資料１－３

第 33 回 JECFA 会合（1988）におけるアルミニウムの評価

（WHO Food Additive Series 24（1989）“ALUMINIUM”より抜粋／
「酸性リン酸アルミニウムナトリウム文献集」文献 2）

COMMENTS

The general population is principally exposed to aluminium from food and water. Aluminium intake from foods, particularly those containing aluminium compounds used as food additives, represents the major route of aluminium exposure excluding persons who regularly ingest aluminium-containing drugs. Previous evaluations by the Committee dealt with sodium aluminium phosphate, a primary sources of dietary aluminium intake.

Recent estimates of aluminium intake from food based on newer methods of analysis and improved quality control are considerably less than previously estimated. Current estimates of aluminium intake range from about 2-6 mg/day for children and 6-14 mg/day for teenagers and adults. Low total body burdens of aluminium coupled with urinary excretion suggest to the Committee that even at high levels of consumption, only a small amount of aluminium is absorbed. Aluminium which is absorbed is located primarily in the heart, spleen, and bone but its presence in these sites was without histopathologic lesions.

Studies are adequate to set a provisional tolerable weekly intake of aluminium from 0-7.0 mg/kg b.w. It was concluded that there was no need to set a separate ADI for sodium aluminium phosphate, basic or acid, as the provisional tolerable weekly intake included aluminium intake occurring from food additive uses.

EVALUATION

Level causing no toxicological effect

Dog: 3% sodium aluminium phosphate (acidic) in the diet, equivalent to 1250 mg/kg bw, equivalent to approximately 110 mg/kg bw aluminium.

Estimate of provisional tolerable weekly intake

7.0 mg/kg bw*

*Includes intake of aluminium from food additive uses.

第 67 回 JECFA 会合（2006）におけるアルミニウムの評価

（WHO Food Additive Series 58（2007）“ALUMINIUM FROM ALL SOURCES, INCLUDING FOOD ADDITIVES”より抜粋／
全文は「酸性リン酸アルミニウムナトリウム文献集」文献 13）

10. EVALUATION

The Committee concluded that aluminium compounds have the potential to affect the reproductive system and developing nervous system at doses lower than those used in establishing the previous PTWI and therefore the PTWI should be revised. However, 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 Al/kg bw per day.

The Committee applied an uncertainty factor of 100 to the lower end of this range of LOELs (50 mg Al/kg bw per day) 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 Al/kg bw, which applies to all aluminium compounds in food, including additives. The previously established ADIs and PTWI for aluminium compounds were withdrawn.

The potential range of exposure from dietary sources is summarized in Table 8.

The Committee noted that the PTWI is likely to be exceeded to a large extent by some population groups, particularly children, who regularly consume foods that include aluminium-containing additives. The Committee also noted that dietary exposure to aluminium is expected to be very high for infants fed on soya-based formula.

Further data on the bioavailability of different aluminium-containing food additives are required.

There is a need for an appropriate study of developmental toxicity and a multigeneration study incorporating neurobehavioural end-points, to be conducted on a relevant aluminium compound(s).

Studies to identify the forms of aluminium present in soya formulae, and their bioavailability, are needed before an evaluation of the potential risk for infants fed on soya formulae can be considered.

第 74 回 JECFA 会合（2011）におけるアルミニウムの評価

（WHO Food Additive Series 65（2012）“ALUMINIUM FROM ALL SOURCES, INCLUDING FOOD ADDITIVES”より抜粋／
全文は「アルミ含有添加物追加関連論文集」文献 3）

5. Evaluation

The new data submitted to the Committee and available in the published literature addressed some of the research needs identified previously, including studies of bioavailability and reproductive, developmental and neurobehavioural effects.

The absorption of aluminium compounds is generally in the region of 0.01–0.3%. Soluble aluminium compounds appear to be more bioavailable, but it is not possible to draw conclusions on quantitative differences in the overall toxicokinetics of different aluminium-containing food additives or between experimental animals and humans.

The recent evidence did not show effects of aluminium on reproductive outcomes. The new studies support previous observations of neurodevelopmental effects in experimental animals, but there continues to be a lack of consistency regarding the reported effects, and there are some limitations to all of the studies. Most of the studies involved administration of aluminium compounds in drinkingwater, rather than in the diet.

At its current meeting, the Committee noted that the new data did not substantially change the LOAEL range of 50–75 mg/kg bw per day, but one of the studies also provided a NOAEL of 30 mg/kg bw per day. This NOAEL was identified from a study in which aluminium citrate was administered in drinking-water. Aluminium citrate is more soluble than many other aluminium compounds and is likely to be more bioavailable from drinking-water than from food. The Committee concluded that the NOAEL of 30 mg/kg bw per day was an appropriate basis for establishing a PTWI for aluminium compounds. Because long-term studies on the relevant toxicological end-points had become available since the sixty-seventh meeting, there was no longer a requirement for an additional safety factor for deficiencies in the database. The Committee therefore established a PTWI of 2 mg/ kg bw from the NOAEL of 30 mg/kg bw per day by applying a safety factor of 100 for interspecies and intraspecies differences. The previous PTWI of 1 mg/kg bw
was withdrawn.

The data submitted on aluminium lactate and potassium aluminium silicate–based pearlescent pigments were insufficient to demonstrate that these food additives differ from other forms of aluminium in their bioavailability or toxicity. The PTWI applies to all aluminium compounds in food, including food additives. The Committee emphasized that whereas substances that have long half-lives and accumulate in the body are not generally considered suitable for use as food additives, consumption of aluminium-containing food additives would not be a health concern, provided that total dietary exposure to aluminium is below the PTWI.

The Committee concluded that, for adults, the estimates of mean dietary exposure to aluminium-containing food additives from consumption of cereals and cereal-based products are up to the PTWI of 2 mg/kg bw. Estimates of dietary exposure of children to aluminium-containing food additives, including high-level dietary exposure, can exceed the PTWI by up to 2-fold.

For potassium aluminium silicate–based pearlescent pigments at the maximum proposed use levels and using conservative estimates, the Committee noted that anticipated dietary exposure at the highest range of estimates is 200 times higher than the PTWI of 2 mg/kg bw.

Therefore, the Committee recommended that provisions for food additives containing aluminium included in the GSFA should be compatible with the revised PTWI for aluminium compounds of 2 mg/kg bw as aluminium from all sources.

There is a need for convincing data to demonstrate that aluminium is not bioavailable from potassium aluminium silicate–based pearlescent pigments.

No data were available to identify the forms of aluminium present in soyabased formula and their bioavailability. Such studies were requested at the sixtyseventh meeting and are still required.