jick SS, Olek MJ, Jick H. 2004. Recombinant hepatitis B vaccine and the risk of multiple sclerosis: a prospective study. Neurology 63(5): 838-842.

Herrmann J. 1987. Aluminium impact on freshwater invertebrates at low pH: A review. In: Landner, L, editor, Speciation of metals in water, sediments and soil systems. Lecture Notes in Earth Sciences. Volume 11: 157-175 [cited in Rosseland et al.1990].

Heyman A, Wilkinson WE, Stafford JA, Helms MJ, Sigmon AH, Weinberg T. 1984. Alzheimer's disease: a study of epidemiological aspects. Ann Neurol 15(4): 335–341.

Höhr D, Abel J, Wilhelm M. 1989. Renal clearance of aluminium: studies in the isolated perfused rat kidney. Toxicol Lett 45: 165-174.

Horst WJ, Klotz F, Szulkiewicz P. 1990. Mechanical impedance increases aluminium tolerance of soybean (*Glycine max* L.). Plant Soil 124: 227–231.

Hosovski E, Mastelica Z, Sunderic D, Radulovic D. 1990. Mental abilities of workers exposed to aluminium. Med Lav 81(2): 119-123.

Hossain MD, Bache DH. 1991. Composition of alum flocs derived from a coloured, low-turbidity water. Aqua 40(5): 298–303.

Hu H, Yang YJ, Li XP, Chen GH. 2005. [Effect of aluminum chloride on motor activity and species-typical behaviors in mice]. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi 23(2): 132-135.

Huh JW, Choi MM, Lee JH, Yang SJ, Kim MJ, Choi J, Lee KH, Lee JE, Cho SW. 2005. Activation of monoamine oxidase isotypes by prolonged intake of aluminum in rat brain. J Inorg Biochem 99(10): 2088-2091.

Hutchinson NJ, Holtze KE, Munro JR, Pawson TW. 1987. Lethal responses of salmonid early life stages to H^+ and Al in dilute waters. Belg. J. Zool. 117 (Suppl. 1): 201– 217.

Hutchinson NJ, Sprague JB. 1987. Reduced lethality of Al, Zn and Cu mixtures to American flagfish by complexation with humic substances in acidified soft waters. Environ Toxicol Chem 6: 755–765.

Hutchinson TC, Bozic L, Munoz-Vega G. 1986. Responses of five species of conifer seedlings to aluminium stress. Water Air Soil Pollut 31: 283–294.

Ilvesniemi H. 1992. The combined effect of mineral nutrition and soluble aluminium on *Pinus sylvestris* and *Picea abies* seedling. For Ecol Manage. 51: 227–238.

[InVS-Afssa-Afssaps] Institut de veille sanitaire-Agence française de sécurité sanitaire des aliments-Agence française de sécurité sanitaire des produits de santé. 2003. Évaluation des risques sanitaires liés à l'exposition de la population française à l'aluminium: eaux, aliments, produits de santé. 1992 p.

[IARC] International Agency for Research on Cancer. 1987. Aluminum production. IARC monograph. 34 (Suppl 7).

[ICMM] International Council on Mining and Metals. 2007. MERAG: Metals environmental risk assessment guidance. London (UK): ICMM. Available from: http://www.icmm.com/document/15.

Ittel T, Gerish P, Nolte E, Sieberth H. 1993. Fractional absosption of Al is dose-dependent: A ^{26}Al tracer study. Nephrol Dial Transplant 8: 993.

Ittel TH, Kluge R, Sieberth HG. 1988. Enhanced gastrointestinal absorption of aluminium in uraemia: time course and effect of vitamin D. Nephrol Dial Transplant 3(5): 617-623.

Jacqmin H, Commenges D, Letenneur L, Barberger-Gateau P, Dartigues JF. 1994. Components of drinking water and risk of cognitive impairment in the elderly. Am J Epidemiol 139(1): 48-57.

Jacqmin-Gadda H, Commenges D, Letenneur L, Dartigues JF. 1996. Silica and aluminum in drinking water and cognitive impairment in the elderly. Epidemiology 7(3): 281-285.

Jeffery EH, Abreo K, Burgess E, Cannata J, Greger JL. 1996. Systemic aluminum toxicity: effects on bone, hematopoietic tissue, and kidney. J Toxicol Environ Health 48(6): 649-665.

Jia Y, Zhong C, Wang Y. 2001b. Effects of aluminum on amino acid neurotransmitters in hippocampus of rats. Zhonghua Yu Fang Yi Xue Za Zhi 35(6): 397-400.

Jia Y, Zhong C, Wang Y, Zhao R. 2001a. Effects of aluminum intake on the content of aluminum, iron, zinc and lipid peroxidation in the hippocampus of rats. Wei Sheng Yan Jiu 30(3): 132-134.

Jing Y, Wang Z, Song Y. 2004. Quantitative study of aluminum-induced changes in synaptic ultrastructure in rats. Synapse 52(4): 292-298.

Johannessen M. 1980. Aluminium, a buffer in acidic waters? In: Drablos D, Tollan A, editors, Ecological impact of acid precipitation. Proceedings of an international conference, March 11-14, Sandefjord, Norway. p. 222-223.

Johnson GV, Jope RS. 1987. Aluminum alters cyclic AMP and cyclic GMP levels but not presynaptic cholinergic markers in rat brain in vivo. Brain Res 403(1): 1-6.

Johnson GV, Watson AL, Jr., Lartius R, Uemura E, Jope RS. 1992. Dietary aluminum selectively decreases MAP-2 in brains of developing and adult rats. Neurotoxicology 13(2): 463-474.

[JECFA] Joint FAO/WHO Expert Committee on Food Additives. 2007. 67th Meeting of the Joint FAO/WHO Expert Committee on Food Additives and Contaminants, 20-29 June. Rome: Food and Agricultural Organization of the United Nations, World Health Organization.

Jonasson B. 1996. Phosphorus transformations in alum sludge amended soils. Swedish Journal of. Agricultural Research 26: 69–79.

Jones G, Henderson V. 2006. Metal concentrations in soils and produce from gardens in Flin Flon, Manitoba, 2002. Flin FLon: Winnipeg. Section de l'aménagement et de l'habitat et de la surveillance des écosystèmes. Direction de la protection de la faune et des écosystèmes. Conservation Manitoba. Report nr 2006-01. 81 p.

Jones G, Philips F. 2003. Metal concentrations in surface soils of Thompson, September 2001. Thompson: Winnipeg. Section de l'aménagement et de l'habitat et de la surveillance des écosystèmes. Direction de la protection de la faune et des écosystèmes. Conservation Manitoba. Report nr 2003-01. 21 p.

Jones JH. 1938. The metabolism of calcium and phosphorus as influenced by the addition to the diet of salts of metals which form insoluble phosphates. Amer J Physiol 124: 230-237.

Jouhanneau P, Raisbeck GM, Yiou F, Lacour B, Banide H, Drueke TB. 1997. Gastrointestinal absorption, tissue retention, and urinary excretion of dietary aluminum in rats determined by using 26Al. Clin Chem 43(6 Pt 1): 1023-1028.

Jyoti A, Sharma D. 2006. Neuroprotective role of Bacopa monniera extract against aluminium-induced oxidative stress in the hippocampus of rat brain. Neurotoxicology 27(4): 451-457.

Kádár E, Salánki J, Powell J, White KN, McCrohan CR. 2002. Effect of sub-lethal concentrations of aluminium on the filtration activity of the freshwater mussel *Anodonta cygnea* L. at neutral pH. Acta Biol Hung 53(4): 485-493.

Kaizer RR, Correa MC, Spanevello RM, Morsch VM, Mazzanti CM, Goncalves JF, Schetinger MR. 2005. Acetylcholinesterase activation and enhanced lipid peroxidation after long-term exposure to low levels of aluminum on different mouse brain regions. J Inorg Biochem 99(9): 1865-1870.

Kaneko N, Yasui H, Takada J, Suzuki K, Sakurai H. 2004. Orally administrated aluminum-maltolate complex enhances oxidative stress in the organs of mice. J Inorg Biochem 98(12): 2022-2031.

Karlsson-Norrgren L, Dickson W, Ljungberg O, Runn P. 1986. Acid water and aluminium exposure: gill lesions and aluminium accumulation in farmed brown trout, *Salmo trutta* L. J Fish Dis 9: 1-9 [cited in Dussault et al., 2001].

Katyal R, Desigan B, Sodhi CP, Ojha S. 1997. Oral aluminum administration and oxidative injury. Biol Trace Elem Res 57(2): 125-130.

Kaur A, Gill KD. 2005. Disruption of neuronal calcium homeostasis after chronic aluminium toxicity in rats. Basic Clin Pharmacol Toxicol 96(2): 118-122.

Kaur A, Gill KD. 2006. Possible peripheral markers for chronic aluminium toxicity in Wistar rats. Toxicol Ind Health 22(1): 39-46.

Kaur A, Joshi K, Minz RW, Gill KD. 2006. Neurofilament phosphorylation and disruption: a possible mechanism of chronic aluminium toxicity in Wistar rats. Toxicology 219(1-3): 1-10.

Kawahara M. 2005. Effects of aluminum on the nervous system and its possible link with neurodegenerative diseases. J Alzheimers Dis 8(2): 171-182; discussion 209-215.

Kiesswetter E, Sch, auml, per M, Buchta M, Schaller KH, Rossbach B, Scherhag H, Zschiesche W, Letzel S. 2007. Longitudinal study on potential neurotoxic effects of aluminium: I. Assessment of exposure and neurobehavioural performance of Al welders in the train and truck construction industry over 4 years. Int Arch Occup Environ Health. 81(1): 41-67.

Kilburn KH. 1998. Neurobehavioral impairment and symptoms associated with aluminum remelting. Arch Environ Health 53(5): 329-335.

Kim K. 2003. Perinatal exposure to aluminum alters neuronal nitric oxide synthase expression in the frontal cortex of rat offspring. Brain Res Bull 61(4): 437-441.

Kimball BA, Callender E, Axtmann EV. 1995. Effects of colloids on metal transport in a river receiving acid mine drainage, upper Arkansas River, Colorado, U.S.A. Applied Geochem 10: 285-306 [cited in Farag et al., 2007].

Kinraide TB. 1997. Reconsidering the rhizotoxicity of hydroxyl, sulphate, and fluoride complexes of aluminium. J Exp Bot 48: 1115-1124.

Kirkwood DE, Nesbitt HW. 1991. Formation and evolution of soils from an acidified watershed: Plastic Lake, Ontario, Canada. Geochim Cosmochim Acta 55: 1295–1308.

Klein GL. 2005. Aluminum: new recognition of an old problem. Curr Opin Pharmacol 5(6): 637-640.

Kobayashi K, Yumoto S, Nagai H, Hosoyama Y, Imamura M, Masuzawa S, Koizumi Y, Ymashita H. 1990. ^{26}Al tracer experiment by accelerator mass spectrometry and its application to the studies for amyotrophic lateral slerosis and Alzheimer's disease. Proceedings of the Japan Academy. Series B, Physical and biological sciences B66: 189-192.

Kohila T, Parkkonen E, Tahti H. 2004. Evaluation of the effects of aluminium, ethanol and their combination on rat brain synaptosomal integral proteins in vitro and after 90-day oral exposure. Arch Toxicol 78(5): 276-282.

Koo WW, Kaplan LA, Krug-Wispe SK. 1988. Aluminum contamination of infant formulas. JPEN J Parenter Enteral Nutr 12(2): 170-173.

Kopáček J, Ulrich K-U, Hejzlar J, Borovec J, Stuchlík E. 2001. Natural inactivation of phosphorus by aluminum in atmospherically acidified water bodies. Water Res 35(16): 3783-3790.

Kram P, Hruska J, Driscoll C, Johnson CE. 1995. Biogeochemistry of aluminum in a forest catchment in the Czech Republic impacted by atmospheric inputs of strong acids. Water Air Soil Pollut 85: 1831–1836.

Krantzberg G. 1989. Metal accumulation by chironomid larvae: the effects of age and body weight on metal body burdens. Hydrobiologia 188/189: 497–506.

Krantzberg G, Stokes PM. 1988. The importance of surface adsorption and pH in metal accumulation by chironomids. Environ Toxicol Chem 7: 653–670.

Krasovskii GN, Vasukovich LY, Chariev OG. 1979. Experimental study of biological effects of leads and aluminum following oral administration. Environ Health Perspect 30: 47-51.

Krewski D, Yokel RA, Nieboer E, Borchelt D, Cohen J, Harry J, Kacew S, Lindsay J, Mahfouz AM, Rondeau V. 2007. Human health risk assessment for aluminium, aluminium oxide, and aluminium hydroxide. J Toxicol Environ Health B Crit Rev. 2007; 10 Suppl 1: 1-269.

Kuja A, Jones R. 2000. Soil contamination in Port Colborne Woodlots: 2000. Port Colborne: Ministry of Environment. Ontario. 30 p.

Kullberg A, Bishop KH, Hargeby A, Jansson M, Peterson RC. 1993. The ecological significance of dissolved organic carbon in acidified waters. Ambio 22(5): 331–337.

Kumar S. 1998. Biphasic effect of aluminium on cholinergic enzyme of rat brain. Neurosci Lett 248(2): 121-123.

Kumar S. 1999. Aluminium-induced biphasic effect. Med Hypotheses 52(6): 557-559.

Kumar S. 2002. Aluminium-induced changes in the rat brain serotonin system. Food Chem Toxicol 40(12): 1875-1880.

Kundert K, Meilke L, Elford T, Maksymetz B, Pernitsky DJ. 2004. Evaluating pH adjustment to investigate seasonal changes in aluminum residuals at a large conventional water treatment plant. In: Proceedings of the 56th Annual Western Canada Water and Wastewater Association Conference and Tradeshow, Calgary, Alberta, October 17-20, 2004. 13 p.

Lacroix GL. 1992. Mitigation of low stream pH and its effects on salmonids. Environ Pollut 78: 157–164.

Lacroix GL, Peterson RH, Belfry CS, Martin-Robichaud DJ. 1993. Aluminum dynamics on gills of Atlantic salmon (*Salmo salar*) fry in the presence of citrate and effects on integrity of gill structures. Aquat Toxicol 27: 373–402.

Lal B, Gupta A, Gupta A, Murthy RC, Ali MM, Chandra SV. 1993. Aluminum ingestion alters behaviour and some neurochemicals in rats. Indian J Exp Biol 31(1): 30-35.

Lamb DS, Bailey GC. 1981. Acute and chronic effects of alum to midge larva (Diptera: Chironomidae). Bull Environ Contam Toxicol 27: 59–67.

Landry B, Mercier M. 1992. *Notions de géologie*. 3rd edition. Mont-Royal (PQ): Modulo. p. 565.

LaZerte BD, van Loon G, Anderson B. 1997. Aluminum in water. In: Yokel R, Golub MS, editors, Research Issues in Aluminum Toxicity. Washington (DC): Taylor and Francis. p. 17-46.

Lee W, Westerhoff P. 2006. Dissolved organic nitrogen removal during water treatment by aluminum sulfate and cationic polymer coagulation. Water Res 40: 3767-3774.

Lee YH, Hultberg H, Sverdrup H, Borg GC. 1995. Are ion exchange processes important in controlling the cation chemistry of soil and runoff water. Water Air Soil Pollut 85: 819–1824.

Lévesque L, Mizzen CA, McLachlan DR, Fraser PE. 2000. Ligand specific effects on aluminum incorporation and toxicity in neurons and astrocytes. Brain Res 877(2): 191-202.

Lewandowski J, Schauser I, Hupfer M. 2003. Long term effects of phosphorus precipitations with alum in hypereutrophic Lake Süsser See (Germany). Water Res 37: 3194-3204.

Lewis RJ. 1992. Sax's dangerous properties of industrial materials. Vol. 3. New York (NY): Van Nostrand Reinhold.

Li XP, Yang YJ, Hu H, Wang QN. 2006. Effect of aluminum trichloride on dissociated Ca2+ in Hippocampus neuron cell as well as learning and memory. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi 24(3): 161-163.

Liao YH, Yu HS, Ho CK, Wu MT, Yang CY, Chen JR, Chang CC. 2004. Biological monitoring of exposures to aluminium, gallium, indium, arsenic, and antimony in optoelectronic industry workers. J Occup Environ Med 46(9): 931-936.

Likens GE, Bormann FH, Pierce RS, Eaton JS, Johnson NM. 1977. Biogeochemistry of a forested ecosystem. New York (NY): Springer-Verlag.

Lima PD, Leite DS, Vasconcellos MC, Cavalcanti BC, Santos RA, Costa-Lotufo LV, Pessoa C, Moraes MO, Burbano RR. 2007. Genotoxic effects of aluminum chloride in cultured human lymphocytes treated in different phases of cell cycle. Food Chem Toxicol 45: 1154-1159.

Lin S, Evans RL, Schnepper D, Hill T. 1984. Evaluation of wastes from the East St. Louis water treatment plant and their impact on the Mississippi River. Springfield (IL): Department of Energy and Natural Resources, (ISWS/CIR-160/84:1-89, 1984).

Lin SD. 1989. No adverse environmental impacts from water plant discharges. Water Engineering & Management 136: 40–41.

Lindsay J, Laurin D, Verreault R, Hébert R, Helliwell B, Hill GB, McDowell I. 2002. Risk factors for Alzheimer's disease: a prospective analysis from the Canadian study of health and aging. Am J Epidemiol 156(5): 445-453.

Lindsay WL, Vlek PLG, Chien SH. 1989. Phosphate minerals. In: Dixon JB, Weed SB, editors, Minerals in soil environments. Madison (WI): Soil Science Society of America. p. 1089–1130.

Liukkonen-Lilja H, Piepponen S. 1992. Leaching of aluminium from aluminium dishes and packages. Food Addit Contam 9(3): 213-223.

Llansola M, Minana MD, Montoliu C, Saez R, Corbalan R, Manzo L, Felipo V. 1999. Prenatal exposure to aluminum reduces expression of neuronal nitric oxide synthase and of soluble guanylate cyclase and impairs glutamatergic neurotransmission in rat cerebellum. J Neurochem 73(2): 712-718.

Loganathan P, Hedley MJ, Grace ND, Lee J, Cronin SJ, Bolan NS, Zanders JM. 2003. Fertiliser contaminants in New Zealand grazed pasture with special reference to cadmium and fluorine: a review. Australian Journal of Soil Research 41: 501-532 [cited in Manoharan et al. 2007].

Long JF, Nagode LA, Steinmeyer CL, Renkes G. 1994. Comparative effects of calcitriol and parathyroid hormone on serum aluminum in vitamin D-depleted rabbits fed an aluminum-supplemented diet. Res Commun Chem Pathol Pharmacol 83(1): 3–14.

Long JF, Renkes G, Steinmeyer CL, Nagode LA. 1991. Effect of calcitriol infusions on serum aluminum in vitamin D-depleted rabbits fed an aluminum-supplemented ration. Res Commun Chem Pathol Pharmacol 74(1): 89-104.

Lopez FE, Cabrera C, Lorenzo ML, Lopez MC. 2002. Aluminum levels in convenience and fast foods: in vitro study of the absorbable fraction. Sci Total Environ 300(1–3): 69-79.

Lydersen E, Poléo ABS, Muniz IP, Salbu B, Bjornstad HE. 1990a. The effects of naturally occurring high and low molecular weight inorganic and organic species on the yolk-sac larvae of Atlantic salmon (*Salmo salar* L.) exposed to acidic aluminium-rich lake water. Aquat Toxicol 18: 219–229.

Lydersen E, Salbu B, Poléo ABS, Muniz IP. 1990b. The influences of temperature on aqueous aluminium chemistry. Water Air Soil Pollut 51: 203-215.

Mackie GL, Kilgour BW. 1995. Efficacy and role of alum in removal of zebra mussel veliger larvae from raw water supplies. Water Res 29: 731–744.

MacLean DC, Hansen KS, Schneider RE. 1992. Amelioration of aluminium toxicity in wheat by fluoride. New Phytol 121: 81-88 [cited in Manoharan et al. 2007].

Maitani T, Kubota H, Hori N, Yoshihira K, Takeda M. 1994. Distribution and urinary excretion of aluminum injected with several organic acids into mice: Relationship with chemical state in serum studied by the HPLC-ICP method. J Appl Toxicol 14: 257-261.

Malley DF, Chang PSS. 1985. Effects of aluminium and acid on calcium uptake by the crayfish *Oronectes virilis*. Arch Environ Contam Toxicol 14: 739-747 [cited in Rosseland et al. 1990].

Malley DF, Findlay DL, Chang PSS. 1982. Ecological effects of acid precipitation on zooplankton. In: D'Itri FN, editor, Acid precipitation: effects on ecological systems. Ann Arbor (MI): Ann Arbor Science, p. 297-327.

Malley DF, Heubner JD, Donkersloot K. 1988. Effects on ionic composition of blood and tissues of *Anodonta grandis grandis* (Bivalvia) of an addition of aluminum and acid to a lake. Arch Environ Contam Toxicol 17: 479–491.

Mameli O, Caria MA, Melsi P, Zambenedetti P, Ramila M, Zatta P. 2006. Effect of aluminum consumption on the vestibule-ocular reflex. Metab Brain Dis 21(2-3): 89-107.

Manoharan V, Loganathan P, Tillman RW, Parfitt RL. 2007. Interactive effects of soil acidity and fluoride on soil solution aluminium chemistry and barley (*Hordeum vulgare* L.) root growth. Environ Poll 145: 778-786.

Marchesi VT. 2005. An alternative interpretation of the amyloid Aβ hypothesis with regard to the pathogenesis of Alzheimer's disease. PNAS 102(26): 9093-9098.

Martin RB. 1996. Ternary complexes of Al^{+3} and F with a third ligand Coord. Chem. Rev. 149: 23-32.

Martyn CN, Coggon DN, Inskip H, Lacey RF, Young WF. 1997. Aluminum concentrations in drinking water and risk of Alzheimer's disease. Epidemiology 8(3): 281-286.

Mathias R, Salusky I, Harman W, Paredes A, Emans J, Segre G, Goodman W. 1993. Renal bone disease in pediatric and young adult patients on hemodialysis in a children's hospital. J Am Soc Nephrol 3(12): 1938-1946.

Matsumoto H. 2000. Cell biology of aluminium toxicity and tolerance in higher plants. Int Rev Cytol 200: 1-46 [cited in Manoharan et al. 2007].

Mattson MP, Lovell MA, Ehmann WD, Markesbery WR. 1993. Comparison of the effects of elevated intracellular aluminum and calcium levels on neuronal survival and tau immunoreactivity. Brain res 602: 21-31.

McCanny SJ, Hendershot WH, Lechowicz MJ, Shipley B. 1995. The effects of aluminum on *Picea rubens*: factorial experiments using sand culture. Can J For Res 25: 8–17.

McCormack KM, Ottosen LD, Sanger VL, Sprague S, Mayor GH, Hook JB. 1979. Effects of prenatal administration of aluminum and parathyroid hormone on fetal development in the rat. Soc Exp Biol Med 161: 74–77.

McCormick LH, Steiner KC. 1978. Variation in aluminum tolerance among six genera of trees. Forest Science 24: 565–568.

McDonald DG, Reader JP, Dalziel TRK. 1989. The combined effects of pH and trace metals on fish ionoregulation. In: Morris R, Taylor EW, Brown DJA, Brown JA, editors, Acid toxicity and aquatic animals. Cambridge (MA): Cambridge University Press. p. 221–242.

McGreer JC, Brix KV, Skeaff JM, DeForest DK, Brigham SI, Adams WJ, Green A. 2003. Inverse relationship between bioconcentration factor and exposure concentration for metals: implications for hazard assessment of metals in the aquatic environment. Environ Toxicol Chem 22(5): 1017-1037.

McLachlan DR, Bergeron C, Smith JE, Boomer D, Rifat SL. 1996. Risk for neuropathologically confirmed Alzheimer's disease and residual aluminum in municipal drinking water employing weighted residential histories. Neurology 46(2): 401-405.

Meek B, Renwick A, Sonich-Mulloch C. 2003. Practical application of kinetic data in risk assessment-an IPCS initiative. Toxicol Lett(138): 151-160.

Merck Index. 2006. An encyclopedia of chemicals, drugs, and biologicals. 14th edition. O'Neil M, Smith A, Heckelman PE, eds. Whitehouse Station (NJ): Merck & Co., Inc.

Meyer-Baron M, Sch, auml, per M, Knapp G, van Thriel C. 2007. Occupational aluminum exposure: Evidence in support of its neurobehavioral impact. Neurotoxicology. 28(6): 1068-1078.

Michel P, Commenges D, Dartigues JF, Gagnon M. 1991. Study of the relationship between aluminium concentration in drinking water and risk of Alzheimer's Disease. In: Iqbal K, McLachlan DRC, Winblad B, Wisniewski HM, editors. Alzheimer's disease: Basic mechanism, diagnosis and therapeutic strategies. New York: John Wiley. p 387-391.

Ministère de l'Environnement du Québec and Environment Canada. 2001. Toxic potential assessment of municipal wastewater treatment plant effluents in Quebec. Montreal (QC): Ministère de l'Environnement du Québec and Environment Canada, St. Lawrence Vision 2000, Phase III – Industrial and Urban component. 136 pp. + appendices.

[MEF] Ministère de l'Environnement et de la faune du Québec and Environnement Canada. 1998. *Évaluation de la toxicité des effluents des stations d'épuration municipales du Québec. Rapport d'étape. Campagne de caractérisation d'hiver.* Montréal (QC) : Ministère de l'environnement et de la faune du Québec and Environnement Canada, Direction de la protection de l'environnement, Région du Québec, Groupe d'intervention et restauration, 89 pp. + appendices.

Ministers' Expert Advisory Panel. 1995. Report of the Ministers' Expert Advisory Panel on the second Priority Substances List under the *Canadian EnvironmentalProtection Act* (CEPA). Ottawa (ON): Government of Canada. 26 p.

[ME and MAFRA] Ministry of the Environment and Ministry of Agriculture, Food and Rural Affairs. 1996. Guidelines for the utilization of biosolids and other wastes on agricultural land. Ministry of the Environment and Ministry of Agriculture, Food and Rural Affairs. March 1996. Available at: http://www.ene.gov.on.ca/envision/gp/3425e.pdf.

Misawa T, Shigeta S. 1993. Effects of prenatal aluminum treatment on development and behavior in the rat. J Toxicol Sci 18(1): 43-48.

Miu AC, Benga O. 2006. Aluminum and Alzheimer's disease: a new look. J Alzheimers Dis 10(2-3): 179-201.

Moreno A, Dominguez P, Dominguez C, Ballabriga A. 1991. High serum aluminum levels and acute reversible encephalopathy in a 4-year old boy with acute renal failure. Eur J Pediatr 150: 513-514.

Morrissey CA, Bendell-Young LI, Elliott JE. 2005. Assessing trace-metal exposure to American dippers in mountain streams of southwestern British Columbia, Canada. Environ Toxicol Chem 24(4): 836-845.

Mortula M, Gibbons MK, Lake CB, Gagnon GA. 2007. The reuse of alum residuals for wastewater treatment: effect on aluminum leachability. In: Proceedings of the 4th Canadian Organic Residuals and Biosolids Management Conference, Moncton, New Brunswick, June 24-27. Canadian Association on Water Quality, Burlington, Ontario.

Mount DR, Ingersoll CG, Gulley DD, Fernandez JD, LaPoint TW, Bergman HL. 1988. Effect of long-term exposure to acid, aluminum, and low calcium on adult brook trout (*Salvelinus fontinalis*). 1. Survival, growth, fecundity, and progeny survival. Can. J. Fish. Aquat. Sci. 45: 1633–1642.

Muller G, Bernuzzi V, Desor D, Hutin MF, Burnel D, Lehr PR. 1990. Developmental alterations in offspring of female rats orally intoxicated by aluminum lactate at different gestation periods. Teratology 42(3): 253-261.

Muller G, Hutin MF, Burnel D, Lehr PR. 1992. Aluminum transfer through milk in female rats intoxicated by aluminum chloride. Biol Trace Elem Res 34: 79-87.

Muller JP, Steinegger A, Schlatter C. 1993. Contribution of aluminum from packaging materials and cooking utensils to the daily aluminum intake. Z Lebensm Unters Forsch 197(4): 332-341.

Muniz IP, Leivestad H. 1980. Toxic effects of aluminum on the brown trout, *Salmo trutta*. In: Drablos D, Tollen A, editors, Proceedings of an International Conference on the Ecological Impact of Acid Precipitation. SNSF Project, Oslo.

Narf RP. 1990. Interactions of Chironomidae and Chaoboridae (Diptera) with aluminum sulfate treated lake sediments. Lake and Reservoir Management 6(1): 33–42.

[NRC] National Research Council. Committee on Fluoride in Drinking Water. 2006. Fluoride in drinking water. A scientific review of EPA's standards. Washington, DC: Academies Press. 507 p.

Nehru B, Anand P. 2005. Oxidative damage following chronic aluminium exposure in adult and pup rat brains. J Trace Elem Med Biol 19(2-3): 203-208.

Nelson WO, Campbell PGC. 1991. Review of the effects of acidification on the geochemistry of Al, Cd, Pb and Hg in freshwater environments. Environ Pollut 71: 91–130.

Neri LC, Hewitt D. 1991. Aluminium, Alzheimer's disease, and drinking water. Lancet 338(8763): 390.

Neri LC, Hewitt D, Rifat SL. 1992. Aluminium in drinking water and risk for diagnoses of presenile alzheimer's type dementia (Abstract 453). Neurobiology of aging. p S115.

Neville CM. 1985. Physiological responses of juvenile rainbow trout, *Salmo gairdneri*, to acid and aluminum — prediction of field responses from laboratory data. Can. J. Fish. Aquat. Sci. 42: 2004–2019.

Neville CM, LaZerte BD, Ralston JG. 1988. Aluminum. Scientific criteria document for development of provincial water quality objectives and guidelines. Toronto (ON): Ontario Ministry of the Environment, Water Quality Management Working Group I, Water Resources Branch.

Newman MC, Jagoe CH. 1994. Ligands and the bioavailability of metals in aquatic environments. In: Hamelink JL, Landrum PF, Bergman HL, Benson WH, editors, Bioavailability: Physical, chemical and biological Interactions. Proceedings of the 13th Pellston workshop, Michigan, August 17-22, 1992, Boca Raton (FL): Lewis Publishers. p. 39-61.

Ng AH, Hercz G, Kandel R, Grynpas MD. 2004. Association between fluoride, magnesium, aluminum and bone quality in renal osteodystrophy. Bone 34(1): 216-224.

Nieboer E, Gibson BL, Oxman AD, Kramer JR. 1995. Health effects of aluminum: a critical review with emphasis on aluminum in drinking water. Environ. Rev. 3: 29-81.

Nilsson R. 1988. Aluminium in natural waters — toxicity to fish and man. In: Astruc M, Lester JN, editors, Heavy metals in the hydrological cycle. London (England): Selper Ltd. p. 11–18.

Nilsson SI, Bergkvist B. 1983. Aluminum chemistry and acidification processes in a spodzol on the Swedish west coast. Water Air Soil Pollut 20: 311–329.

Noble AD, Fey MV, Sumner ME. 1988a. Calcium-aluminum balance and the growth of soybean roots in nutrient solutions. Soil Sci Soc Am J 52: 1651-1656 [cited in Manoharan et al. 2007].

Noble AD, Sumner ME, Alva AK. 1988b. Comparison of aluminum and 8-hydroxyquinoline methods in the presence of fluoride for assaying phytotoxic aluminum. Soil Sci. Soc. Am. J. 52: 1059–1063.

Nolte E, Beck E, Winklhofer C, Steinhausen C. 2001. Compartmental model for aluminium biokinetics. Hum Exp Toxicol 20(2): 111-117.

Nordstrom DK, May HM. 1995. The chemistry of aluminum in surface waters. *In:* Sposito G, editor, The environmental chemistry of aluminum. 2nd edition. Boca Raton (FL): CRC Press. p. 39–80.

Novak JT, Knocke WR, Geertsema W, Dove D, Taylor A, Mutter R. 1995. An assessment of cropland application of water treatment residuals. Denver (CO): American Water Works Association Research Foundation, 71 p.

Nozaki Y. 1997. A fresh look at element distribution in the North Pacific. Eos, Transactions, American Geophysical Union 78(21): 221-227. Available from: http://www.agu.org/eos_elec/07025e.html.

Nriagu JO, Wong HTK. 1986. What fraction of the total metal flux into lakes is retained in the sediments? Water Air Soil Pollut 31: 999–1006.

Oneda S, Takasaki T, Kuriwaki K, Ohi Y, Umekita Y, Hatanaka S, Fujiyoshi T, Yoshida A, Yoshida H. 1994. Chronic toxicity and tumorigenicity study of aluminum potassium sulfate in B6C3F1 mice. In Vivo 8(3): 271-278.

Orians KJ, Bruland KW. 1985. Dissolved aluminium in the central North Pacific. Nature 316: 427-429.

Orr PL, Craig GR, Nutt SG, Stephenson J. 1992. Evaluation of acute and chronic toxicity of Ontario sewage treatment plant effluents. Toronto (ON): Ontario Ministry of the Environment, Municipal Section, Municipal and Industrial Strategic Abatement. p. 1–314.

Oteiza PI, Keen CL, Han B, Golub MS. 1993. Aluminum accumulation and neurotoxicity in Swiss-Webster mice after long-term dietary exposure to aluminum and citrate. Metabolism 42(10): 1296-300.

Ott SM, Maloney NA, Klein GL, Alfrey AC, Sherrard DJ. 1982. The prevalence of bone aluminum deposition in renal osteodystrophy and its relation to the reponse to calcitriol therapy. N Engl J Med 307: 709-713.

Otto C, Svensson BS. 1983. Properties of acid brown water streams in south Sweden. Arch Hydrobiol 99: 15–36 [cited in Wren and Stephenson 1991].

Owen LMW, Crews HM, Bishop Nj, Massey RC. 1994. Aluminium uptake from some foods by guinea pigs and the characterizatrion of aluminium in in vivo intestinal digesta by SEC-ICP-MS. Food Chem Toxicol 32(8): 697-705.

Pagenkopf GK. 1983. Gill surface interaction model for trace-metal toxicity to fishes: role of complexation, pH and water hardness. Environ Sci Technol 17: 342–347.

Pai SM, Melethil S. 1989. Kinetics of aluminum in rats I: Dose-dependent elimination from blood after intravenous administration. J Pharm Sci 78(3): 200-202.

Pandya JD, Dave KR, Katyare SS. 2001. Effect of long-term aluminum feeding on lipid/phospholipid profiles of rat brain synaptic plasma membranes and microsomes. J Alzheimers Dis 3(6): 531-539.

Pandya JD, Dave KR, Katyare SS. 2004. Effect of long-term aluminum feeding on lipid/phospholipid profiles of rat brain myelin. Lipids Health Dis 3: 13.

Parametrix. 1995. Persistence, bioaccumulation and toxicity of metals and metal compounds. London (UK): International Council on Metals in the Environment [cited in ICMM 2007].

Parent L, Campbell PGC. 1994. Aluminum bioavailability to the green alga *Chlorella pyrenoidosa* in acidified synthetic soft water. Environ Toxicol Chem 13: 587–598.

Parent L, Twiss MR, Campbell PGC. 1996. Influences of natural dissolved organic matter on the interaction of aluminum with the microalga *Chlorella*: a test of the free-ion model of trace metal toxicity. Environ Sci Technol 30: 1713–1720.

Parker DR, Bertsch PM. 1992a. Identification and quantification of the "Al13" tridecameric polycation using ferron. Environ Sci Technol 26: 908–914.

Parker DR, Bertsch PM. 1992b. Formation of the "Al13" tridecameric polycation under diverse synthesis conditions. Environ Sci Technol 26: 914–921.

Parker DR, Zelazny LW, Kinraide TB. 1989. Chemical speciation and plant toxicity of aqueous aluminum. In: Lewis TE, editor, Environmental chemistry and toxicology of aluminum. Chelsea (MI): Lewis Publishers. p. 117–145.

Parkhurst BR, Bergman HL, Fernandez J, Gulley DD, Hocket JR, Sanchez DA. 1990. Inorganic monomeric aluminum and pH as predictors of acidic water toxicity to brook trout (*Salvelinus fontinalis*). Can. J. Fish. Aquat. Sci. 47: 1631–1640.

Paternain JL, Domingo JL, Llobet JM, Corbella J. 1988. Embryotoxic and teratogenic effects of aluminum nitrate in rats upon oral administration. Teratology 38: 253–257.

Pellerin BA, Fernandez IJ, Norton SA, Kahl JS. 2002. Soil aluminum distribution in the near-stream zone at the Bear Brook watershed in Maine. Water Air Soil Pollut 134: 189-204.

Pennington JA. 1988. Aluminium content of foods and diets. Food Addit Contam 5(2): 161-232.

Perl DP, Good PF. 1987. Uptake of aluminium into central nervous system along nasal-olfactory pathways. Lancet 1: 1028.

Perry RH, Green DW, editors. 1984. Perry's chemical engineers' handbook. 6th edition. New York (NY): McGraw-Hill Book Company.

Peterson RH, Bourbonniere RA, Lacroix GL, Martin-Robichaud DJ, Takats P, Brun G. 1989. Responses of Atlantic salmon (*Salmo salar*) alevins to dissolved organic carbon and dissolved aluminum at low pH. Water Air Soil Pollut 46: 399–413.

Pettersen JC, Hackett DS, Zwicker GM, Sprague GL. 1990. Twenty-six week toxicity study with Kasal (basic sodium aluminum phosphate) in beagle dogs. Environ Geochem Health 12(1-2): 121-123.

Peuranen S, Keinänen M, Tigerstedt C, Kokko J, Vuorinen PJ. 2002. The effects of Fe and Al exposure with or without humic acid at two pH levels on the gills, oxygen consumption and blood and plasma parameters of juvenile grayling (*Thymallus thymallus*). Arch. Hydrobiol. Supplement 141(3-4): 241-261.

Pichard A. 2005. Aluminium et ses dérivés. Fiche de données toxicologiques et environnementales des substances chimiques. INERIS. Available from : http://www.ineris.fr/index.php?module=doc&action=getDoc&id_doc_object=134.

Pidwirny M, Gow T. 2002. The changing atmosphere. In: Pidwirny M, editor, Land use and environmental change in the Thompson-Okanagan. Victoria (BC): Royal British Columbia Museum. Available from: http://www.livinglandscapes.bc.ca/thomp-ok/env-changes/index.html

Pierre F, Baruthio F, Diebold F, Biette P. 1995. Effect of different exposure compounds on urinary kinetics of aluminium and fluoride in industrially exposed workers. Occup Environ Med 52(6): 396-403.

Pilgrim W, Schroeder B. 1997. Multi-Media concentrations of heavy metals and major ions from urban and rural sites in New Brunswick, Canada. Environ Monit Assess 47: 89-108.

Pintro J, Barloy J, Fallavier P. 1996. Aluminum effects on the growth and mineral composition of corn plants cultivated in nutrient solution at low aluminum activity. J Plant Nutr 19: 729–741.

Poléo ABS. 1995. Aluminium polymerization – a mechanism of acute toxicity of aqueous aluminium to fish. Aquat Toxicol 31: 347-356.

Poléo ABS, Bjerkely F. 2000. Effect of unstable aluminium chemistry on Arctic char (*Salvelinus alpinus*). Can. J. Fish. Aquat. Sci. 57: 1423-1433.

Poléo ABS, Hytterød S. 2003. The effect of aluminium in Atlantic salmon (*Salmo salar*) with special emphasis on alkaline water. J Inorg Biochem 97: 89-96.

Poléo ABS, Lydersen E, Rosseland BO, Kroglund F, Salbu B, Vogt RD, Kvellestad A. 1994. Increased mortality of fish due to changing Al chemistry of mixing zones between limed streams and acidic tributaries. Water Air Soil Pollut 75: 339-351.

Poléo ABS, Øxnevad SA, Østbye K, Andersen RA, Oughton DH, Vøllestad LA. 1995. Survival of curcian carp, *Carassius carassius*, exposed to a high low-molecular weight inorganic aluminium challenge. Aquat Sci 57: 350-359 [cited in Alstad et al. 2005].

Polizzi S, Ferrara M, Bugiani M, Barbero D, Baccolo T. 2007. Aluminium and iron air pollution near an iron casting and aluminium foundry in Turin district (Italy). J Inorg Biochem. p 1339-43.

Poulos BK, Perazzolo M, Lee VM, Rudelli R, Wisniewski HM, Soifer D. 1996. Oral aluminum administration during pregnancy and lactation produces gastric and renal lesions in rat mothers and delay in CNS development of their pups. Mol Chem Neuropathol 29(1): 15-26.

Powell J, Thompson R. 1993. The chemistry of aluminium in the gastrointestinal lumen and its uptake and absorption. Proc Nutr Soc 52: 241-253.

Pratico D, Uryu K, Sung S, Tang S, Trojanowski JQ, Lee VM. 2002. Aluminum modulates brain amyloidosis through oxidative stress in APP transgenic mice. FASEB J 16(9): 1138-1140.

Priest ND. 1993. The bioavailability and metabolism of aluminium compounds in man. Proc Nutr Soc 52(1): 231-240.

Priest ND. 2004. The biological behaviour and bioavailability of aluminium in man, with special reference to studies employing aluminium-26 as a tracer: review and study update. J Environ Monit 6(5): 375-403.

Priest ND, Newton D, Day JP, Talbot RJ, Warner AJ. 1995. Human metabolism of aluminium-26 and gallium-67 injected as citrates. Hum Exp Toxicol 14(3): 287-293.

Priest ND, Talbot RJ, Austin JG, Day JP, King SJ, Fifield K, Cresswell RG. 1996. The bioavailability of 26Al-labelled aluminium citrate and aluminium hydroxide in volunteers. Biometals 9(3): 221-228.

Priest ND, Talbot RJ, Newton D, Day JP, King SJ, Fifield LK. 1998. Uptake by man of aluminium in a public water supply. Hum Exp Toxicol 17(6): 296-301.

Quartin VL, Azinheira HG, Nunes MA. 2001. Phosphorus deficiency is responsible for biomass reduction of triticale in nutrient solution with aluminum. J Plant Nutr 24(12): 1901-1911.

Quartley B, Esselmont G, Taylor A, Dobrota M. 1993. Effect of oral aluminium citrate on short-term tissue distribution of aluminium. Food Chem Toxicol 31(8): 543-548.

Radunovic A, Ueda F, Raja KB, Simpson RJ, Templar J, King SJ, Lilley JS, Day JP, Bradbury MW. 1997. Uptake of 26-Al and 67-Ga into brain and other tissues of normal and hypotransferrinaemic mice. Biometals 10(3): 185-191.

Rahnema S, Jennings F. 1999. Accumulation and depletion of aluminum from various tissues of rats following aluminum citrate ingestion. OHIO J Sci 99(5): 98-101.

Rajasekaran K. 2000. Effects of combined exposure to aluminium and ethanol on food intake, motor behaviour and a few biochemical parameters in pubertal rats. Environ Toxicol Pharmacol 9(1-2): 25-30.

Ramamoorthy S. 1988. Effects of pH on speciation and toxicity of aluminum in rainbow trout (*Salmo gardneri*). Can. J. Fish. Aquat. Sci. 45: 634–642.

Rasmussen PE, Subramanian KS, Jessiman BJ. 2001. A multi-element profile of housedust in relation to exterior dust and soils in the city of Ottawa, Canada. Sci Total Environ 267(1-3): 125-140.

Ravi SM, Prabhu BM, Raju TR, Bindu PN. 2000. Long-term effects of postnatal aluminium exposure on acetylcholinesterase activity and biogenic amine neurotransmitters in rat brain. Indian J Physiol Pharmacol 44(4): 473-478.

Razniewska G, Trzcinka-Ochocka M. 2003. ET-AAS as a method for determination of aluminum in blood serum and urine. Chemia Analityczna 48: 107-113.

Reiber S, Kukull W, Standish-Lee P. 1995. Drinking water aluminium and bioavailability. Journal AWWA: 86-100.

Reimann C, Garrett RG. 2005. Geochemical background--concept and reality. Sci Total Environ 350(1-3): 12-27.

Rifat SL, Eastwood MR, McLachlan DR, Corey PN. 1990. Effect of exposure of miners to aluminium powder. Lancet 336(8724): 1162-1165.

Ritchie GSP. 1995. Soluble aluminium in acidic soils: principles and practicalities. Plant Soil 171: 17–27.

[RMOC] Region of Ottawa-Carleton. 2000. Regional Facilities Environmental Effects Monitoring Project. Preliminary Study of Ottawa-Carleton's Water Purification and Wastewater Treatment Plants. Prepared by the Surface Water Quality Branch, Water Environment Protection Division, Environment and Transportation Department, Region of Ottawa Carleton.

Roberts MH, Diaz RD. 1985. Assessing the effects of alum sludge discharges into coastal streams. Recent advances in sludge treatment and disposal. Denver (CO): American Water Works Association [cited in Cornwell et al. 1987].

Rodella L, Rezzani R, Lanzi R, Bianchi R. 2001. Chronic exposure to aluminium decreases NADPH-diaphorase positive neurons in the rat cerebral cortex. Brain Res 889(1-2): 229-233.

Rodella LF, Ricci F, Borsani E, Rezzani R, Stacchiotti A, Mariani C, Bianchi R. 2006. Exposure to aluminium changes the NADPH-diaphorase/NPY pattern in the rat cerebral cortex. Arch Histol Cytol 69(1): 13-21.

Rogers MA, Simon DG. 1999. A preliminary study of dietary aluminium intake and risk of Alzheimer's disease. Age Ageing 28(2): 205–209.

Roig JL, Fuentes S, Teresa Colomina M, Vicens P, Domingo JL. 2006. Aluminum, restraint stress and aging: behavioral effects in rats after 1 and 2 years of aluminum exposure. Toxicology 218(2-3): 112-124.

Romano LS. 1971. Windsor nutrient removal studies. Sewage treatment. City of Windsor, Ontario, September. 4 p.

Rondeau V, Commenges D, Jacqmin-Gadda H, Dartigues JF. 2000. Relation between aluminum concentrations in drinking water and Alzheimer's disease: an 8-year follow-up study. Am J Epidemiol 152(1): 59-66.

Rondeau V, Jacqmin-Gadda H, Commenges D, Dartigues JF. 2001. Re: aluminum in drinking water and cognitive decline in elderly subjects: the Paquid cohort. Am J Epidemiol 154(3): 288-290.

Roskams AJ, Connor JR. 1990. Aluminum access to the brain: a role for transferrin and its receptor. Proc. Natl. Acad. Sci. USA 87: 9024-9027.

Rosseland BO, Blakar IA, Bulgar A, Krogland F, Kvellstad A, Lydersen E, Oughton DH, Salbu B, Staurnes M, Vogt R. 1992. The mixing zone between limed and acidic river waters: complex aluminium chemistry and extreme toxicity for salmonids. Environ Pollut 78: 3–8.

Rosseland BO, Eldhuset TD, Staurnes M. 1990. Environmental effects of aluminium. Environ Geochem Health 12(1-2): 17-27.

Roy AK, Sharma A, Talukder G. 1991. Effects of aluminum salts on bone marrow chromosomes in rats *in vivo*. Cytobios 66 : 105-111.

Roy AK, Talukder G, Sharma A. 1991. Similar effects in vivo of two aluminum salts on the liver, kidney, bone, and brain of Rattus norvegicus. Bull Environ Contam Toxicol 47(2): 288-295.

Roy R. 1999a. The chemistry, bioaccumulation and toxicity of aluminum in the aquatic environment for the PSL2 assessment of aluminum salts. Report prepared by Fisheries and Oceans Canada for Environment Canada. Montreal (QC): Environment Canada. 110 pp. Unpublished report.

Roy R. 1999b. A preliminary environmental assessment of aluminum salts in the aquatic environment. Report prepared by Fisheries and Oceans Canada for Environment Canada. Montreal (QC): Environment Canada. 18 p. Unpublished report.

Roy R, Campbell PGC. 1995. Survival time modeling of exposure of juvenile Atlantic salmon (*Salmo salar*) to mixtures of Al and Zn in soft water at low pH. Aquat Toxicol 33: 155–176.

Roy R, Campbell PGC. 1997. Decreased toxicity of aluminum to juvenile Atlantic salmon (*Salmo salar*) in acidic soft water containing natural organic matter: a test of the free-ion model. Environ Toxicol Chem 16: 1962–1969.

Ruby MV, Schoof R, Brattin W, Goldade M, Post G, Harnois M, Mosby DE, Casteel SW, Berti W, Carpenter M and others. 1999. Advances in evaluating the oral bioavailability of inorganics in soil for use in human health risk assessment. Environ Sci Technol 33(21): 3697-3705.

Rundgren S, Nilsson P. 1997. Sublethal effects of aluminium on earthworms in acid soil – the usefulness of *Dendrodrilus rubidus* (SAV.) in a laboratory test system. Pedobiologia 41: 417-436.

Rustad LE, Cronan CS. 1995. Biogeochemical controls on aluminum chemistry in the O horizon of a red spruce (*Picea rubens* Sarg.) stand in central Maine, USA. Biogeochemistry 29: 107–129.

Sadler K, Lynam S. 1985. The mineral content of some freshwater invertebrates in relation to stream pH and calcium concentration. Central Electric Research Laboratory, Leatherland, Surrey.

Sadler K, Lynam S. 1988. The influence of calcium on aluminium-induced changes in the growth rate and mortality of brown trout, *Salmo trutta* L. J Fish Biol 33: 171–179.

Sadovnick AD, Scheifele DW. 2000. School-based hepatitis B vaccination programme and adolescent multiple sclerosis. Lancet 355(9203): 549-550.

Sahin G, Taskin T, Benli K, Duru S. 1995. Impairment of motor coordination in mice after ingestion of aluminum chloride. Biol Trace Elem Res 50(1): 79-85.

Salib E, Hillier V. 1996. A case-control study of Alzheimer's disease and aluminium occupation. Br J Psychiatry 168(2): 244-249.

Sanchez DJ, Gomez M, Llobet JM, Corbella J, Domingo JL. 1997. Effects of aluminium on the mineral metabolism of rats in relation to age. Pharmacol Toxicol 80(1): 11–17.

Santschi PH, Nyffeler VP, Anderson RF, Schiff SL, O'Hara P, Hesslein RH. 1986. Response of radioactive trace metals to acid–base titrations in controlled ecosystems: evaluation of transport parameters for applications to whole-lake radio-tracer experiments. Can. J. Fish. Aquat. Sci. 43: 60–77.

Sarin S, Julka D, K.D. G. 1997. Regional alterations in calcium homeostasis in the primate brain following chronic aluminum exposure. Mol Cell Boiochem 168: 95–100.

Savory J. 2000. Aluminium - Mechanism report. Charlottesville, VA: Department of Pathology and Biochemistry and Molecular Genetics. University of Virginia, Health System. 1-57 p.

Savory J, Herman MM, Ghribi O. 2006. Mechanisms of aluminum-induced neurodegeneration in animals: Implications for Alzheimer's disease. J Alzheimers Dis: 135-144.

Schecher WD, McAvoy D. 1994. "MINEQL+: A chemical equilibrium program for personal computers". Version 3.01. Hallowell, Maine: Environmental Research Software; 107 p.

Schemel LE, Kimball BA, Bencala KE. 2000. Colloid formation and metal transport through two mixing zones affected by acid mine drainage near Silverton, Colorado. Appl Geochem 15: 1000-1018 [cited in Farag et al. 2007].

Schier GA. 1996. Effect of aluminum on growth of newly germinated and 1-year-old red spruce (*Picea rubens*) seedlings. Can J For Res 26: 1781–1787.

Schindler DW. 1988. Effect of acid rain on freshwater ecosystems. Science 239: 149–157.

Schindler DW, Hesslein RH, Wageman R, Broecker WS. 1980. Effects of acidification on mobilization of heavy metals and radionuclides from the sediments of a freshwater lake. Can. J. Fish. Aquat. Sci. 37: 373–377.

Schmidt PF, Zumkley H, Bertram H, Lison A, Winterberg B, Barckhaus R. 1984. Localization of aluminum in bone of patients with dialysis osteomalacia. In: Schramel PBaP, editor. Trace Elements-Analytical Chemistry in Medicine and Biology. New York: Walter de Gruyter & Co. p 475-482.

Schonholzer KW, Sutton RA, Walker VR, Sossi V, Schulzer M, Orvig C, Venczel E, Johnson RR, Vetterli D, Dittrich-Hannen B and others. 1997. Intestinal absorption of trace amounts of aluminium in rats studied with 26aluminium and accelerator mass spectrometry. Clin Sci (Lond) 92(4): 379-383.

Sedman AB, Wilkening GN, Warady BA. 1984. Clinical and laboratory observations. Encephalopathy in childhood secondary to aluminum toxicity. J Pediatr 105: 836-838.

Seip HM, Andersen S, Henriksen A. 1990. Geochemical control of aluminum concentrations in acidified surface waters. J Contam Hydrol 116: 299–305.

Servos MR, Rooke JB, Mackie GL. 1985. Reproduction of selected mollusca in some low alkalinity lakes in south-central Ontario. Can J Zool 63: 511–515.

Shah NR, Oberkircher OR, Lobel JS. 1990. Aluminum-induced microcytosis in a child with moderate renal insufficiency. Am J Pediatr Hematol Oncol 12(1): 77-79.

Shakoor A, Gupta PK, Kataria M. 2003. Influence of aluminium on neurotoxicity of lead in adult male albino rats. Indian J Exp Biol 41(6): 587-591.

Sharma P, Mishra KP. 2006. Aluminum-induced maternal and developmental toxicity and oxidative stress in rat brain: response to combined administration of Tiron and glutathione. Reprod Toxicol 21(3): 313-321.

Shcherbatykh I, Carpenter DO. 2007. The role of metals in the etiology of Alzheimer's disease. J Alzheimers Dis: 191-205.

Sherrard DJ, Walker JV, Boykin JL, Dis. AJK. 1988. Precipitation of dialysis dementia by deferoxamine treatment of aluminum-related bone disease. Am J Kidney Dis 12: 126-130.

Shi-Lei S, Guang-Yu MA, Bachelor LH, Bachelor ZY, Dong HM, Xu XH. 2005. Effect of naloxone on aluminum-induced learning and memory impairment in rats. Neurol India 53(1): 79-82.

Shock SS, Bessinger BA, Lowney YW, Clark JL. 2007. Assessment of the solubility and bioaccessibility of barium and aluminum in soils affected by mine dust deposition. Environ Sci Technol 41(13): 4813-4820.

Silva VS, Cordeiro JM, Matos MJ, Oliveira CR, Goncalves PP. 2002. Aluminum accumulation and membrane fluidity alteration in synaptosomes isolated from rat brain cortex following aluminum ingestion: effect of cholesterol. Neurosci Res 44(2): 181-193.

Silva VS, Duarte AI, Rego AC, Oliveira CR, Goncalves PP. 2005. Effect of chronic exposure to aluminium on isoform expression and activity of rat (Na+/K+)ATPase. Toxicol Sci 88(2): 485-494.

Silva VS, Goncalves PP. 2003. The inhibitory effect of aluminium on the (Na+/K+)ATPase activity of rat brain cortex synaptosomes. J Inorg Biochem 97(1): 143-150.

Sim M, Dick R, Russo J, Bernard B, Grubb P, Krieg E, Jr., Mueller C, McCammon C. 1997. Are aluminium potroom workers at increased risk of neurological disorders? Occup Environ Med 54(4): 229-235.

Sjogren B, Elinder CG, V. L, G. C. 1988. Uptake and urinary excretion of aluminum among welders. Int Arch Occup Environ Health 60: 77-79.

Sjogren B, Gustavsson P, Hogstedt C. 1990. Neuropsychiatric symptoms among welders exposed to neurotoxic metals. Br J Ind Med 47(10): 704-707.

Sjogren B, Iregren A, Frech W, Hagman M, Johansson L, Tesarz M, Wennberg A. 1996. Effects on the nervous system among welders exposed to aluminium and manganese. Occup Environ Med 53(1): 32-40.

Sjogren B, Lidums V, Håkansson M, Hedström L. 1985. Exposure and urinary excretion of aluminum during welding. Scand J Work Environ Health 11: 39-13.

Skinner BJ, Porter SC. 1989. The dynamic earth. Toronto (ON): John Wiley & Sons. 541 p.

Smeltzer E. 1990. A successful alum/aluminate treatment of Lake Morey, Vermont. Lake and Reservoir Management 6: 9–19.

Smith LF. 1995. Public health role, aluminium and alzheimer's disease. Environmetrics 6: 277-286.

Somova LI, Missankov A, Khan MS. 1997. Chronic aluminum intoxication in rats: dose-dependent morphological changes. Methods Find Exp Clin Pharmacol 19(9): 599–604.

Soucek DJ. 2006. Effects of freshly neutralized aluminum on oxygen consumption by freshwater invertebrates. Arch Environ Contam Toxicol 50: 353-360.

Sparks DL, Friedland R, Petanceska S, Schreurs BG, Shi J, Perry G, Smith MA, Sharma A, Derosa S, Ziolkowski C and others. 2006. Trace Copper Levels in the Drinking Water, but not Zinc or Aluminum Influence CNS Alzheimer-Like Pathology. J Nutr Health Aging 10(4): 247-254.

Sparling DW, Lowe TP. 1996. Environmental hazards of aluminum to plants, invertebrates, fish, and wildlife. Rev Environ Contam Toxicol 145: 1–127.

Sposito G, editor. 1996. The environmental chemistry of aluminum. 2nd edition. Boca Raton (FL): CRC Press.

Spry DJ, Wiener JG. 1991. Metal bioavailability and toxicity to fish in low-alkalinity lakes — a critical review. Environ Pollut 71: 243–304.

Srinivasan PT, Viraghavan T, Kardash B, Bergman J. 1998. Aluminum speciation during drinking water treatment. Water Quality Research Journal of Canada 33: 377–388.

Stauber JL, Florence TM, Davies CM, Adams MS, Buchanan SJ. 1999. Bioavailability of Al in alum-treated drinking water. AWWA 91(11): 84-93.

Steiner KC, Barbour JR, McCormick LH. 1984. Response of *Populus* hybrids to aluminum toxicity. Forest Science 30: 404–410.

Steinhausen C, Kislinger G, Winklhofer C, Beck E, Hohl C, Nolte E, Ittel TH, Alvarez-Bruckmann MJ. 2004. Investigation of the aluminium biokinetics in humans: a 26Al tracer study. Food Chem Toxicol 42(3): 363-371.

Stevens DP, McLaughlin MJ, Alston AM. 1997. Phytotoxicity of aluminium-fluoride complexes and their uptake from solution culture by *Avena sativa* and *Lycopersicon esculentum*. Plant Soil 192: 81-93 [cited in Manoharan et al. 2007].

Strong MJ, Garruto RM, Joshi JG, Mundy WR, Shafer TJ. 1996. Can the mechanisms of aluminum neurotoxicity be integrated into a unified scheme? J Toxicol Environ Health 48(6): 599-613.

Stumm W, Morgan JJ. 1981. Aquatic chemistry. An introduction emphasizing chemical equilibria in natural waters. New York (NY): John Wiley and Sons.

Sturkenboom M, Wolfson C, Rollet E, Heinzlef O, Abenhaim L. 2000. Demyelination multiple sclerosis and hepatitis B vaccination: a population based study in the UK. Neurology 54(A166).

Su C, Evans LJ. 1996. Soil solution chemistry and alfalfa response to $CaCO_3$ and $MgCO_3$ on an acidic gleysol. Canadian Journal of Soil Science 76: 41–47.

Suarez-Fernandez MB, Soldado AB, Sanz-Medel A, Vega JA, Novelli A, Fernandez-Sanchez MT. 1999. Aluminum-induced degeneration of astrocytes occurs via apoptosis and results in neuronal death. Brain Res 835(2): 125-136.

Swegert CV, Dave KR, Katyare SS. 1999. Effect of aluminium-induced Alzheimer like condition on oxidative energy metabolism in rat liver, brain and heart mitochondria. Mech Ageing Dev 112(1): 27-42.

Szerdahelyi P, Kasa P. 1988. Intraventricular administration of the cholinotoxin AF64A increases the accumulation of aluminum in the rat parietal cortex and hippocampus, but not in the frontal cortex. Brain res 444: 356-360.

Takita E, Koyama H, Hara T. 1999. Organic acid metabolism in aluminium-phosphate utilizing cells of carrot (*Daucus carota* L.). Plant Cell Physiol 40: 489-495 [cited in Manoharan et al. 2007].

Talbot RJ, Newton D, Priest ND, Austin JG, Day JP. 1995. Inter-subject variability in the metabolism of aluminium following intravenous injection as citrate. Hum Exp Toxicol 14(7): 595-599.

Tanaka A, Tadano T, Yamamoto K, Kananura N. 1987. Comparison of toxicity to plants among Al^{3+}, $AlSO_4^+$ and AlF complex ions. Soil Sci. Plant Nutr. 33: 43-55 [cited in Manoharan et al. 2007].

Taugbol G, Seip HM. 1994. Study of interaction of DOC with aluminium and hydrogen ion in soil and surface water using a simple equilibrium model. Environ Int 20: 353–361.

Taylor GA, Ferrier IN, McLoughlin IJ, Fairbairn AF, McKeith IG, Lett D, Edwardson JA. 1992. Gastrointestinal absorption of aluminium in Alzheimer's disease: response to aluminium citrate. Age Ageing 21(2): 81-90.

Tessier A, Campbell PGC. 1990. Partitioning of trace metals in sediments and its relationship to their accumulation in benthic organisms. In: Broekaert JAC, Guter S, Adams FB, editors, Metal speciation in the environment. Berlin (Germany): Springer-Verlag. p. 545–569.

Thomas KW, Pellizzari ED, Clayton CA, Whitaker DA, Shores RC, Spengler J, Ozkaynak H, Froehlich SE, Wallace LA. 1993. Particle Total Exposure Assessment Methodology (PTEAM) 1990 study: method performance and data quality for personal, indoor, and outdoor monitoring. J Expo Anal Environ Epidemiol 3(2): 203-226.

Thorne BM, Cook A, Donohoe T, Lyon S, Medeiros DM, Moutzoukis C. 1987. Aluminum toxicity and behavior in the weanling Long-Evans rat. Bull Psychon Soc 25(2): 129-132.

Thorne BM, Donohoe T, Lin KN, Lyon S, Medeiros DM, Weaver ML. 1986. Aluminum ingestion and behavior in the Long-Evans rat. Physiol Behav 36(1): 63-67.

Thornton FC, Schaedle M, Raynal DJ. 1986a. Effects of aluminum on the growth, development, and nutrient composition of honeylocust (*Gleditsia triacanthos* L.) seedlings. Tree Physiol 2: 307–316.

Thornton FC, Schaedle M, Raynal DJ, Zipperer C. 1986b. Effects of aluminium on honeylocust (*Gleditsia triacanthos* L.) seedlings in solution culture. J Exp Bot 37: 775–785.

Tietge JE, Johnson RD, Bergman HL. 1988. Morphometric changes in gill secondary lamellae of brook trout (Salvelinus fontinalis) after long-term exposure to acid and aluminum. Can. J. Fish. Aquat. Sci. 45: 1643-1648.

Tipping E. 1994. WHAM [Windermere Humic Acid Model] – A chemical equilibrium model and computer code for waters, sediments, and soils incorporating a discrete site electrostatic model of ion-binding by humic substances. Comput Geosci 20: 73-1023.

Touze E, Fourrier A, Rue-Fenouche C, Ronde-Oustau V, Jeantaud I, Begaud B, Alperovitch A. 2002. Hepatitis B vaccination and first central nervous system demyelinating event: a case-control study. Neuroepidemiology 21(4): 180-186.

Touze E, Gout O, Verdier-Taillefer MH, Lyon-Caen O, Alperovitch A. 2000. The first episode of central nervous system demyelinization and hepatitis B virus vaccination. Rev Neurol 156(3): 242-246.

Troutman DE, Peters NE. 1982. Deposition and transport of heavy metals in three lake basins affected by acidic precipitation in the Adirondack Mountains, New York. In: Keith LH editor, Energy and environmental chemistry. Vol. 2. Ann Arbor (MI): Ann Arbor Science, p. 33–61.

Tsunoda M, Sharma RP. 1999a. Modulation of tumor necrosis factor alpha expression in mouse brain after exposure to aluminum in drinking water. Arch Toxicol 73(8-9): 419-426.

Tsunoda M, Sharma RP. 1999b. Altered dopamine turnover in murine hypothalamus after low-dose continuous oral administration of aluminum. J Trace Elem Med Biol 13(4): 224-231.

Turmel MC, Courchesne F. 2007. Influence of microbial activity and trace metal speciation in the rhizosphere on metal uptake by wheat. Unpublished manuscript. Département de géographie, Université de Montréal, Montréal, Québec.

Urban NR, Gorham E, Underwood JK, Martin FB, Ogden JG. 1990. Geochemical processes controlling concentrations of Al, Fe, and Mn in Nova Scotia lakes. Limnol Oceanogr 35: 1516–1534.

Valkonen S, Aitio A. 1997. Analysis of aluminium in serum and urine for the biomonitoring of occupational exposure. Sci Total Environ 199(1-2): 103-110.

van Coillie R, Thellen C, Campbell PGC, Vigneault Y. 1983. *Effets toxiques del'aluminium chez les salmonidés en relation avec des conditions physico-chimiques acides*. Can. Tech. Rep. Fish. Aquat. Sci. No. 1237. 88 p.

Van Gestel CAM, Hoogerwerf G. 2001. Influence of soil pH on the toxicity of aluminium for Eisenia Andrei (Oligochaeta: Lumbricidae) in an artificial soil substrate. Pedobiologia 45: 385-395.

Van Ginkel MF, van der Voet GB, D'Haese PC, De Broe ME, Wolff FA. 1993. Effect of citric acid and maltol on the accumulation of aluminum in rat brain and bone. J Lab Clin Med 121: 453-460.

Vance GF, Stevenson FJ, Sikora FJ. 1996. Environmental chemistry of aluminum-organic complexes. In: Sposito, G. (ed.), The environmental chemistry of aluminum. Boca Raton (FL): CRC Press. p. 169-220.

Varner JA, Horvath WJ, Huie CW, Naslund HR, Isaacson RL. 1994. Chronic aluminum fluoride administration. I. Behavioral observations. Behav Neural Biol 61(3): 233–241.

Varner JA, Huie CW, Horvath W, Jensen KF, Isaacson RL. 1993. Chronic ALF, Administration: II Selected histological observations. Neurosci Res Commun 13(2): 99-103.

Varner JA, Jensen KF, Horvath W, Isaacson RL. 1998. Chronic administration of aluminum-fluoride or sodium-fluoride to rats in drinking water: alterations in neuronal and cerebrovascular integrity. Brain Res 784(1-2): 284-298.

Vasiloff GN. 1991. Phytotoxicology Section investigation in the vicinity of Welland Chemical, Sarnia on August 23, 1989. Toronto (ON): Ontario Ministry of the Environment, Report PIBS 1434.

Vasiloff GN. 1992. Phytotoxicology surveillance investigation in the vicinity of Welland Chemical, Sarnia, 1991. Toronto (ON): Ontario Ministry of the Environment, Report PIBS 2072E.

Verbost PM, Berntssen MHG, Kroglund F, Lydersen E, Witters HE, Rosseland BO, Salbu B, Wendelaar Bonga SE. 1995. The toxic mixing zone of neutral and acidic river water: Acute aluminium toxicity in brown trout (*Salmo trutta* L.). Water Air Soil Pollut 85(2): 341-346.

Verreault R, Laurin D, Lindsay J, De Serres G. 2001. Past exposure to vaccines and subsequent risk of Alzheimer's disease. Can Med Assoc J 165(11): 1495-1498.

Verstraeten SV, Erlejman AG, Zago MP, Oteiza PI. 2002. Aluminum affects membrane physical properties in human neuroblastoma (IMR-32) cells both before and after differentiation. Arch Biochem Biophys 399(2): 167-73.

Verstraeten SV, Keen CL, Golub MS, Oteiza PI. 1998. Membrane composition can influence the rate of Al3+ -mediated lipid oxidation: effect of galoactolipids. Biochem journal 333: 833-838.

Vogt T. 1986. Water quality and health. A story of a possible relationship between aluminium in drinking water and age-related dementia. Oslo, Norway. 145 p.

von Linstow Roloff E, Platt B, Riedel G. 2002. Long-term study of chronic oral aluminum exposure and spatial working memory in rats. Behav Neurosci 116(2): 351-356.

Walker VR, Sutton RA, Meirav O, Sossi V, Johson R, Klein J, Fink D, Middleton R. 1994. Tissue disposition of ^{26}aluminum i rats measured by accelerator mass spectrometry. Clin Invest Med 17: 420-425.

Walton J, Hams G, Wilcox D. 1994. Bioavailability of aluminium from drinking water: co-exposure with foods and beverage. Water Services Association of Australia. Report nr WSAA No.83.

Wang M, Chen JT, Ruan DY, Xu YZ. 2002a. The influence of developmental period of aluminum exposure on synaptic plasticity in the adult rat dentate gyrus in vivo. Neuroscience 113(2): 411-419.

Wang M, Ruan DY, Chen JT, Xu YZ. 2002b. Lack of effects of vitamin E on aluminium-induced deficit of synaptic plasticity in rat dentate gyrus in vivo. Food Chem Toxicol 40(4): 471-478.

Weatherley NS, Rutt GP, Thomas SP, Ormerod SJ. 1991. Liming acid streams - aluminium toxicity to fish in mixing zones. Water Air Soil Pollut 55: 345–353.

Weberg R, Berstad A. 1986. Gastrointestinal absorption of aluminium from single doses of aluminium containing antacids in man. Eur J Clin Invest 16(5): 428-432.

Wettstein A, Aeppli J, Gautschi K, Peters M. 1991. Failure to find a relationship between mnestic skills of octogenarians and aluminum in drinking water. Int Arch Occup Environ Health 63(2): 97-103.

Wheeler DM, Dodd MB. 1995. Effect of aluminium on yield and plant chemical concentrations of some temperate legumes. Plant Soil 173: 133–145.

Wheeler DM, Edmeades DC, Christie RA. 1992. Effect of aluminum on relative yield and plant chemical concentrations for cereals grown in solution culture at low ionic strength. J Plant Nutr 15: 403–418.

White DM, Longstreth WT, Jr., Rosenstock L, Claypoole KH, Brodkin CA, Townes BD. 1992. Neurologic syndrome in 25 workers from an aluminum smelting plant. Arch Intern Med 152(7): 1443-1448.

Wier, Dixon. 2008. Director of Water and Wastewater Services, City of Ottawa. Personal communication with John Pasternak, Environment Canada, 6 August 2008.

Wilkinson KJ, Campbell PGC. 1993. Aluminum bioconcentration at the gill surface of juvenile Atlantic salmon in acidic media. Environ Toxicol Chem 12: 2083–2095.

William M, Dave M. 2000. Phytotoxicology Soil investigation- School Yards and Beaches Port Colborne (2000). Port Colborne: Ministry of Environmen,. Ontario. 30 p.

Wisniewski HM, Lidsky TI. 1997. The role of aluminium in alzheimer's disease. In: Press MU, editor. Managing Health in the Aluminium Industry. London. p 263-273.

Witters H, Vangenechten JHD, Van Puymbroeck S, Vanderborght OLJ. 1984. Interference of aluminium and pH on the Na-influx in an aquatic insect *Corixa punctata* (Illig.). Bull Environ Contam Toxicol 32: 575-579.

Witters HE, Van Puymbroeck S, Stouthart AJHX, Bonga SEW. 1996. Physicochemical changes of aluminium in mixing zones: mortality and physiological disturbances in brown trout (*Salmo trutta* L.). Environ Toxicol Chem 15: 986–996.

Witters HE, Van Puymbroeck S, Vangenechten JHD, Vanderborght OLJ. 1990. The effect of humic substances on the toxicity of aluminium to adult rainbow trout, *Oncorhynchus mykiss* (Walbaum). J Fish Biol 37: 43–53.

Wobma P, Kjartanson K, Bellamy B, Pernitsky D. 2001. Effects of cold water temperatures on water treatment unit processes. In: New Horizons in Drinking Water, Proceedings of the Annual Conference of the American Water Works Association, Washington, D.C., June 17-21, 2001.

Wold LA, Moore BC, Dasgupta N. 2005. Life-history responses of *Daphnia pulex* with exposure to aluminum sulfate. Lake and Reservoir Management 21(4): 383-390.

Wong HKT, Nriagu JO, McCabe KJ. 1989. Aluminum species in porewaters of Kejimkujik and Mountain lakes, Nova Scotia. Water Air Soil Pollut 46: 155–164.

Wood CM, McDonald DG, Booth CE, Simons BP, Ingersoll CG, Bergman HL. 1988a. Physiological evidence of acclimation to acid/aluminum stress in adult brook trout (*Salvelinus fontinalis*). 1. Blood composition and net sodium fluxes. Can. J. Fish. Aquat. Sci. 45: 1587–1596.

Wood CM, Simons BP, Mount DR, Bergman HL. 1988b. Physiological evidence of acclimation to acid/aluminum stress in adult brook trout (*Salvelinus fontinalis*). 2. Blood parameters by cannulation. Can. J. Fish. Aquat. Sci. 45: 1597–1605.

Wood DJ, Cooper C, Stevens J, Edwardson J. 1988. Bone mass and dementia in hip fracture patients from areas with different aluminium concentrations in water supplies. Age Ageing 17(6): 415-419.

[WHO] World Health Organization. 1997. Aluminium. Geneva.

Wren CD, Stephenson GL. 1991. The effect of acidification on the accumulation and toxicity of metals to freshwater invertebrates. Environ Pollut 71: 205–241.

Wright RJ, Baligar VC, Wright SF. 1987. Estimation of phytotoxic aluminium in soil solution using three spectrophotometric methods. Soil Sci 144: 224-233 [cited in Manoharan et al. 2007].

Wu J, Zhou CY, Wong MK, Lee HK, Ong CN. 1997. Urine levels of aluminum after drinking tea. Biol Trace Elem Res 57(3): 271-280.

Xu ZX, Pai SM, Melethil S. 1991. Kinetics of aluminum in rats. II: Dose-dependent urinary and biliary excretion. J Pharm Sci 80(10): 946-951.

Yang MS, Wong MH. 2001. Changes in Ca, Cu, Fe, Mg, and Zn contents in mouse brain tissues after prolonged oral ingestion of brick tea liquor containing a high level of Al. Biol Trace Elem Res 80(1): 67-76.

Yokel R. 2006. Blood-brain barrier flux of aluminum, manganese, iron and other metals suspected to contribute to metal-induced neurodegeneration. J Alzheimers Dis 10: 223-253.

Yokel RA. 1985. Toxicity of gestational aluminum exposure to the maternal rabbit and offspring. Toxicol Appl Pharmacol 79: 121-133.

Yokel RA. 2000. The toxicology of aluminum in the brain: a review. Neurotoxicology 21(5): 813-28.

Yokel RA. 2001. Aluminum toxicokinetics at the blood-barrier. In: Exley C, editor. Aluminium and Alzheimer's Disease. New York: Elsevier.

Yokel RA. 2007. Brain aluminum influx rate determined with the tracer ^{26}Al in the rat. Poster presented at the 46th Annual Meeting of the Society of Toxicology, March 25-29, 2007. Charlotte, NC.

Yokel RA, Florence RL. 2006. Aluminum bioavailability from the approved food additive leavening agent acidic sodium aluminum phosphate, incorporated into a baked good, is lower than from water. Toxicology 227: 86-93.

Yokel RA, Hicks CL, Florence RL. 2008. Aluminum bioavailability from basic sodium aluminum phosphate, an approved food additive emulsifying agent, incorporated in cheese. Food Chem Toxicol 46: 2261-2266.

Yokel RA, McNamara PJ. 1985. Aluminum bioavailability and disposition in adult and immature rabbits. Toxicol Appl Pharmacol 77(2): 344-352.

Yokel RA, McNamara PJ. 1988. Influence of renal impairment, chemical form, and serum protein binding on intravenous and oral aluminum kinetics in the rabbit. Toxicol Appl Pharmacol 95(1): 32-43.

Yokel RA, McNamara PJ. 2000. Aluminum bioavailability (a compilation and critical review). Prepared for the Environmental Substances Division, Health Canada.

Yokel RA, McNamara PJ. 2001. Aluminium toxicokinetics: an updated minireview. Pharmacol Toxicol 88(4): 159-167.

Yokel RA, Rhineheimer SS, Brauer RD, Sharma P, Elmore D, McNamara PJ. 2001a. Aluminum bioavailability from drinking water is very low and is not appreciably influenced by stomach contents or water hardness. Toxicology 161: 93-101.

Yokel RA, Rhineheimer SS, Sharma P, Elmore D, McNamara PJ. 2001b. Entry, half-life, and desferrioxamine-accelerated clearance of brain aluminum after a single (26)Al exposure. Toxicol Sci 64(1): 77-82.

Young LB, Harvey HH. 1991. Metal concentrations in chironomids in relation to the geochemical characteristics of surficial sediments. Arch Environ Contam Toxicol 21: 202–211.

Yuan B, Klein MH, Contiguglia RS, Mishell JL, Seligman PA, Miller NL, Molitoris BA, Alfrey AC, Shapiro JI. 1989. The role of aluminum in the pathogenesis of anemia in an outpatient hemodialysis population. Ren Fail 11: 91-96.

Yuan G, Soma M, Seyama H, Theng BKG, Lavkukich LM, Takamatsu T. 1998. Assessing the surface composition of soil particules from some Podzolic soils by X-Ray photoelectron spectroscopy. Geoderma 86: 169-181.

Yumoto S, Nagai H, Matsuzaki H, Kobayashi T, Tada W, Ohki Y, Kakimi S, Kobayashi K. 2000. Transplacental passage of ^{26}Al from pregnant rats to fetuses and ^{26}Al transfer through maternal milk to suckling rats. Nucl Instrum Methods Phys Res B 172: 925-929.

Yumoto S, Nagai H, Matsuzaki H, Matsumura H, Tada W, Nagatsuma E, Kobayashi K. 2001. Aluminium incorporation into the brain of rat fetuses and sucklings. Brain Res Bull 55(2): 229-234.

Zafar TA, Weaver CM, Martin BR, Flarend R, Elmore D. 1997. Aluminum (26AI) metabolism in rats. Proc Soc Exp Biol Med 216(1): 81-85.

Zatta P, Ibn-Lkhayat-Idrissi M, Zambenedetti P, Kilyen M, Kiss T. 2002. In vivo and in vitro effects of aluminum on the activity of mouse brain acetylcholinesterase. Brain Res Bull 59(1): 41-45.

Zatta P, Zambenedetti P, Reusche E, Stellmacher F, Cester A, Albanese P, Meneghel G, Nordio M. 2004. A fatal case of aluminium encephalopathy in a patient with severe chronic renal failure not on dialysis. Nephrol Dial Transplant 19(11): 2929-2931.

Zatta PF, Favarato M, Nicolini M. 1993. Deposition of aluminium in brain tissues of rats exposed to inhalation of aluminum acetylacetonate. Neuro Rep 4: 1119-1122.

Zheng YX, Liang YX. 1998. The antagonistic effects of L-do J Inorg Biochem and eserine on Al-induced neurobehavioral deficits in rats. Biomed Environ Sci 11(4): 321-330.

Zhou Y, Harris WR, Yokel RA. 2008. The influence of citrate, maltolate and fluoride on the gastrointestinal absorption of aluminum at a drinking water-relevant concentration: a ^{26}Al and ^{14}C study. J Inorg Biochem 102(4): 798-808.

Zhou Y, Yokel RA. 2005. The chemical species of aluminum influences its paracellular flux across and uptake into Caco-2 cells, a model of gastrointestinal absorption. Toxicol Sci 87(1): 15-26.

Zipp F, Weil JG, Einhaupl KM. 1999. No increase in demyelinating diseases after hepatitis B vaccination. Nat Med 5(9): 964-5.

APPENDICES

Appendix A

Search methodology for aluminum PSL2 draft assessment

Appendix B

Table B1 Epidemiological Investigations into neurological disease and aluminum in drinking water

Appendix C

Table C1 Subset of experimental animal studies for consideration in the exposure-response analysis: neurotoxic effects in exposed adults.

Table C2 Subset of experimental animal studies for consideration in the exposure-response analysis: developmental neurotoxicity or reproductive effects (prenatal exposure and/or exposure during lactation).

Appendix A

Search Methodology, PSL2 Draft Assessment, Aluminum Salts

Toxicological and Epidemiological Data

A comprehensive search of the toxicological and epidemiological literature in relation to the health effects of aluminum was carried out in preparation of the SOS report published in 2000 (Environment Canada and Health Canada 2000). Since publication of this report, literature searches were conducted using the databases Toxline, Pubmed, and Current Contents as well as the organizational Web sites from the standard Existing Substances Division literature search list (ATSDR, ECETOC, IPCS, NICNAS, Health Canada, National Toxicology Program, WHO/Air, WHO/Water). The keywords (in truncated forms) included "aluminum" plus "toxicity", "neurotoxicity", "epidemiology", "bioavailability", "mode of action", "reproductive" and "developmental". For databases functioning on the basis of CAS registration numbers, the CAS RN of aluminum chloride (7446-70-0), aluminum nitrate (13473-90-0) and aluminum sulphate (10043-01-3) were used.

The comprehensive literature search was conducted through 2007. Some articles published in 2008 may also be included.

In addition to evaluating original study reports in the peer-reviewed literature, Health Canada consulted four recent comprehensive reviews of the literature on the toxic effects of aluminum: ATSDR (2006); InVS-Afssa-Afssaps (2003); JECFA (2006); and Krewski et al. (2007). These reviews were used primarily to supplement the literature search and are also cited as sources for some toxicological and exposure information, where appropriate. However, for all issues central to Health Canada's evaluation of human health risks, the original articles were consulted and cited.

Exposure Data (see text for sources of data for exposure estimates).

Environmental evaluation

Data relevant to the risk characterization of aluminum chloride, aluminum nitrate and aluminum sulphate to the environment were identified from existing review documents, published reference texts and online searches of the following databases: Aqualine, ASFA (Aquatic Sciences and Fisheries Abstracts, Cambridge Scientific Abstracts; 1996), BIOSIS (Biosciences Information Services; 1990–1996), CAB (Commonwealth Agricultural Bureaux), CESARS (Chemical Evaluation Search and Retrieval System, Ontario Ministry of the Environment and Michigan Department of Natural Resources; 1996), Chemical Abstracts (Chemical Abstracts Service, Columbus, Ohio), CHRIS (Chemical Hazard Release Information System; 1964–1985), Current Contents (Institute for Scientific Information; 1993–1996), ELIAS (Environmental Library Integrated Automated System, Environment Canada library; January 1996), Enviroline (R.R. Bowker Publishing Co.; November 1995–June 1996), Environmental Abstracts (1975–February 1996), Environmental Bibliography (Environmental

Studies Institute, International Academy at Santa Barbara; 1990–1996), GEOREF (Geo Reference Information System, American Geological Institute; 1990–1996), HSDB (Hazardous Substances Data Bank, U.S. National Library of Medicine; 1990–1996), Life Sciences (Cambridge Scientific Abstracts; 1990–1996), NTIS (National Technical Information Service, U.S. Department of Commerce), Pollution Abstracts (Cambridge Scientific Abstracts, U.S. National Library of Medicine), POLTOX (Cambridge Scientific Abstracts, U.S. National Library of Medicine; 1990–1995), RTECS (Registry of Toxic Effects of Chemical Substances, U.S. National Institute for Occupational Safety and Health; 1996), Toxline (U.S. National Library of Medicine; 1990–1996), TRI93 (Toxic Chemical Release Inventory, U.S. Environmental Protection Agency, Office of Toxic Substances; 1993), USEPA-ASTER (Assessment Tools for the Evaluation of Risk, U.S. Environmental Protection Agency; up to December 21, 1994), WASTEINFO (Waste Management Information Bureau of the American Energy Agency; 1973–September 1995) and Water Resources Abstracts (U.S. Geological Survey, U.S. Department of the Interior; 1990–1996). A further search of the scientific literature was conducted in 2007 using SciFinder, an electronic interface that allows access to six databases: CA Plus (Literature from journals, patents, books, conferences, etc.), Registry (substances), Chemlist (regulatory listing), ChemCats (commercial chemical suppliers), CASReact (reaction database) and Medline.

As well as retrieving references from literature database searches, direct contacts were made with researchers, academics and other government agencies. In addition, a survey of Canadian industry was carried out under authority of section 16 of CEPA (Environment Canada 1997b), and a second review aimed at identifying changes in use trends and quantities was conducted in 2007 (Cheminfo Services Inc. 2008). Companies were required to provide information on uses, releases, environmental concentrations, effects or other data that were available to them and related to aluminum salts. Ongoing scans were conducted of the open literature, conference proceedings and the Internet for relevant information. Data obtained to August 2008 were considered in this assessment report.

Appendix B

Tables

Table B1 Epidemiological investigations into neurological disease and aluminum in drinking water					
Location Collection period	References Study type	Study population and health outcomes	Exposure measure	Results	Comments
Ontario 1981–1991	McLachlan et al. (1996) Case-control study	Cases and controls based on brains donated to Canadian Brain Tissue Bank. Cases: a1—296 AD based on clinical history of dementia and histopathology criteria (neuritic plaques and NFTs in specific brain regions); a2—89 AD as above coexisting with other neuropathologic process. Controls: c1—125 with no brain histopathology; c2—170 with other neurodegenerative diseases.	Total Al in drinking water based on the data of the Water Quality Surveillance Programme of the Ontario Ministry of the Environment for municipal supplies serving place of residence and residential history (1981–1991).	Not weighted for residential history: al vs c1 + c2: Al≥100 vs <100 µg/L, OR = 1.7 (95% CI 1.2–2.6) Al≥125 vs <125 µg/L, OR = 3.6 (95% CI 1.4–9.9) Al≥150 vs <150 µg/L, OR = 4.4 (95% CI 0.98–20) Al≥175 vs <175 µg/L, OR = 7.6 (95% CI 0.98–61) a1 + a2 vs c1 + c2: Al≥100 vs <100 µg/L, OR = 1.7 (95% CI 1.2–2.5) Weighted for 10-year residential history: a1 vs c1 + c2: Al≥100 vs <100 µg/L, OR = 2.6 (95% CI 1.2–5.7) a1 + a2 vs c1 + c2: Al≥100 vs <100 µg/L, OR = 2.5 (95% CI 1.2–5.3) a1 vs c2: Al≥100 vs <100 µg/L, OR = 2.5 (95% CI 1.1–5.6)	No control for age, sex, education, occupation, etc. Exposure weighted for 10-year residential history for 119 cases and 51 controls. AD clinical diagnostic criteria not stated.
Ontario 1984–1991	Forbes et al. (1995b) Forbes and McLachlan (1996) Cross-sectional study	AD or presenile dementia based on death certificate data (ICD-9 331.0 and ICD-9 290.1) from LSA cohort. Forbes et al. (1995b): ≈3,000 death certificates reporting dementia (AD and presenile dementia). Forbes and McLachlan (1996): 1,041 death certificates reporting AD (≥85 years of age).	Total Al in drinking water based on the data of the Water Quality Surveillance Programme of the Ontario Ministry of the Environment for municipal supplies serving place of residence at time of death.	Forbes et al. (1995b): For individuals of ≥75 years of age with AD: For Al alone: Al≤67 µg/L, RR = 1.00 Al = 68–200 µg/L, RR = 0.91 (95% CI 0.82–1.01) Al≥336 µg/L, RR = 3.15 (95% CI 1.85–5.36) Adjustment for pH: Al≤67 µg/L, pH<7.85, RR = 1.00 Al = 68–200 µg/L, pH = 7.85–7.95, RR = 0.91 (95% CI 0.82–1.00) Al≥336 µg/L, pH≥7.95, RR = 3.27 (95% CI 1.92–5.57) Adjustment for F: Al≤67 µg/L, RR = 1.00	No control for sex, education, occupation, etc. Possible inaccuracies in death certificate data due to the different certification practices of local doctors. No information on duration of

Table B1 Epidemiological investigations into neurological disease and aluminum in drinking water					
Location Collection period	References Study type	Study population and health outcomes	Exposure measure	Results	Comments
				Al = 68–200 µg/L, F<300 µg/L, RR = 0.95 (95% CI 0.84–1.06) Al≥336 µg/L, F≥860 µg/L, RR = 3.10 (95% CI 1.81–5.27) Adjustment for Al/F interaction term: Al≤67 µg/L, F<300 µg/L, RR = 1.00 Al = 68–200 µg/L, RR = 1.11 (95% CI 0.92–1.33) Al≥336 µg/L, RR = 3.88 (95% CI 2.22–6.77) Al≤67 µg/L, F≥860 µg/L, RR = 1.00 Al = 68–200 µg/L, RR = 0.85 (95% CI 0.74–0.98) Al≥336 µg/L, RR = 0.98 (95% CI 0.14–6.97) Adjustment for Si: Al≤67 µg/L, RR = 1.00 Al = 68–200 µg/L, Si<1.5 mg/L, RR = 0.90 (95% CI 0.81–1.00) Al≥336 µg/L, Si≥1.5 mg/L, RR = 3.14 (95%CI 1.84–5.34) Adjustment for Al/Si interaction term: Al≤67 µg/L, Si<1.5 mg/L, RR = 1.00 Al = 68–200 µg/L, RR = 1.00 (95% CI 0.89–1.13) Al≥336 µg/L, RR = 4.04 (95% CI 2.32–7.03) Al≤67 µg/L, Si≥1.5 mg/L, RR = 1.00 Al = 68–200 µg/L, RR = 0.67 (95% CI 0.55–0.82) Al≥336 µg/L, RR = 0.88 (95% CI 0.12–6.29) Similar analyses with individuals with AD and presenile dementia, with presenile dementia alone, and with AD individuals of all ages were presented. The RRs were smaller. Forbes and McLachlan (1996): For individuals ≥85 years of age: For Al alone: Al = 68–250 µg/L vs ≤67 µg/L, RR = 0.85, p<0.05 Al>250 µg/L vs ≤67 µg/L, RR = 4.76, p<0.05 Adjustment for water source: Al = 68–250 µg/L vs ≤67 µg/L, RR = 0.88, p>0.05 Al>250 µg/L vs ≤67 µg/L, RR = 4.93, p<0.05	exposure. RR corresponds to rate ratio where the population reference was from Ontario Longitudinal Study of Aging.

Table B1 Epidemiological investigations into neurological disease and aluminum in drinking water					
Location Collection period	References Study type	Study population and health outcomes	Exposure measure	Results	Comments
				Adjustment for water source, Si: Al = 68–250 µg/L vs ≤67 µg/L, RR = 0.91, p>0.05 Al>250 µg/L vs ≤67 µg/L, RR = 5.07, p<0.05 Adjustment for water source, Si, Fe: Al = 68–250 µg/L vs ≤67 µg/L, RR = 0.89, p>0.05 Al>250 µg/L vs. ≤67 µg/L, RR = 6.27, p<0.05 Adjustment for water source, Si, Fe, pH: Al = 68–250 µg/L vs ≤67 µg/L, RR = 0.91, p>0.05 Al>250 µg/L vs ≤67 µg/L, RR = 7.38, p<0.05 Adjustment for water source, Si, Fe, pH, F: Al = 68–250 µg/L vs ≤67 µg/L, RR = 0.90, p>0.05 Al>250 µg/L vs. ≤ 67 µg/L, RR= 7.56, p < 0.05 Adjustment for water source, Si, Fe, pH, F, turbidity: Al = 68–250 µg/L vs ≤67 µg/L, RR = 0.89, p>0.05 Al>250 µg/L vs ≤ 67 µg/L, RR = 9.95, p<0.05	
Ontario 1990–1991	Forbes et al. (1992) Forbes et al. (1994) Forbes and Agwani (1994) Forbes et al. (1995a) Cross-sectional study	Males with cognitive impairment based on interview/questionnaire with modified mental status test for subjects from the LSA cohort. For deceased persons, the questionnaires were administered to survivors or proxy respondants. Forbes et al. (1992): 485 males. Forbes et al. (1994): 290 males for analysis restricted to treated surface drinking water and 485 males for other analysis.	Total Al in drinking water based on the data of the Water Quality Surveillance Programme of the Ontario Ministry of the Environment for municipal supplies serving place of residence and residential history. Medians of Al and F	Forbes et al. (1992): Based on treated water: Al≥84.7 µg/L vs Al<84.7 µg/L OR = 1.14 (p>0.05) Al<84.7 µg/L, F>880 µg/L, OR = 1.00 Al≥84.7 µg/L, F>880 µg/L, OR = 1.69 (p>0.05) Al<84.7 µg/L, F<880 µg/L, OR = 2.21 (p<0.05) Al≥84.7 µg/L, F<880 µg/L, OR = 2.72 (p<0.01) Al<84.7 µg/L, F<880 µg/L, OR = 1.00 Al<84.7 µg/L, F>880 µg/L, OR = 0.45 (p<0.05) Al≥84.7 µg/L, F<880 µg/L, OR = 1.23 (p>0.05) Al≥84.7 µg/L, F<880 µg/L, OR = 1.00 other combinations of Al and F, OR≈0.61 (p>0.05) Al<84.7 µg/L, F>880 µg/L, OR = 1.00 Al≥84.7 µg/L, F>880 µg/L, OR = 1.69 (p>0.05) other combinations of Al and F, OR = 1.95 (p<0.05) Similar analyses with raw water concentrations were presented but no significant association was reported.	Forbes et al. (1992), Forbes et al. (1994), Forbes and Agwani, (1994), Forbes et al.(1995a): Exposure not weighted for residential history. Cognitive impairments generally slight. Forbes et al. (1992), Forbes and Agwani, (1994): No control for age, education, occupation, etc.

Table B1 Epidemiological investigations into neurological disease and aluminum in drinking water					
Location Collection period	References Study type	Study population and health outcomes	Exposure measure	Results	Comments
		Forbes and Agwani (1994): 530 males. Forbes et al. (1995a): 494–541 males for each analysis.	concentrations are the cut-off values.	Forbes et al. (1994): Restricted to treated surface drinking water (N = 290): Al≥84.7 vs <84.7 µg/L, OR = 1.53 (95% CI 0.94–2.51) Al<84.7 µg/L, F≥880 µg/L, OR = 1.00 Al≥84.7 µg/L, F≥880 µg/L, OR = 2.13 (95% CI 1.09–4.12) Al<84.7 µg/L, F<880 µg/L, OR = 2.75 (95% CI 1.20–6.27) Al≥84.7 µg/L, F<880 µg/L, OR = 3.98 (95% CI 1.72–9.19) Forbes et al. (1994): Increased ORs when analysis restricted to subjects residing >5 years at current address. Analyses based on all treated drinking water (N = 485): pH<7.85 (N = 68) Al≥84.7 vs <84.7 µg/L, OR = 0.76 (95% CI 0.28–2.06) Al≥84.7 vs <84.7 µg/L with F<880 µg/L, OR = 0.91 (95% CI 0.30–2.74) pH = 7.85–8.05 (N = 54) Al≥84.7 vs <84.7 µg/L, OR = 0.68 (95% CI 0.21–2.19) Al≥84.7 vs <84.7 µg/L with F<880 µg/L, OR = 0.67 (95% CI 0.07–6.41) pH>8.05 (N = 363) Al≥84.7 vs <84.7 µg/L, OR = 1.30 (95% CI 0.85–2.04) Al≥84.7 vs <84.7 µg/L with F<880 µg/L, OR = 1.36 (95% CI 0.55–3.39) Al≥84.7 vs <84.7 µg/L, F≥880 vs <880 µg/L, OR = 0.87 (95% CI 0.50–1.52) Al<84.7 µg/L, F≥880 vs <880 µg/L, OR = 0.47 (95% CI 0.23–0.97) Logistic regression adjusted for F, pH, water source, age, education, health, income and number of moves: Al≥84.7 vs <84.7 µg/L, OR = 1.72 (95% CI 1.08–2.75) Forbes and Agwani (1994): Logistic regression adjusted for F, pH, turbidity, dissolved organic	Forbes et al. (1994), Forbes et al. (1995a): Selected analyses included control for education, health status at age 62, income at age 45, number of moves and age.

Table B1 Epidemiological investigations into neurological disease and aluminum in drinking water					
Location Collection period	References Study type	Study population and health outcomes	Exposure measure	Results	Comments
				carbon and water source: Al≥84.7 vs <84.7 µg/L, OR = 1.97 (95% CI 1.21–3.22) Logistic regression adjusted for F, pH, turbidity, dissolved organic carbon, water source and detailed source: Al≥84.7 vs <84.7 µg/L, OR = 2.27 (95% CI 1.27–4.07) Forbes et al. (1995a): Logistic regression adjusted for F, pH, turbidity, dissolved organic carbon, Si, Fe, water source, education, health status, income and number of moves (N = 530): Without age term: Al≥84.7 vs <84.7 µg/L, OR = 2.19 (95% CI 1.29–3.71) With age term: Al≥84.7 vs <84.7 µg/L, OR = 2.19 (95% CI 1.29–3.71) With age term and Al/Si interaction term: Al≥84.7 vs <84.7 µg/L, OR = 2.35 (95% CI 1.32–4.18) Logistic regression adjusted for F, pH, Si, water source and Al/Si interaction (N = 541): Al≥84.7 vs <84.7 µg/L, OR = 1.98 (95% CI 1.20–3.26) Analysis for Si (N = 494): Al≥84.7 vs <84.7 µg/L, OR = 1.47 (95% CI 0.99–2.20) Al<84.7 µg/L, Si≥790 vs <790 µg/L, OR = 2.20 (95% CI 1.02–4.74) Al≥84.7 µg/L, Si≥790 vs <790 µg/L, OR = 0.89 (95% CI 0.54–1.47)	
Ontario 1986–1987	Neri and Hewitt (1991) Neri et al. (1992) Case-control	Cases: AD and presenile dementia based on ICD criteria from individuals' hospital discharge data. Controls: other diagnoses (not psychiatric or neurological) matched to	Total Al in drinking water based on the data of the Water Quality Surveillance Programme of the Ontario	Neri and Hewitt (1991); Neri et al. (1992): Significant dose-response between AD and concentrations ≥10 µg/L (p<0.05). Neri and Hewitt (1991): <10 µg/L, RR = 1.0 10–99 µg/L, RR = 1.13 100–199 µg/L, RR = 1.26	Control for age and sex. Stronger dose-response upon reanalysis restricted to age >75 years (Smith 1995). No information on

Table B1 Epidemiological investigations into neurological disease and aluminum in drinking water					
Location Collection period	References Study type	Study population and health outcomes	Exposure measure	Results	Comments
		cases for age/sex. ≥55 years of age. Neri and Hewitt (1991): 2,232 cases/2,232 controls. Neri et al. (1992): 2,258 cases/2,258 controls.	Ministry of the Environment for municipal supplies serving place of current residence.	>200 µg/L, RR = 1.46 95% CI or p value are not mentioned Neri et al. (1992): <10 µg/L, RR = 1.00 10–99 µg/L, RR = 1.15 100–199 µg/L, RR = 1.45 >200 µg/L, RR = 1.46 95% CI or p value are not mentioned	the history of exposure. Possible inaccuracies in death certificate data due to the different certification practices of local doctors.
Quebec (Saguenay-Lac-Saint-Jean) 1994	Gauthier et al. (2000) Case-control study	Cases: 68 probable and possible AD based on a three-step procedure: (1) MMS examination, (2) DSM-IV criteria, (3) NINCDS-ADRDA and ICD-10. Controls: 68 free of cognitive impairment, matched with cases for age and sex. ≥70 years of age.	Al in drinking water based on water samples of 54 municipalities collected four times from 1995 to 1996. Al species (e.g., dissolved, monomeric, polymeric) were quantified. The fourth quartile of the concentration of each Al species was the cut-off value.	For long-term exposure to Al (1945 to onset): No significant association for any Al species. For exposure estimated at onset (vs <fourth quartile): Total (>77.2 µg/L): OR = 2.10 (95% CI 0.83–5.35) Total dissolved (>38.9 µg/L): OR = 1.93 (95% CI 0.79–4.67) Monomeric organic (>12.2 µg/L): OR = 2.67 (95% CI 1.04–6.90) Monomeric inorganic (>8.4 µg/L): OR = 0.71 (95% CI 0.29–1.72) Al-OH (>8 µg/L): OR = 0.53 (95% CI 0.20–1.42) Al-F (>0.3 µg/L): OR = 0.67 (95% CI 0.26–1.67) Al-Si (>0.04 µg/L): OR = 0.67 (95% CI 0.26–1.69) Polymeric (>14.6 µg/L): OR = 1.98 (95% CI 0.79–4.98)	Examination of the speciation of Al in drinking water. Control for age, sex, education level, family history, ApoE ε4 allele and occupational exposure.
France (southwestern: Gironde and Dordogne) 1988–1989	Jacqmin et al. (1994) Jacqmin-Gadda et al. (1996) Cross-	Cognitive impairment based on the MMS examinations of individuals ≥65 years of age from the PAQUID cohort. Jacqmin et al. (1994): 3,469 individuals.	Total Al in drinking water based on data from treatment plant or distribution system serving	Jacqmin et al. (1994): No significant association with Al without adjustment for pH; association positive for pH≤7.3, association negative for pH≥7.3 (p values not mentioned). Logistic regression adjusted for age, sex, education, occupation, calcium, pH:	Control for age, sex, education levels, principal lifetime occupation and calcium. Exposure not

Table B1 Epidemiological investigations into neurological disease and aluminum in drinking water					
Location Collection period	References Study type	Study population and health outcomes	Exposure measure	Results	Comments
	sectional study	Jacqmin-Gadda et al. (1996): 3,430 individuals.	place of residence (from two analysis surveys). Data from distribution system were weighted to take into account the period length of use of each treatment plant over the previous 10 years (1981–1991) and the hourly flow or the relative contribution of the treatment plant.	OR = 5.2 (95% CI 1.1–25.1),with increase of logarithm of the Al concentration (1 mg Al/L) OR = 0.80 (95% CI 0.65–0.98), with increase of logarithm of the Al concentration (1 mg Al/L) with the pH/Al interaction term No significant association (p>0.05) when adjusted for education and occupation. Jacqmin-Gadda et al. (1996): Logistic regression adjusted for age, sex, education, occupation, calcium, pH, Si: Only significant association ($p<0.05$) with Al when the cutpoint was the first quartile of Al (vs median and third quartile): Al≥3.5 µg/L vs <3.5 µg/L: OR = 1.65 (95% CI 0.80–3.39) (without Al/Si interaction term) OR = 3.94 (95% CI 1.39–11.2) (with Al/Si interaction term) Logistic regression adjusted for personal characteristics and calcium: Al<3.5 µg/L, pH<7.35, Si<10.4 mg/L, OR = 1.00 Al≥3.5 µg/L: pH≥7.35, Si≥10.4 mg/L, OR = 0.75 (95% CI 0.59–0.96) pH≥7.35, Si<10.4 mg/L, OR = 0.89 (95% CI 0.64–1.22) pH<7.35, Si≥10.4 mg/L, OR = 0.74 (95% CI 0.53–1.02) pH < 7.35, Si < 10.4 mg/L, OR = 1.30 (95%CI 0.75-2.24)	weighted for residential history.
France (southwestern: Gironde and Dordogne) 1988–1989 to 1997	Rondeau et al. (2000) Rondeau et al. (2001) Longitudinal study (follow-up analysis in eight years)	Dementia and AD based on a two-step procedure: (1) DSM-III criteria, (2) for those with positive DSM results or decline of MMS score (>2 points), NINCDS-ADRDA criteria for AD and Hachinski score for vascular dementia. Re-evaluation of the subjects one, three, five and eight years after the initial visit (the subjects from Dordogne were not re-evaluated after one	Total Al in drinking water based on data from treatment plant or distribution system serving place of residence (from two analysis surveys). Data from distribution	RR for 253 cases of dementia: Adjustment for age and sex: Al≥100 vs <100 µg/L, RR = 2.33 (95% CI 1.42–3.82) Increase of 100 µg/L Al, RR = 1.36 (95% CI 1.15–1.61) Adjustment for age, sex, educational level, wine consumption and place of residence: Al<3.8 µg/L, RR = 1 Al≥3.8 vs <11.0 µg/L, RR = 1.03 (95% CI 0.74–1.43) Al≥11.0 vs <100 µg/L, RR = 0.98 (95% CI 0.69–1.40) Al≥100 µg/L, RR = 2.00 (95% CI 1.15–3.50) Al≥100 vs <100 µg/L, RR = 1.99 (95% CI 1.20–3.28) Increase of 100 µg/L Al, RR = 1.25 (95% CI 1.05–1.50)	Control for age, sex, education, wine consumption and place of residence. Exposure not weighted for residential history.

Table B1 Epidemiological investigations into neurological disease and aluminum in drinking water					
Location Collection period	References Study type	Study population and health outcomes	Exposure measure	Results	Comments
		year). Initially, 2,698 nondemented subjects ≥65 years of age from the PAQUID cohort participated in this study	system were weighted to take into account the period length of use of each treatment plant over the previous 10 years (1981–1991) and the hourly flow or the relative contribution of the treatment plant.	RR for 182 cases of AD: Adjustment for age and sex: Al≥100 vs <100 µg/L, RR = 2.20 (95% CI 1.24–3.84) Increase of 100 µg/L Al, RR = 1.46 (95% CI 1.23–1.74) Adjustment for age, sex, educational level, wine consumption and place of residence: Al<3.8 µg/L, RR = 1 Al≥3.8 vs <11.0 µg/L, RR = 1.16 (95% CI 0.78–1.72) Al≥11.0 vs <100 µg/L, RR = 0.97 (95% CI 0.63–1.49) Al≥100 µg/L, RR = 2.27 (95% CI 1.19–4.34) Al≥100 vs <100 µg/L, RR = 2.14 (95% CI 1.21–3.80) Increase of 100 µg/L Al, RR = 1.35 (95% CI 1.11–1.62) RR for 105 cases of dementia (among 1,638 individuals): Adjustment for mineral water consumption, age, sex, education level, wine consumption and place of residence: Al≥100 vs <100 µg/L, RR = 3.36 (95% CI 1.74–6.49)	
France (southwestern: Gironde and Dordogne) 1988–1989	Michel et al. (1991) Cross-sectional study	Possible and probable AD based on a two-step procedure: (1) DSM-III, (2) NINCDS-ADRDA criteria in 2,731 individuals ≥65 years of age from the PAQUID cohort.	Total Al in drinking water based on data from treatment plant or distribution system serving place of residence (years of collection not mentioned).	Spearman rank correlation between Al concentration and AD was significantly different from zero (p<0.05). Logistic regression adjusted for age, education and place of residence: Increase of 10 µg/L, RR = 1.16, p = 0.0014 Increase of 100 µg/L, RR = 4.53 (95% CI 3.36–6.10)	Control for age, education, rural and urban residence. Relationship between Al and AD discounted based on updated analyses of water Al levels post-publication (Smith 1995; WHO 1997).
Eight regions of England and Wales 1986–1992	Martyn et al. (1997) Case-control study	Cases: 106 with clinical diagnosis of AD or normal computer tomography (CT) scan or cerebral atrophy, with a progressive deterioration of cognition in the absence of other causes for dementia. Controls: 99 patients with other types of dementia	Al in drinking water based on data from treatment plant or distribution system serving place of residence and residential history from age	No significant association between AD and drinking water concentrations based on several OR (27 OR were presented and were not significant p>0.05): Al = 15–44, Al = 45–109 and Al≥110 µg/L in comparison to Al<15 µg/L When: Al concentrations were averaged over 10 years before diagnosis Al concentrations were averaged from age 25 to 10 years before	Control for age, neuroradiology centre where diagnosis was made and distance of residence from neuroradiology centre. AD clinical

Table B1 Epidemiological investigations into neurological disease and aluminum in drinking water					
Location Collection period	References Study type	Study population and health outcomes	Exposure measure	Results	Comments
		(normal CT), 226 patients with brain cancer and 441 patients with other neurological disorders. Cases and controls were all males born between 1916 and 1945.	of 25 years to diagnosis.	diagnosis Al concentrations were averaged over 10 years before diagnosis For the three sets of controls (i.e., other dementia, brain cancer, other diagnoses). No significant association between AD and Al in drinking water when Si<6 mg/L (again based on 27 OR, with ≈40 cases, ≈34 patients with other dementia, ≈60 patients with brain cancer and ≈166 patients with other diagnoses).	diagnostic criteria not stated.
Northern England 1990–1992	Forster et al. (1995) Case-control study	Cases: 109 AD-type presenile dementia diagnosed before 65 years of age based on a three-step procedure: (1) hospital case notes (NINCDS-ADRDA and DSM criteria), (2) MMS examination, (3) geriatric mental state examination. Controls: 109 from general population paired for age and sex with exclusion of potentially dementia.	Al in drinking water based on data from water treatment plant serving place of residence, and residential history for longest residence in the 10 years before disease onset. Consumption of tea and of antacid based on interview data.	Al in drinking water 10 years before dementia onset: Al<50 vs >50 µg/L, OR = 1.2 (95% CI 0.67–2.37) Al>50 vs <50 µg/L, OR = 0.8 (95% CI 0.42–1.50) Al>99 vs <99 µg/L, OR = 0.8 (95% CI 0.44–1.49) Al>149 vs <149 µg/L, OR = 1.0 (95% CI 0.41–2.43) Same conclusions when the exposure is based on Al in drinking water at birthplace (N = 80 cases/control). >4 cups tea/day, OR = 1.4 (95% CI 0.81–2.63) Prolonged antacids used, OR = 1.6 (95% CI 0.77–3.51)	Control for age and sex. Same conclusions with control for family history of dementia. No information on presence or absence of Al in antacids.
Northern England (three districts: North Tyneside, Sunderland and Durham) 1982–1985	Wood et al. (1988) Cross-sectional study	Dementia in 386 patients with hip fracture >55 years of age (no information about the mental test).	Al in drinking water based on data from water treatment plants either in two districts where water is not treated with aluminum coagulants (low Al) or in a district where water is treated	No significant difference in mental test scores between the residents from district with high-Al level (180–250 µg/L) and those from districts with low-Al levels (≤50 µg/L).	Control for age and sex. Primary focus of study was bone mass/hip fracture. No information on the history of exposure. Details of mental test scores not

Table B1 Epidemiological investigations into neurological disease and aluminum in drinking water					
Location Collection period	References Study type	Study population and health outcomes	Exposure measure	Results	Comments
			with alum (high Al) (1982–1985), and place of residence.		provided.
Switzerland (Zurich) ≈1989	Wettstein et al. (1991) Cross-sectional study	Cognitive impairment based on MMS scores in 805 residents of two districts aged 81–85 years (400/district) and residing in each district >15 years.	Al in drinking water based on data from water treatment plants either in a district where water is not treated with aluminum coagulants (low Al) or in a district where water is treated with alum (high Al), and place of residence.	No significant difference in MMS scores between the residents from the district with low mean Al level (4 µg/L) and those from the district with high meanAl level (98 µg/L).	Control for socioeconomic status, age and education. No significant differences in Al serum, Al urine or Al urine/creatinine ratio in 20 patients with probable AD in comparison to 20 control patients.

Notes:
AD = Alzheimer's disease
Al = Aluminium
F = Fluoride
LSA = Ontario Longitudinal Study of Aging
NFT = neurofibrillary tangles
OR = Odds ratio
PAQUID = Principle Lifetime Occupation and Cognitive Impairment in a French Elderly Cohort study (≥65 years old)
RR = Relative risk
Si = Silicon
Criteria for Alzheimers or dementia diseases:
ADRDA = Alzheimer's Disease and Related Disorders Associations
DSM = Diagnostic and Statistical Manual of Mental Disorders
ICD = International Classification of Diseases (World Health Organization)
MMS = mini-mental state examination
NINCDS = National Institute of Neurological and Communicative Disorders and Stroke

Appendix C

Tables

Table C1 Subset of experimental animal studies for consideration in the exposure-response analysis: neurotoxic effects in exposed adults				
Species, sex, strain and number Al species (number of dose levels in addition to control)	Exposure Dose levels in study: D_a (administered dose), or D_c (combined dose)	Critical neurotoxic effects in adults (>90-day exposure studies)	LOEL or NOEL (mg Al/kg bw/d) D_a = administered dose D_c = combined dose	References
RATS				
Male Sprague-Dawley rats (five per group) Al sulphate	Drinking water, for various periods up to 12 months One dose level: D_a: 165 mg Al/kg bw/d	Decrease in nitroxidergic neurons in the somatosensory cortex.	**LOEL** = 165 (D_a)	Rodella et al. (2006)
Wistar rats (3 age groups: 3, 10, 24 months) (20 per dose per age group) Al chloride	Drinking water, for 90 days Three dose levels: D_a: 11.1, 21.5 or 43.1 mg Al/kg bw/d	Impaired vestibulo-ocular reflex (results not influenced by age)	**LOEL** = 43.1 (D_a) **NOEL** = 21.5 (D_a)	Mameli et al. (2006)
Male Sprague-Dawley rats (six per group) Al maltolate	Drinking water, for 12 months One dose level: D_a: 0.38 mg Al/kg bw/d*	Induced apoptosis in brain; Increased efficiency of monoamine oxidases; Increase in level of caspase 3 and 12 in brain.	**LOEL** = 1.0 (D_c)	Huh et al. (2005)
Male Wistar rats (seven per group) Al chloride	Gavage (101 mg Al/kg bw/d), for one month, drinking water (45 mg Al/kg bw/d) for additional four months One dose level: D_a: 56 mg Al/kg bw/d* (weighted average dose)	Impaired performance in Morris water maze; Increased expression of amyloid precursor protein and caspase 3 in hippocampus.	**LOEL** = 56 (D_a)	Gong et al. (2005)
Male Wistar rats (ten per group) Al chloride	Diet for four months One dose level: D_a: 19 mg Al/kg bw/d** (assuming same weight gain as in 2002)	Decrease in Na+/K+-ATPase activity in brain cortex synaptosomes.	**LOEL** = 19 (D_a)	Silva et al. (2005)
Sprague-Dawley rats (nine per group)	Gavage, for three months One dose level:	Impaired performance in Morris water maze; Decrease in long-term potentiation in hippocampal	**LOEL** = 121 (D_a)	Shi-Lei et al. (2005)

Table C1 Subset of experimental animal studies for consideration in the exposure-response analysis: neurotoxic effects in exposed adults

Species, sex, strain and number Al species (number of dose levels in addition to control)	Exposure Dose levels in study: D_a (administered dose), or D_c (combined dose)	Critical neurotoxic effects in adults (>90-day exposure studies)	LOEL or NOEL (mg Al/kg bw/d) D_a = administered dose D_c = combined dose	References
Al chloride	D_a: 121 mg Al/kg bw/d	slices.		
Male rats (strain not specified) (20–40 per group) Al species not specified (indicated to be water-soluble)	Gavage, for three months One dose level: D_a: 500 mg Al/kg bw/d	Impaired performance in Morris water maze; Altered synapses in hippocampus and frontal cortex.	**LOEL** = 500 (D_a)	Jing et al. (2004)
Male Wistar rats (ten per group) Al nitrate	Drinking water, for eight months One dose level: D_a: 36 mg Al/kg bw/d*	Evidence of increased lipid peroxidation in brain.	**LOEL** = 36 (D_a)	Flora et al. (2003)
Male Wistar rats (ten per group) Al chloride	Diet for four months One dose level: D_a: 19 mg Al/kg bw/d**	Increase in synaptosomal membrane fluidity; Decrease in cholesterol/phospholipid ratio in synaptosomes.	**LOEL** = 19 (D_a)	Silva et al. (2002)
Male Lister hooded rats (11–24 per group) Al sulphate	Drinking water, for up to seven months One dose level: D_a: 140 mg Al/kg bw/d*	Progressive working memory in water maze.	**NOEL** = 140 (D_a)	Von Linstow Roloff et al. (2002)
Male Sprague-Dawley rats (ten per group) Al nitrate with citrate (two dose levels)	Drinking water, for 6.5 months Two dose levels: D_a: 50 or 100 mg Al/kg bw/d	No effects on open field activity or on shuttle box performance (passive avoidance).	**NOEL** = 100 (D_a) No information on base diet (see Sanchez et al. 1997) where lab chow intake is estimated up to 13 mg/kg bw/d. D_c = 113.	Domingo et al. (1996)
Male Druckrey albino rats (40 per group) Al chloride	Drinking water, for 12 months One dose level: D_a: 36 mg Al/kg bw/d**	Increase in lipid peroxidation in brain.	**LOEL** = 36 (D_a)	Gupta and Shukla (1995)
Wistar rats (6–8 per group) Al citrate	Diet for six months One dose level: D_a: 50 mg Al/kg bw/d*	Cytoplasmic vacuolation in astrocytes and neurons.	**LOEL** = 50 (D_c)	Florence et al. (1994)
Male Druckrey albino rats (90 per exposure group; 6 to 10 animals per test group)	Drinking water, for six months One dose level:	Reduction in spontaneous motor activity; Impaired learning (shuttle box, maze); Increase in brain lipid peroxidation;	**LOEL** = 52 (D_a)	Lal et al. (1993)

Table C1 Subset of experimental animal studies for consideration in the exposure-response analysis: neurotoxic effects in exposed adults				
Species, sex, strain and number Al species (number of dose levels in addition to control)	Exposure Dose levels in study: D_a (administered dose), or D_c (combined dose)	Critical neurotoxic effects in adults (>90-day exposure studies)	LOEL or NOEL (mg Al/kg bw/d) D_a = administered dose D_c = combined dose	References
Al chloride	D_a: 52 mg Al/kg bw/d**	Reduction in Mg^{2+}- and $Na^{+}K^{+}$-ATPase activities.		
Male Sprague-Dawley rats (4–6 per group) Al sulphate	Drinking water, for three months One dose level: D_a: 420 mg Al/kg bw/d*	Decrease in levels of microtubule associated protein-2 and spectrin in hippocampus.	**LOEL** = 420 (D_a)	Johnson et al. (1992)
Male Sprague-Dawley rats (8-14 per group) Al chloride	Diet for 11 months One dose level: D_a: 50 mg Al/kg bw/d*	Reduction in motor activity; Impaired learning (shuttle box).	**LOEL** = 50 (D_a)	Commissaris et al. (1982)
MICE				
CD mice (10 per group) Al lactate	Gavage, for three months One dose level: D_a: 333 mg Al/kg bw/d*	Increase in acetylcholinesterase activity.	**LOEL** = 333 (D_a)	Zatta et al. (2002)
Swiss Webster mice (10–12 per group) Al lactate	Diet for 90 days One dose level: D_c: 160 mg Al/kg bw/d**	Decrease in motor activity, hindlimb grip strength, and auditory and air puff startle responsiveness.	**LOEL** = 160 (D_c)	Golub et al. (1992)
DOGS				
Beagle dogs (6M, 6F per dose) Acidic SALP	Diet for 6 months Three dose levels: D_a: 9.5, 29.0 or 90.0 mg Al/kg bw/d	No difference in body weight; No ocular changes; No effect on haematological parameters; No change in organ weight.	**NOEL** = 90 (D_a)	Katz et al. (1984)

* Dose calculated with Health Canada's reference values for body weights and intakes (Health Canada 1994).
** Dose calculated with author's reported body weights and intakes.

Table C2 Subset of experimental animal studies for consideration in the exposure-response analysis: developmental neurotoxicity or reproductive effects (prenatal exposure and/or exposure during lactation)				
Species, strain and number Al species (number of dose levels in addition to control)	Exposure GD = gestational day PND = postnatal day	Critical effects in pups (or dams where indicated)	LOEL or NOEL (mg Al/kg bw/d) D_a = administered dose D_c = combined dose	References
RATS				
Sprague-Dawley rats (12 per group) Al nitrate with citrate	Drinking water, during gestation and lactation Two maternal dose levels: D_a: 50 or 100 mg Al/kg bw/d	Biphasic effect on learning: improved performance at D_a= 50 mg/kg bw/d, but no difference compared to controls at D_a= 100 mg/kg bw/d; No effect on motor activity.	**NOEL** = 103 (D_c)	Roig et al. (2006)
Wistar rats (eight per group) Al chloride	Gavage, during gestation and lactation One maternal dose level: D_a: 70 mg Al/kg bw/d	Decrease in placental and fetal weight; Increase in number of resorptions; Increase in skeletal malformations; Increase in oxidative stress in brains of mothers/fetuses and sucklings.	**LOEL** = 70 (D_a)	Sharma and Mishra (2006);
Sprague-Dawley rats (5–6 per group) Al chloride	Gavage, during lactation, pups also exposed 39 days after weaning via gavage One maternal dose level: D_a: 100 mg Al/kg bw/d	Increased lipid peroxidation, decrease in superoxide dismutase and catalase activity in cerebrum and cerebellum.	**LOEL** = 100 (D_a)	Nehru and Anand (2005)
Sprague-Dawley rats (10–14 per group) Al nitrate with citrate	Drinking water, during gestation and lactation Two maternal dose levels: D_a: 50 or 100 mg Al/kg bw/d	Increase in number of days to sexual maturation.	**LOEL** = 53 (D_c) (females) **LOEL** = 103 (D_c) (males)	Colomina et al. (2005)
		Improved performance in learning tests (passive avoidance, water maze).	**LOEL** = 103 (D_c)	
		Reduction in forelimb strength in males.	**LOEL** = 103 (D_c) **NOEL** = 53 (D_c)	
Wistar rats (≈ seven pups per group) Al chloride	Drinking water, during lactation One maternal dose level: D_a: 85 mg Al/kg bw/d*	Deficits in synaptic plasticity in dentate gyrus of hippocampus.	**LOEL** = 85 (D_a)	Chen et al. (2002)

Table C2 Subset of experimental animal studies for consideration in the exposure-response analysis: developmental neurotoxicity or reproductive effects (prenatal exposure and/or exposure during lactation)

Species, strain and number Al species (number of dose levels in addition to control)	Exposure GD = gestational day PND = postnatal day	Critical effects in pups (or dams where indicated)	LOEL or NOEL (mg Al/kg bw/d) D_a = administered dose D_c = combined dose	References
Wistar rats (4–10 per group) Al chloride	Drinking water, in three groups: gestation, lactation, and lactation and lifetime One maternal dose level: D_a: 85 mg Al/kg bw/d* (same dose for pups following lactation)	Reduced body weight; Deficits in synaptic plasticity in dentate gyrus of hippocampus. (greatest effect in rats exposed from parturition throughout life, while prenatal exposure was associated with the least effect)	**LOEL** = 85 (D_a)	Wang et al. (2002a)
Wistar rats (number not specified) Al sulphate	Drinking water, during gestation One maternal dose level: D_a: 63 mg Al/kg bw/d*	Decrease in pup body weight; Decreased number of cells in cerebellum; Disaggregation of microtubules and neuronal death in cerebellar neuron cultures.	**LOEL** = 663 (D_a)	Llansola et al. (1999)
Long Evans rats (number not specified) Al lactate	Drinking water, during gestation or prior to mating and then during gestation and lactation One maternal dose level: D_a: 450 mg Al/kg bw/d*	Delayed expression of phosphorylated high molecular weight neurofilament protein in tracts in diencephalon; Maternal toxicity.	**LOEL** = 450 (D_a)	Poulos et al. (1996)
THA rats (8–20 pups per group) Al chloride	Gavage, dams exposed one time (GD8) 2 maternal dose levels: D_a: 183 or 366 mg Al/kg bw/d	Maternal toxicity; Decreased pup weight; Delay in pinna detachment and eye opening in females; Delayed development of auditory startle in males.	**LOEL** = 183 (D_a)	Misawa and Shigeta (1993)
Sprague-Dawley rats (15–19 dams per group) Al hydroxide with and without citrate	Gavage, during gestation One maternal dose level: D_a: 133 mg Al/kg bw/d	Fetal body weight reduced; Skeletal variations increased in Al hydroxide + citrate group.	**LOEL** = 133 (D_a)	Gomez et al. (1991)
Wistar rats (6–9 dams per group) Al lactate	Diet during gestation One maternal dose level: D_a: 400 mg Al/kg bw/d	Impaired negative geotaxis; Impaired performance in suspension and locomotor coordination tests.	**LOEL** = 400 (D_a)	Muller et al. (1990)
		No effects in righting or grasping reflex.	**NOEL** = 400 (D_a)	

Table C2 Subset of experimental animal studies for consideration in the exposure-response analysis: developmental neurotoxicity or reproductive effects (prenatal exposure and/or exposure during lactation)

Species, strain and number Al species (number of dose levels in addition to control)	Exposure GD = gestational day PND = postnatal day		Critical effects in pups (or dams where indicated)	LOEL or NOEL (mg Al/kg bw/d) D_a = administered dose D_c = combined dose	References
Wistar rats (6–12 dams per group) Al chloride and Al lactate	Diet during gestation Three maternal dose levels	Al chloride: 100, 300 and 400 mg Al/kg bw/d	Impaired grasping reflex and impaired righting reflex.	**LOEL** = 300 (D_a) **NOEL** = 100(D_a)	Bernuzzi et al. (1989b)
			Negative geotaxis and locomotor coordination.	**LOEL** = 400 (D_a) **NOEL** = 300 (D_a)	
		Al lactate: 100, 200 and 400 mg Al/kg bw/d	Impaired grasping reflex.	**LOEL** = 100 (D_a)	
			Impaired righting reflex.	**LOEL** = 200 (D_a) **NOEL** = 100 (D_a)	
			Negative geotaxis.	**NOEL** = 400 (D_a)	
			Impaired locomotor coordination.	**LOEL** = 400 (D_a) **NOEL** = 200 (D_a)	
Wistar rats (12 to 14 dams per groups) Al chloride	Diet, during gestation Two maternal dose levels: D_a: 160 or 200 mg Al/kg bw/d		Reduced body weight of pups; Impaired negative geotaxis.	**LOEL** = 160 (D_a)	Bernuzzi et al. (1986)
Wistar rats (6–8 per group) Al chloride	Diet during gestation Two maternal dose levels: D_c: 25 or 50 mg Al/kg bw/d*		No differences in number of live fetuses and resorbed/dead fetuses, fetal body weight and length, or in skeletal anomalies.	**NOEL** = 50 (D_a)	McCormack et al. (1979)
MICE					
Swiss Webster mice (15–17 pups per dose group per sex) Al lactate Less than optimal diet—trace element reduction in lab chow based on deficiencies measured in U.S. women.	Diet during gestation and lactation, continued exposure of pups via diet for 14 days. Three maternal dose levels: D_c: 10, 50 and 100 mg Al/kg bw/d		Decreased weight gain in pups; Impaired learning of maze with respect to cue utilization (females).	**LOEL** = 50 (D_c) **NOEL** = 10 (D_c)	Golub and Germann (2001b)
			Impaired performance in rotarod test (males).	**LOEL** = 100 (D_c) **NOEL** = 50 (D_c)	
Swiss Webster mice (15–19 pups per dose group) Al lactate	Diet during gestation and lactation, continued exposure of pups via diet to PND 35 One maternal dose level: D_c: 100 mg Al/kg bw/d		Reduced forelimb and hindlimb grip strength; Decreased thermal sensitivity.	**LOEL** = 100 (D_c)	Golub et al. (2000)