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# Aluminium in drinking-water

Background document for development of
WHO *Guidelines for Drinking-water Quality*

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## Preface

One of the primary goals of the World Health Organization (WHO) and its Member States is that "all people, whatever their stage of development and their social and economic conditions, have the right to have access to an adequate supply of safe drinking water." A major WHO function to achieve such goals is the responsibility "to propose ... regulations, and to make recommendations with respect to international health matters ...."

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as *International Standards for Drinking-water*. It was subsequently revised in 1963 and in 1971 under the same title. In 1984–1985, the first edition of the WHO *Guidelines for Drinking-water Quality* (GDWQ) was published in three volumes: Volume 1, Recommendations; Volume 2, Health criteria and other supporting information; and Volume 3, Surveillance and control of community supplies. Second editions of these volumes were published in 1993, 1996 and 1997, respectively. Addenda to Volumes 1 and 2 of the second edition were published in 1998, addressing selected chemicals. An addendum on microbiological aspects reviewing selected microorganisms was published in 2002. The third edition of the GDWQ was published in 2004, the first addendum to the third edition was published in 2006 and the second addendum to the third edition was published in 2008. The fourth edition will be published in 2011.

The GDWQ are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking-water are subject to periodic review, and documentation related to aspects of protection and control of public drinking-water quality is accordingly prepared and updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other supporting information to the GDWQ, describing the approaches used in deriving guideline values and presenting critical reviews and evaluations of the effects on human health of the substances or contaminants of potential health concern in drinking-water. In the first and second editions, these constituted Volume 2 of the GDWQ. Since publication of the third edition, they comprise a series of free-standing monographs, including this one.

For each chemical contaminant or substance considered, a lead institution prepared a background document evaluating the risks for human health from exposure to the particular chemical in drinking-water. Institutions from Canada, Japan, the United Kingdom and the United States of America (USA) prepared the documents for the fourth edition.

Under the oversight of a group of coordinators, each of whom was responsible for a group of chemicals considered in the GDWQ, the draft health criteria documents were submitted to a number of scientific institutions and selected experts for peer review. Comments were taken into consideration by the coordinators and authors. The draft documents were also released to the public domain for comment and submitted for final evaluation by expert meetings.

During the preparation of background documents and at expert meetings, careful consideration was given to information available in previous risk assessments carried out by the International Programme on Chemical Safety, in its Environmental Health Criteria monographs and Concise International Chemical Assessment Documents, the International Agency for Research on Cancer, the Joint FAO/WHO Meetings on Pesticide Residues and the Joint FAO/WHO Expert Committee on Food Additives (which evaluates contaminants such as lead, cadmium, nitrate and nitrite, in addition to food additives).

Further up-to-date information on the GDWQ and the process of their development is available on the WHO Internet site and in the current edition of the GDWQ.

**Acknowledgements**

The update of Aluminium in Drinking-water, Background document for development of WHO *Guidelines for Drinking-water Quality* (GDWQ), was prepared by Mr J.K. Fawell, United Kingdom, to whom special thanks are due. This original background document was published in the addendum to the second edition in 1998.

The work of the following working group coordinators was crucial in the development of this document and others contributing to the fourth edition:

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The draft text was discussed at the Expert Consultation for the fourth edition of the GDWQ, held on 9–13 November 2009. The final version of the document takes into consideration comments from both peer reviewers and the public. The input of those who provided comments and of participants at the meeting is gratefully acknowledged.

The WHO coordinators were Mr R. Bos and Mr B. Gordon, WHO Headquarters. Ms C. Vickers provided a liaison with the International Programme on Chemical Safety, WHO Headquarters. Mr M. Zaim, WHO Pesticide Evaluation Scheme, Vector Ecology and Management, WHO Headquarters, provided input on pesticides added to drinking-water for public health purposes.

Ms P. Ward provided invaluable administrative support at the Expert Consultation and throughout the review and publication process. Ms M. Sheffer of Ottawa, Canada, was responsible for the scientific editing of the document.

Many individuals from various countries contributed to the development of the GDWQ. The efforts of all who contributed to the preparation of this document and in particular those who provided peer or public domain review comments are greatly appreciated.

## Acronyms and abbreviations used in the text

| | |
|---|---|
| AAS | atomic absorption spectrometry |
| DNA | deoxyribonucleic acid |
| FAO | Food and Agriculture Organization of the United Nations |
| JECFA | Joint FAO/WHO Expert Committee on Food Additives |
| $LD_{50}$ | median lethal dose |
| LOAEL | lowest-observed-adverse-effect level |
| LOEL | lowest-observed-effect level |
| NOAEL | no-observed-adverse-effect level |
| NOEL | no-observed-effect level |
| PTWI | provisional tolerable weekly intake |
| USA | United States of America |
| WHO | World Health Organization |

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## *1. GENERAL DESCRIPTION*

### *1.1 Identity*

Aluminium is the most abundant metallic element and constitutes about 8% of Earth's crust. It occurs naturally in the environment as silicates, oxides and hydroxides, combined with other elements, such as sodium and fluoride, and as complexes with organic matter.

| Compound | Chemical Abstracts Service Registry No. | Molecular formula |
|---|---|---|
| Aluminium | 7429-90-5 | Al |
| Aluminium chloride | 7446-70-0 | $AlCl_3$ |
| Aluminium hydroxide | 21645-51-2 | $Al(OH)_3$ |
| Aluminium nitrate (anhydrous) | 13473-90-0 | $Al(NO_3)_3$ |
| Aluminium nitrate (nonahydrate) | 7784-27-2 | $Al(NO_3)_3 \cdot 9H_2O$ |
| Aluminium oxide | 1344-28-1 | $Al_2O_3$ |
| Aluminium sulfate | 10043-01-3 | $Al_2(SO_4)_3$ |

### *1.2 Physicochemical properties (Lide, 1993)*

| Property | Al | $AlCl_3$ | $Al(OH)_3$ | $Al(NO_3)_3$ | $Al_2O_3$ | $Al_2(SO_4)_3$ |
|---|---|---|---|---|---|---|
| Melting point (°C) | 660 | 190 | 300 | 72.8 (n) | 2072 | 770 (d) |
| Boiling point (°C) | 2467 | 262 (d) | – | 135 (n) (d) | 2980 | – |
| Density at 20 °C ($g/cm^3$) | 2.70 | 2.44 | 2.42 | 1.72 (n) | 3.97 | 2.71 |
| Water solubility (g/l) | (i) | 69.9 | (i) | 734 at 20 °C<br>673 (n) | (i) | 31.3 at 0 °C |

d, decomposes; i, insoluble; n, nonahydrate

### *1.3 Organoleptic properties*

Use of aluminium salts as coagulants in water treatment may lead to increased concentrations of aluminium in finished water. Where residual concentrations are high, aluminium may be deposited in the distribution system. Disturbance of the deposits by change in flow rate may increase aluminium levels at the tap and lead to undesirable colour and turbidity (Ainsworth, Oliphant & Ridgway, 1980). Concentrations of aluminium at which such problems may occur are highly dependent on a number of water quality parameters and operational factors at the water treatment plant, such as coagulation pH and coagulant dose.

### *1.4 Major uses*

Aluminium metal is used as a structural material in the construction, automotive and aircraft industries, in the production of metal alloys, in the electric industry, in cooking utensils and in food packaging. Aluminium compounds are used as antacids, antiperspirants and food additives (ATSDR, 2008). Aluminium salts are also widely used in water treatment as coagulants to reduce organic matter, colour, turbidity and microorganism levels. The process usually consists of addition of an aluminium salt

(often sulfate) at optimum pH and dosage, followed by flocculation, sedimentation and filtration (Health Canada, 1993).

### *1.5 Environmental fate*

Aluminium is released to the environment mainly by natural processes. Several factors influence aluminium mobility and subsequent transport within the environment. These include chemical speciation, hydrological flow paths, soil–water interactions and the composition of the underlying geological materials. Acid environments caused by acid mine drainage or acid rain can cause an increase in the dissolved aluminium content of the surrounding waters (WHO, 1997; ATSDR, 2008).

Aluminium can occur in a number of different forms in water. It can form monomeric and polymeric hydroxy species, colloidal polymeric solutions and gels, and precipitates, all based on aquated positive ions or hydroxylated aluminates. In addition, it can form complexes with various organic compounds (e.g. humic or fulvic acids) and inorganic ligands (e.g. fluoride, chloride and sulfate), most but not all of which are soluble. The chemistry of aluminium in water is complex, and many chemical parameters, including pH, determine which aluminium species are present in aqueous solutions. In pure water, aluminium has a minimum solubility in the pH range 5.5–6.0; concentrations of total dissolved aluminium increase at higher and lower pH values (CCME, 1988; ISO, 1994).

## *2. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE*

### *2.1 Air*

Aluminium enters the atmosphere as a major constituent of atmospheric particulates originating from natural soil erosion, mining or agricultural activities, volcanic eruptions or coal combustion. Atmospheric aluminium concentrations show widespread temporal and spatial variations. Airborne aluminium levels range from 0.0005 µg/m$^3$ over Antarctica to more than 1 µg/m$^3$ in industrialized areas (WHO, 1997).

### *2.2 Water*

The concentration of aluminium in natural waters can vary significantly depending on various physicochemical and mineralogical factors. Dissolved aluminium concentrations in waters with near-neutral pH values usually range from 0.001 to 0.05 mg/l but rise to 0.5–1 mg/l in more acidic waters or water rich in organic matter. At the extreme acidity of waters affected by acid mine drainage, dissolved aluminium concentrations of up to 90 mg/l have been measured (WHO, 1997).

Aluminium levels in drinking-water vary according to the levels found in the source water and whether aluminium coagulants are used during water treatment. In Germany, levels of aluminium in public water supplies averaged 0.01 mg/l in the western region, whereas levels in 2.7% of public supplies in the eastern region exceeded 0.2 mg/l (Wilhelm & Idel, 1995). In a 1993–1994 survey of public water supplies in Ontario, Canada, 75% of all average levels were less than 0.1 mg/l, with a range of 0.04–0.85 mg/l (OMEE, 1995). More recently, in drinking-water treatment

systems in Canada that have surface water sources and use aluminium salts, the mean total aluminium concentration was estimated to be 101 µg/l. Mean concentrations for the different provinces varied from 20.0 to 174 µg/l (Environment Canada & Health Canada, 2010). In a large monitoring programme in 1991 in the United Kingdom, concentrations in 553 samples (0.7%) exceeded 0.2 mg/l (MAFF, 1993). In a survey of 186 community water supplies in the United States of America (USA), median aluminium concentrations for all finished drinking-water samples ranged from 0.03 to 0.1 mg/l; for facilities using aluminium sulfate coagulation, the median level was 0.1 mg/l, with a maximum of 2.7 mg/l (Miller et al., 1984). In another survey in the USA, the average aluminium concentration in treated water at facilities using aluminium sulfate coagulation ranged from 0.01 to 1.3 mg/l, with an overall average of 0.16 mg/l (Letterman & Driscoll, 1988; ATSDR, 2008).

### *2.3 Food*

Aluminium is present in foods naturally or from the use of aluminium-containing food additives. The use of aluminium cookware, utensils and wrappings can increase the amount of aluminium in food; however, the magnitude of this increase is generally not of practical importance. Foods naturally high in aluminium include potatoes, spinach and tea. Processed dairy products, flour and infant formula may be high in aluminium if they contain aluminium-based food additives (Pennington & Schoen, 1995; WHO, 1989, 1997).

Adult dietary intakes of aluminium have been reported in several countries: Australia (1.9–2.4 mg/day), Finland (6.7 mg/day), Germany (8–11 mg/day), Japan (4.5 mg/day), the Netherlands (3.1 mg/day), Sweden (13 mg/day), Switzerland (4.4 mg/day), the United Kingdom (3.9 mg/day) and the USA (7.1–8.2 mg/day). Intakes of children 5–8 years old were 0.8 mg/day in Germany and 6.5 mg/day in the USA. Infant intakes of aluminium in Canada, the United Kingdom and the USA ranged from 0.03 to 0.7 mg/day (WHO, 1997).

### *2.4 Estimated total exposure and relative contribution of drinking-water*

Aluminium intake from foods, particularly those containing aluminium compounds used as food additives, represents the major route of aluminium exposure for the general public, excluding persons who regularly ingest aluminium-containing antacids and buffered analgesics, for whom intakes may be as high as 5 g/day (WHO, 1997).

At an average adult intake of aluminium from food of 5 mg/day and a drinking-water aluminium concentration of 0.1 mg/l, the contribution of drinking-water to the total oral exposure to aluminium will be about 4%. The contribution of air to the total exposure is generally negligible.

## *3. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS*

In experimental animals, absorption of aluminium via the gastrointestinal tract is usually less than 1%. The main factors influencing absorption are solubility, pH and chemical species. Organic complexing compounds, notably citrate, increase absorption. Aluminium absorption may interact with calcium and iron transport

systems. Aluminium, once absorbed, is distributed in most organs within the body, with accumulation occurring mainly in bone at high dose levels. To a limited but as yet undetermined extent, aluminium passes the blood–brain barrier and is also distributed to the fetus. Aluminium is eliminated effectively in the urine in experimental animals (WHO, 1997).

In humans, aluminium and its compounds appear to be poorly absorbed, with levels of absorption of up to about 1% (Priest et al., 1998; Stauber et al., 1998; Priest 2004). The mechanism of gastrointestinal absorption has not yet been fully elucidated. Variability results from the chemical properties of the element and the formation of various chemical species, which is dependent upon the pH, ionic strength, presence of competing elements (e.g. silicon) and presence of complexing agents within the gastrointestinal tract (e.g. citrate). The urine is the most important route of aluminium excretion in humans (WHO, 1997; FAO/WHO, 2007).

## *4. EFFECTS ON EXPERIMENTAL ANIMALS AND IN VITRO TEST SYSTEMS*

### *4.1 Acute exposure*

The oral median lethal dose ($LD_{50}$) of aluminium nitrate, chloride and sulfate in mice and rats ranges from 200 to 1000 mg of aluminium per kilogram of body weight (WHO, 1997).

### *4.2 Short-term exposure*

Groups of 25 male Sprague-Dawley rats were fed diets containing basic sodium aluminium phosphate or aluminium hydroxide at 0, 5, 67, 141 or 288/302 mg of aluminium per kilogram of body weight per day for 28 days. No treatment-related effects on organ and body weights, haematology, clinical chemistry parameters and histopathology were observed, and there was no evidence of deposition of aluminium in bones. The no-observed-effect levels (NOELs) were 288 and 302 mg of aluminium per kilogram of body weight per day for sodium aluminium phosphate and aluminium hydroxide, respectively (Hicks, Hackett & Sprague, 1987).

In a study in which a wide range of end-points was examined, groups of 10 female Sprague-Dawley rats received drinking-water containing aluminium nitrate for 28 days at 0, 1, 26, 52 or 104 mg of aluminium per kilogram of body weight per day. The only effects noted were mild histopathological changes in the spleen and liver of the high-dose group. Although tissue aluminium concentrations were generally higher in treated animals, the increases were significant only for spleen, heart and gastrointestinal tract of the high-dose group. The no-observed-adverse-effect level (NOAEL) was 52 mg of aluminium per kilogram of body weight per day (Gomez et al., 1986).

Groups of 10 female Sprague-Dawley rats received aluminium nitrate in their drinking-water at doses of 0, 26, 52 or 260 mg of aluminium per kilogram of body weight per day for 100 days. Organ and body weights, histopathology of the brain, heart, lungs, kidney, liver and spleen, haematology and plasma chemistry were examined. The only effect observed was a significant decrease in body weight gain associated with a decrease in food consumption at 260 mg of aluminium per kilogram

of body weight per day. Aluminium did not accumulate in a dose-dependent manner in the organs and tissues examined. The NOAEL in this study was 52 mg of aluminium per kilogram of body weight per day (Domingo et al., 1987a).

Sodium aluminium phosphate, a leavening acid, was administered to groups of six male and six female Beagle dogs at dietary concentrations of 0%, 0.3%, 1.0% or 3.0% for 6 months. Statistically significant decreases in food consumption occurred sporadically in all treated groups of female dogs, but there was no associated decrease in body weight. No significant absolute or relative organ weight differences were found between any of the treated groups and controls. Haematological, blood chemistry and urinalysis data showed no toxicologically significant trend. The NOAEL was the highest dose tested, approximately 70 mg of aluminium per kilogram of body weight per day (Katz et al., 1984).

Beagle dogs (four per sex per dose) were fed diets containing basic sodium aluminium phosphate at 0, 10, 22–27 or 75–80 mg of aluminium per kilogram of body weight per day for 26 weeks. The only treatment-related effect was a sharp, transient decrease in food consumption and concomitant decrease in body weight in high-dose males. The lowest-observed-adverse-effect level (LOAEL) was 75–80 mg/kg of body weight per day (Pettersen, Hackett & Zwicker, 1990).

Wistar rats exposed to aluminium chloride in their drinking-water at reported aluminium doses of 5 and 20 mg/kg of body weight for 6 months showed reduced body weight and reduced erythrocyte counts and associated parameters, but there were no clear dose–response relationships (Somova & Khan, 1996). Results of histopathological examinations indicated spongiform changes and neurofibrillary degeneration in the hippocampus and atrophy and fibrosis in the kidney at 20 mg/kg of body weight (Somova, Missankov & Khan, 1997).

### *4.3 Long-term exposure*

No adverse effects on body weight or longevity were observed in Charles River mice (54 males and 54 females per group) receiving 0 or 5 mg of aluminium (as potassium aluminium sulfate) per kilogram of diet during their lifetime (Schroeder & Mitchener, 1975a; WHO, 1989).

Two groups of Long-Evans rats (52 of each sex) received 0 or 5 mg of aluminium (as potassium aluminium sulfate) per litre of drinking-water during their lifetime. No effects were found on body weight; average heart weight; glucose, cholesterol and uric acid levels in serum; and protein and glucose content and pH of urine. The lifespan was not affected (Schroeder & Mitchener, 1975b; WHO, 1989).

### *4.4 Reproductive and developmental toxicity*

Aluminium nitrate was administered by gavage to groups of pregnant Sprague-Dawley rats on day 14 of gestation through day 21 of lactation at doses of 0, 13, 26 or 52 mg of aluminium per kilogram of body weight per day. These doses did not produce overt fetotoxicity, but growth of offspring was significantly delayed (body weight, body length and tail length) from birth to weaning in aluminium-treated groups (Domingo et al., 1987b). In a similar study, aluminium nitrate was dosed to

males for 60 days prior to mating and to virgin females for 14 days prior to mating and throughout mating, gestation, parturition and weaning of the litters. No reproductive effects on fertility (number of litters produced), litter size or intrauterine or postnatal offspring mortality were reported. There was a decrease in the numbers of corpora lutea in the high-dose group. A dose-dependent delay in the growth of the pups was observed in all treatment groups; female offspring were affected at 13 mg of aluminium per kilogram of body weight per day and males at 26 and 52 mg of aluminium per kilogram of body weight per day. Because of the study design, it is not clear whether the postnatal growth effects in offspring represented general toxicity to male or female parents or specific effects on reproduction or development (Domingo et al., 1987c).

Aluminium hydroxide did not produce either maternal or developmental toxicity when it was administered by gavage during embryogenesis to mice at doses up to 92 mg of aluminium per kilogram of body weight per day (Domingo et al., 1989) or to rats at doses up to 265 mg of aluminium per kilogram of body weight per day (Gomez et al., 1990). When aluminium hydroxide at a dose of 104 mg of aluminium per kilogram of body weight per day was administered with ascorbic acid to mice, no maternal or developmental toxicity was seen, in spite of elevated maternal placenta and kidney concentrations of aluminium (Colomina et al., 1994); on the other hand, aluminium hydroxide at a dose of 133 mg of aluminium per kilogram of body weight per day administered with citric acid produced maternal and fetal toxicity in rats (Gomez, Domingo & Llobet, 1991). Aluminium hydroxide (57 mg of aluminium per kilogram of body weight) given with lactic acid (570 mg/kg of body weight) to mice by gavage was not toxic, but aluminium lactate (57 mg of aluminium per kilogram of body weight) produced developmental toxicity, including poor ossification, skeletal variations and cleft palate (Colomina et al., 1992).

In studies on Swiss-Webster mice given 500 or 1000 mg of aluminium per kilogram of diet as aluminium lactate with a control of 7 mg of aluminium per kilogram of diet (reported to provide doses of <1, 50 or 100 mg of aluminium per kilogram of body weight in adult mice) from conception to weaning, grip strength was reduced in both treatment groups without showing a dose–response relationship. Elevated aluminium concentrations were reported in brain, spinal cord and liver without a dose–response relationship (Golub et al., 1995). These investigators also carried out a similar study with the same control diet and an additional treatment of 100 mg of aluminium per kilogram of diet (10 mg/kg of body weight per day) from conception to 35 days of age. There were no differences in reproductive indices, but, by weaning, both males and females in the two highest dose groups had lower body weights than other groups (Golub & Germann, 2001).

Guo, Lu & Hsu (2005) gave male CD-1 mice 0, 7 or 13 mg of aluminium per kilogram of body weight per day for 14 days, by subcutaneous injection, before mating. There was an initial reduction in mating frequency in treated groups that returned to control levels, but significantly higher numbers of post-implantation losses, fetal mortality and induced petechial haemorrhage, but not fetal abnormalities, were reported in treated groups. The weights of testes decreased as aluminium accumulation increased, and spermatogenic impairment was apparent, but these effects had disappeared by the end of the study.

Aluminium nitrate (nonahydrate) was given to female Sprague-Dawley rats in drinking-water at doses of 0, 50 and 100 mg of aluminium per kilogram of body weight per day for 15 days before mating and throughout gestation, lactation and post-weaning. The aluminium content of the feed was 42 mg/kg. In order to enhance gastrointestinal absorption, citric acid doses of 355 and 710 mg/kg of body weight per day were added to the drinking-water of the 50 and 100 mg of aluminium per kilogram of body weight per day groups, respectively. Controls received water supplemented with citric acid at 710 mg/kg of body weight per day. Doses were adjusted to maintain a constant uptake of aluminium. Body weight was decreased relative to controls on postnatal days 12–21 in pups treated with 100 mg of aluminium per kilogram of body weight per day. Sexual maturation was delayed in all aluminium-treated females and in aluminium-treated males at 100 mg/kg of body weight per day. Forelimb grip strength was reduced in males at 100 mg of aluminium per kilogram of body weight per day (Colomina et al., 2005).

Thirty-one time-mated Charles River CD dams were given aluminium lactate solution by gavage at a dose of 0, 5, 25, 50, 250, 500 or 1000 mg of aluminium per kilogram of body weight per day from days 5 to 15 of gestation. No information was provided on the dietary aluminium content, so the total dose of aluminium is uncertain. The 390 offspring were evaluated for morphological and physiological parameters of reproductive functioning, including birth weight, anogenital distance, timing of vaginal opening, regularity of estrous cycles, duration of pseudopregnancy, number of superovulated oocytes and gonadal weight. No consistent or reproducible findings were reported in these parameters, with the exception of the regularity of estrous cycles. A temporary increase in the proportion of aberrant estrous cycles was detected in the first four cycles after vaginal opening in the group at 250 mg/kg of body weight per day, with none by the fifth consecutive cycle. The authors suggested that aluminium does not have a toxic effect on reproductive functioning in offspring (Agarwal et al., 1996).

Swiss Webster mice were fed diets containing aluminium at 25 (control), 500 or 1000 mg/kg (as aluminium lactate) from conception through weaning. Reported maternal intakes were 5, 100 and 200 mg of aluminium per kilogram of body weight, respectively, at the beginning of pregnancy and 10, 210 and 420 mg of aluminium per kilogram of body weight, respectively, near the end of lactation. Pups were assessed for growth, neurobehavioural development and toxic signs before weaning, immediately after weaning and 2 weeks after weaning, during which time they were maintained on control (25 mg of aluminium per kilogram) diet. No maternal or reproductive toxicity was detected, and there were no group differences in pup mortality, growth, toxic signs or neurobehavioural development before weaning. In general, dietary aluminium was associated with dose-related greater foot splay, decreased sensitivity to heat and greater forelimb and hindlimb grip strength shortly after weaning and, to some extent, after a 2-week recovery period on control diet (Donald et al., 1989).

Male Swiss Webster mice were fed diets containing 7 (control, with and without citrate), 100, 500, 750 or 1000 mg of aluminium per kilogram diet as aluminium lactate (with 3.2% citrate to promote aluminium absorption) from the beginning of puberty (45 days of age) for either 4 or 8 weeks. There was no effect of aluminium content on food intake in any of the treatment groups or on liver, spleen and tibia

weights. A decrease in brain weight was recorded in the animals that received 1000 mg of aluminium per kilogram of diet (which the authors considered to provide an aluminium dose of 100 mg/kg of body weight per day) for 4 weeks, but not in the same group treated for the longer duration. A dose-related effect of aluminium on forelimb grip strength was recorded in the groups exposed for 4 weeks (i.e. in pubertal mice), but this effect disappeared in young adulthood, despite continued administration of aluminium (Golub & Keen, 1999).

Groups of 18 male and female Swiss Webster mice were fed diets containing aluminium at a dose of 1000 mg/kg of diet in the form of aluminium lactate, from conception and throughout their lifespan. The authors considered this diet to provide a dose to adult mice of 100 mg of aluminium per kilogram of body weight per day; the control diet provided less than 1 mg of aluminium per kilogram of body weight per day. Animals in the control and treated groups had a similar mortality rate, and no evidence of gross neurodegeneration was seen. There were no consistent differences in neurobehavioural tests based on grip strength, temperature sensitivity or maze negotiation. The only toxic signs reported were red eyes, fur loss and circling (motor stereotypy), all with a low incidence (no group incidences reported) (Golub et al., 2000).

In the study described in section 4.4, Swiss Webster mice received diets containing 7 (control), 100, 500 or 1000 mg of aluminium per kilogram of diet as aluminium lactate throughout development (conception to age 35 days) and were subjected to behavioural tests as adults (aged more than 90 days). The authors considered these dietary doses to be equivalent to <1, 10, 50 and 100 mg of aluminium per kilogram of body weight per day in adult mice. By weaning, both males and females in the groups at 500 or 1000 mg of aluminium per kilogram of diet weighed significantly less than controls. One offspring from each litter was used for behavioural testing. Subtle deficits in several neurological parameters, including impaired learning in a maze, were observed in the animals that received diet containing 1000 mg of aluminium per kilogram, but not at the lower doses. A reduction in hindlimb grip strength was reported in approximately 15% of animals receiving the highest dose; this was no longer significant after adjustment for body weight (Golub & Germann, 2001).

### *4.5 Mutagenicity and related end-points*

Aluminium can form complexes with deoxyribonucleic acid (DNA) and cross-link chromosomal proteins and DNA, but it has not been shown to be mutagenic in bacteria or induce mutation or transformation in mammalian cells in vitro. Chromosomal aberrations have been observed in bone marrow cells of exposed mice and rats (WHO, 1997).

### *4.6 Carcinogenicity*

There is no indication that aluminium is carcinogenic. The Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) evaluated the limited studies of Schroeder & Mitchener (1975a,b; section 4.3) and concluded that there was no evidence of an increase in tumour incidence related to the administration of potassium aluminium sulfate in mice or rats (WHO, 1989).

### *4.7 Neurotoxicity*

Behavioural impairment has been reported in laboratory animals exposed to soluble aluminium salts (e.g. lactate, chloride) in the diet or drinking-water in the absence of overt encephalopathy or neurohistopathology. Both rats (Commissaris et al., 1982; Thorne et al., 1987; Connor, Jope & Harrell, 1988) and mice (Yen-Koo, 1992) have demonstrated such impairments at doses exceeding 200 mg of aluminium per kilogram of body weight per day. Although significant alterations in acquisition and retention of learned behaviour were documented, the possible role of organ damage (kidney, liver, immunological) due to aluminium was incompletely evaluated in these studies (WHO, 1997).

In studies on brain development in mice and rats, grip strength was impaired in offspring of dams fed 100 mg of aluminium (as aluminium lactate) per kilogram of body weight per day in the diet, in the absence of maternal toxicity (WHO, 1997).

Additional studies on neurobehavioural development are discussed in section 4.4 above.

## *5. EFFECTS ON HUMANS*

There is little indication that aluminium is acutely toxic by oral exposure despite its widespread occurrence in foods, drinking-water and many antacid preparations (WHO, 1997).

In 1988, a population of about 20 000 individuals in Camelford, England, was exposed for at least 5 days to unknown but increased levels of aluminium accidentally distributed to the population from a water supply facility using aluminium sulfate for treatment. Symptoms including nausea, vomiting, diarrhoea, mouth ulcers, skin ulcers, skin rashes and arthritic pain were noted. It was concluded that the symptoms were mostly mild and short-lived. No lasting effects on health could be attributed to the known exposures from aluminium in the drinking-water (Clayton, 1989).

Following the observation that high levels of aluminium in dialysis fluid could cause a form of dementia in dialysis patients, a number of studies were carried out to determine if aluminium could cause dementia or cognitive impairment as a consequence of environmental exposure over long periods. Aluminium was identified, along with other elements, in the amyloid plaques that are one of the diagnostic lesions in the brain for Alzheimer disease, a common form of senile and pre-senile dementia. Numerous epidemiological studies have been carried out to try to determine the validity of this hypothesis. These have been reviewed in detail by several authorities, including JECFA (FAO/WHO, 2007; WHO, 2007), the United Kingdom Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT, 2005), the United States Agency for Toxic Substances and Disease Registry (ATSDR, 2008) and Environment Canada & Health Canada (2010).

Investigators have identified a number of difficulties in carrying out such studies on conditions for which the causes are multifactorial. In addition, there are questions regarding the levels of exposure of aluminium from different sources and the relative

bioavailability from these sources. Most of the studies have focused on aluminium in drinking-water—although this is a very minor source of exposure—and Alzheimer disease. Most of the studies do not consider the speciation of aluminium, and the assessment of exposure from both drinking-water and food is not usually well characterized. In particular, there are difficulties in determining recollected exposure when the subject has a degenerative neural condition affecting cognitive performance. The conclusion of the recent JECFA evaluation (FAO/WHO, 2007) was that "some of the epidemiology studies suggest the possibility of an association of Alzheimer disease with aluminium in water, but other studies do not confirm this association…. All studies lack information on ingestion of aluminium from food and how concentrations of aluminium in food affect the association between aluminium in water and Alzheimer disease." There are suggestions that some genetic variants may absorb more aluminium than others, but there is a need for more analytical research to determine whether aluminium from various sources has a significant causal association with Alzheimer disease and other neurodegenerative diseases.

## *6. PRACTICAL ASPECTS*

### *6.1 Analytical methods and analytical achievability*

Aluminium is reacted with pyrocatechol violet followed by spectrometric measurement of the resulting coloured complex. The method is restricted to the determination of the aquated cations and other forms of aluminium readily converted to that cationic form by acidification. The limit of detection is 2 µg/l (ISO, 1994). The limit of detection for the determination of aluminium by inductively coupled plasma atomic emission spectroscopy ranges from 40 to 100 µg/l (ISO, 1996).

Flame and graphite furnace atomic absorption spectrometric (AAS) methods are applicable for the determination of aluminium in water at concentrations of 5–100 mg/l and 0.01–0.1 mg/l, respectively. The working range of the graphite furnace AAS method can be shifted to higher concentrations either by dilution of the sample or by using a smaller sample volume (ISO, 1997).

### *6.2 Treatment and control methods and performance*

A number of approaches are available for minimizing residual aluminium concentrations in treated water. These include use of optimum pH in the coagulation process, avoiding excessive aluminium dosage, sufficient mixing at the point of application of the coagulant, optimum mixing conditions for flocculation and efficient filtration of the aluminium floc (Letterman & Driscoll, 1988; WRc, 1997). Residual aluminium concentration is affected not only by obvious factors, such as operational conditions and raw water quality, but also by more obscure factors, such as water treatment plant capacity and the size of the water supplier (Ohno et al., 2009). Under good operating conditions, concentrations of aluminium of 0.1 mg/l or less are achievable in large water treatment facilities. Small facilities (e.g. those serving fewer than 10 000 people) might experience some difficulties in attaining this level, because the small size of the plant provides little buffering for fluctuation in operation, and small facilities often have limited resources and access to expertise to solve specific operational problems. For these small facilities, 0.2 mg/l or less is a practicable level for aluminium in finished water (WRc, 1997).

## *7. CONCLUSIONS*

The Environmental Health Criteria document for aluminium (WHO, 1997) concluded that:

> On the whole, the positive relationship between aluminium in drinking-water and AD [Alzheimer disease], which was demonstrated in several epidemiological studies, cannot be totally dismissed. However, strong reservations about inferring a causal relationship are warranted in view of the failure of these studies to account for demonstrated confounding factors and for total aluminium intake from all sources.
>
> Taken together, the relative risks for AD from exposure to aluminium in drinking-water above 100 µg/litre, as determined in these studies, are low (less than 2.0). But, because the risk estimates are imprecise for a variety of methodological reasons, a population attributable risk cannot be calculated with precision. Such imprecise predictions may, however, be useful in making decisions about the need to control exposures to aluminium in the general population.

In 2007, JECFA developed a provisional tolerable weekly intake (PTWI) for aluminium from all sources of 1 mg/kg of body weight (FAO/WHO, 2007). The Committee concluded the following:

> …the available studies have many limitations and are not adequate for defining the dose–response relationships. The Committee therefore based its evaluation on the combined evidence from several studies. The relevance of studies involving administration of aluminium compounds by gavage was unclear because the toxicokinetics after gavage were expected to differ from toxicokinetics after dietary administration, and the gavage studies generally did not report total aluminium exposure including basal levels in the feed. The studies conducted with dietary administration of aluminium compounds were considered most appropriate for the evaluation. The lowest LOELs for aluminium in a range of different dietary studies in mice, rats and dogs were in the region of 50–75 mg/kg bw [body weight] per day expressed as Al.
>
> The Committee applied an uncertainty factor of 100 to the lower end of this range of LOELs (50 mg/kg bw per day expressed as Al) to allow for inter- and intraspecies differences. There are deficiencies in the database, notably the absence of NOELs in the majority of the studies evaluated and the absence of long-term studies on the relevant toxicological end-points. The deficiencies are counterbalanced by the probable lower bioavailability of the less soluble aluminium species present in food. Overall, an additional uncertainty factor of three was considered to be appropriate. The Committee confirmed that the resulting health-based guidance value should be expressed as a PTWI, because of the potential for bioaccumulation. The Committee established a PTWI of 1 mg/kg bw for Al, which applies to all aluminium compounds in food, including additives.

A health-based value derived from the JECFA PTWI would be 0.9 mg/l (rounded value), based on an allocation of 20% of the PTWI to drinking-water and assuming a 60 kg adult drinking 2 litres of water per day. However, there remain uncertainties as to the extent of aluminium absorption from drinking-water, which depends on a number of parameters, such as the aluminium salt administered, pH (for aluminium speciation and solubility), bioavailability and dietary factors.

The beneficial effects of the use of aluminium as a coagulant in water treatment are recognized. Taking this into account and considering the potential health concerns (i.e. neurotoxicity) of aluminium, a practicable level is derived based on optimization of the coagulation process in drinking-water plants using aluminium-based coagulants, to minimize aluminium levels in finished water. For large, well-operated and well-controlled plants, a residual aluminium concentration in the final water of

0.1 mg/l should be achievable. For smaller facilities, a residual concentration of 0.2 mg/l is a more reasonable expectation.

As indicated above, a health-based value based on the JECFA PTWI would be 0.9 mg/l (rounded value). However, as also noted above, practicable levels based on optimization of the coagulation process in drinking-water plants using aluminium-based coagulants are 0.1 mg/l or less in large water treatment facilities and 0.2 mg/l or less in small facilities. In view of the importance of optimizing coagulation to prevent microbial contamination and the need to minimize deposition of aluminium floc in distribution systems, it is important to ensure that average residuals do not exceed these values.

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