FOOD SAFETY

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Abamectin (Avermectin)

Summary

Food Safety Commission of Japan

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of an insecticide, abamectin (CAS No. 71751-41-2), based on results from various studies. The insecticide is consisted of avermectin B_1a (CAS No. 65195-55-3) and avermectin B_1b (CAS No. 65195-56-4), both macrolides having a structure of 16-membered ring. Major adverse effects of abamectin observed are neurological symptoms such as tremor/convulsion and mydriasis. FSCJ considered that abamectin causes tremor/convulsion through the GABA-ergic action with hyperpolarization of nerve/muscle cells. Neither carcinogenicity, reproductive toxicity, developmental neurotoxicity nor genotoxicity was observed. Based on the above results, abamectin and its isomeric 8,9-Z avermectin B_1a, a photolytic product of avermectin B_1a, were identified as chemicals for the residue definition for dietary risk assessment in agricultural products. The lowest value among the no-observed-adverse-effect levels (NOAELs) and the lowest-observed-adverse-effect levels (LOAELs) obtained in all the studies was the LOAEL of 0.12 mg/kg bw/day in a developmental neurotoxicity study in rats. FSCJ specified an acceptable daily intake (ADI) of 0.0006 mg/kg bw/day, applying a safety factor of 200 (10 for species difference, 10 for individual difference, and additional 2 for the use of LOAEL). The lowest NOAEL for adverse effects that would be likely to be elicited by a single oral administration of abamectin was 0.5 mg/kg bw/day consistently obtained in the acute neurotoxicity study in rats, and in the 18-week subacute toxicity study, the 85-day subacute toxicity study and the one-year chronic toxicity study in dogs. FSCJ specified an acute reference dose (ARfD) of 0.005 mg/kg bw, applying a safety factor of 100 to the NOAEL.

Conclusion in Brief

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of an insecticide, abamectin (CAS No. 71751-41-2), based on results from various studies. The insecticide is consisted of avermectin B_1a (CAS No. 65195-55-3) and avermectin B_1b (CAS No. 65195-56-4), both macrolides having a structure of 16-membered ring. The newly submitted data include on the residues in crops (tomatoes, cucumbers, grapes, celery, etc)*.

The data used in the assessment include on fate in animals (rats), fate in plants (tomatoes, celery, etc), residues in crops, acute neurotoxicity (rats), subacute toxicity (rats and dogs), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), developmental neurotoxicity (rats), and genotoxicity, and also on the mechanism.

Major adverse effects of abamectin observed are neurological symptoms such as tremor/convulsion and mydriasis. FSCJ considered that abamectin causes tremor/convulsion through the GABA-ergic action with hyperpolarization of

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nerve/muscle cells. Neither carcinogenicity, reproductive toxicity, developmental neurotoxicity nor genotoxicity was observed.

In a developmental toxicity study in rabbits, various changes including cleft palate, omphalocele, clubbed forefoot, sternebrae malformation, and malformation/incomplete ossification of lumber vertebrae were observed. The changes observed are likely to occur rather secondarily through the severe maternal toxicities, but not a direct fetal effect of abamectin.

In an 18-week subacute toxicity study and one-year chronic toxicity study in dogs, fatalities observed shortly after administration of abamectin were directly attributed to the administration. The exact mechanism of fatality is not clearly understood, although a postulated genetic polymorphism including Pgp protein in dog population is possibly involved in the fatalities.

Based on the above results, abamectin and its isomeric 8,9-Z avermectin B_1a, a photolytic product of avermectin B_1a, were identified as chemicals for the residue definition for dietary risk assessment in agricultural products.

The lowest value among the no-observed-adverse-effect levels (NOAELs) and the lowest-observed-adverse-effect levels (LOAELs) obtained in all the studies was the LOAEL of 0.12 mg/kg bw/day in a developmental neurotoxicity study in rats. FSCJ specified an acceptable daily intake (ADI) of 0.0006 mg/kg bw/day, applying a safety factor of 200 (10 for species difference, 10 for individual difference, and additional 2 for the use of LOAEL).

The lowest NOAEL for adverse effects that would be likely to be elicited by a single oral administration of abamectin was 0.5 mg/kg bw/day consistently obtained in the acute neurotoxicity study in rats, and in the 18-week subacute toxicity study, the 85-day subacute toxicity study and the one-year chronic toxicity study in dogs. FSCJ specified an acute reference dose (ARfD) of 0.005 mg/kg bw, applying a safety factor of 100 to the NOAEL.

* At the request of the Ministry of Health, Labour and Welfare (MHLW), FSCJ conducted the risk assessment of abamectin and submitted its report (first version) to MHLW on February 9, 2012. To establish the maximum residue limits on additional crops, ie, tomatoes, cucumbers, etc for domestic pesticide registration and grapes, celery, etc for import tolerance, MHLW requested FSCJ to conduct the current risk assessment of abamectin.