This is provisional English translation of an excerpt from the original full report.

Risk Assessment Report

Calcium Carbonate

(Food Additives)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted a risk assessment based on results from various studies, of calcium carbonate (CAS No. 471-34-1), an additive used for nutritional enrichment and food manufacturing agents (leavening) such as baker's yeast, gum base, baking powder and others.

Calcium carbonate is dissociated into carbonate and calcium ions in the stomach after the ingestion as a food additive. FSCJ thus conducted a risk assessment of calcium carbonate using the data on calcium carbonate and other anion salts.
The assessment reports on calcium acetate and calcium oxide were also referred in this assessment.

Based on the data on toxicokinetics of calcium carbonate and other calcium salts, FSCJ recognized the necessity to consider that the homeostatic control for calcium in the body in a risk assessment of calcium carbonate.

No toxicities relevant to human health have been suggested from the data on genotoxicity, acute toxicity, carcinogenicity, and reproductive and developmental toxicity of calcium carbonate and other calcium salts.
Data enough to evaluate are not available in the repeated dose toxicity studies and thus the no-observed-adverse-effect level (NOAEL) could not be specified only from these studies. However, calcium carbonate at the dose far beyond the requirement, when administered, has been known to reduce the body weight gain, to reduce feed intake, to decrease feed efficiency, and to alter the body balance of various minerals. Therefore, FSCJ judged that far excess intakes of calcium carbonate affect body weight, feed consumption and homeostasis of minerals in the body, although NOAEL could not be specified or the quantitative assessment could not be completed.
Associations of excessive intake of calcium have been suggested in human clinical studies with milk-alkali syndrome, a renal calculus, prostatic carcinomas and circulatory diseases.
Associations of excessive intake of calcium have been suggested in human clinical studies with milk-alkali syndrome, a renal calculus, prostatic carcinomas and circulatory diseases. The association of calcium intake with prostatic carcinomas or with circulatory diseases, are not consistent and not well supported from the point of the biological mechanism and the time lapse. FSCJ, however, granted the positive association between calcium intake and milk-alkali syndrome. FSCJ paid attention also to the positive association of calcium intake with a renal calculus, based on the human intervention studies of Burtis et al. (1994) and Jackson et al. (2006). It was difficult to specify NOAEL and lowest-observed-adverse-effect level (LOAEL) based on these studies, due to the subject

populations used in the study of Burtis et al. (patients of a renal calculus) and of Jackson (subjects taking vitamin D which facilitate calcium absorption).

It is therefore appropriate to evaluate calcium intake based on the case reports of milk-alkali syndrome in the assessment, which deal relatively low levels of the calcium intake (Table 33, in the full document). Some of these case reports were, however, not included from the following events: Nabhan et al. (2004) and Caruso et al. (2007) reported the cases where vitamin D has been taken for certain period, Kaklamanos & Perros (2007) reported the case where the patient has a history of apepsy due to gastric mucosal erosion, The patient of case-2 in the report by Irtiza-Ali et al. (2008) had a history of renal disease, The patient in the report by AlMusawi et al. (2012) had medical histories of gastroesophageal reflux disease, hypothyroidism and others, and Kashouty et al. (2011) studied the patient with the history of reflux gastritis. Among the available, the report by Gordon et al. (2005) was judged to be appropriate to specify the LOAEL of 3,000 mg/person per day in pregnant women. The subject in the report was a pregnant woman with no medical history and the milk-alkali syndrome, diagnosed after extradietary intake of calcium at ca. 3,000 mg/person per day for one month.

Calcium absorption in pregnant woman is expected to be augmented and thus have the increasing risk of milk-alkaline syndrome incidence, as reports by Uenishi et al. (2003) and by Bailey et al. (2008). The LOAEL for ordinal population can be specified based on the report by Gordon et al. (2005) and applied to Japanese population despite the report using a nondomestic ethnic (Australian) at where the dietary intake of calcium differs from that in Japan.

Consequently, FSCJ specified the LOAEL of 3,000 mg/person per day.

In conclusion, FSCJ judged it appropriate to specify the ULS[1] of 2,000 mg/person per day using UF1.5, for an upper limit of extradietary intake of calcium.

In addition to the conclusion mentioned above, the estimated intake of calcium in Japan will be 711.37 mg/person per day at maximum as calcium derived from additives after amendment of standards for calcium carbonate as an additive. According to the National Health and Nutrition Survey in 2014, average daily intake of calcium was 497 mg/person per day. Available value of the daily intake of calcium silicate, based on the maximal consumption for excipient use, appears to be overestimated and thus the actual status of use is yet uncertain.

[1] UL as a supplement. The upper limit of extradietary intake.