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

Risk Assessment Report

Guanidineacetic acid

(Feed Additives)

Food Safety Commission of Japan (FSCJ)
August 2018

ABSTRACT

FSCJ conducted a risk assessment of guanidineacetic acid (CAS No. 352-97-6), a feed additive, based on the documents of the request for designating it as a feed additive.

The data used in the assessment are the followings: pharmacokinetics (rats, chicken and humans. Humans for its metabolite Creatine); residues (pigs, chicken, and quail's eggs); genotoxicity; acute toxicity (rats); and subacute toxicity (rats). A reproductive toxicity study was also conducted in chicken and quales, while chronic toxicity, carcinogenicity and reproductive developmental toxicity were not studied.

Genotoxicity study was not conducted *in vivo*, while the bacterial reverse mutation tests, gene mutation tests using cultured cells, and chromosomal aberration tests using human peripheral blood lymphocytes were conducted and the data from all these *in vitro* studies were negative. Hence, FSCJ judged that guanidineacetic acid (GAA) has no genotoxicity relevant to human health.

Major adverse effects observed in subacute toxicity studies were a decrease in body weight, bladder stone and decreased plasma cholesterol (Chol).

While chronic toxicity study, carcinogenicity study and reproductive developmental toxicity study were not conducted, reference materials showed that no adverse effects were observed in chicken (sperm) and quales (reproductivity).

The lowest value of the NOAELs obtained in subacute toxicity studies was 66 mg/kg bw/day specified based on the decrease in plasma Chol observed in a 90-day subacute toxicity study.

Humans ingest GAA and/or its metabolite, creatine daily since these substances are endogenous substances of food animals. Moreover, 120 g of creatine is present in a human body of 70 kg body weight, and about 1.7 % (ca.2g) of this creatine is metabolized into creatinine a day. The metabolized portion of creatine is recovered by biosynthesis or dietary ingestion of creatine.
In residue studies in pigs and chicken using GAA at the dose of normal use as a feed additive, no increase in intramuscular concentrations of GAA and Hey was observed in the GAA-administered animals compared to the control animals. Although creatine concentration in GAA-administered chicken tended to increase, the concentration was not so different from the intramuscular concentration reported in food animals.
FSCJ concluded that an ADI for GAA is not necessary to be specified as long as it is used appropriately as a feed additive, based on the comprehensive evaluation of the available findings.