The European Agency for the Evaluation of Medicinal Products
Veterinary Medicines and Information Technology

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COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

DELTAMETHRIN
(extension to fin fish)

SUMMARY REPORT (2)

1. Deltamethrin, (S)-α-cyano-3-phenoxybenzyl, (1R)-cis-3-(2,2-dibromovinyl)-2,2-dimethylcyclo-propane carboxylate, is a synthetic type II pyrethroid insecticide and acaricide. Deltamethrin (98% cis isomer) is used topically for the control of ectoparasites in cattle, sheep and poultry. It is also widely used as a pesticide on crops.

   An ADI of 10 µg/kg bw, i.e. 600 µg per person, had been previously established by the Committee for Veterinary Medicinal Products.

   Currently deltamethrin is included in Annex III of Council Regulation No 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs	Target tissue	Other provisions
Deltamethrin	Deltamethrin	Bovine	10 µg/kg 50 µg/kg 10 µg/kg 10 µg/kg 20 µg/kg	Muscle Fat Liver Kidney Milk	Provisional MRL expire on 1.7.2001
		Ovine	10 µg/kg 50 µg/kg 10 µg/kg 10 µg/kg	Muscle Fat Liver Kidney	Provisional MRL expire on 1.7.2001 Not for use in animals from which milk is produced for human consumption
		Chicken	10 µg/kg 50 µg/kg 10 µg/kg 10 µg/kg 50 µg/kg	Muscle Skin + fat Liver Kidney Eggs	Provisional MRL expire on 1.7.2001

   An application has now been submitted for an extension of the MRLs to fish (Atlantic salmon and rainbow trout). Deltamethrin is recommended in Atlantic salmon and rainbow trout to treat sea lice (*Lepeophteirus salmonis* and *Caligus elongatus*). The recommended bath dosages are 2 µg deltamethrin/l for 30 minutes in a closed container or 3 µg deltamethrin/l for 40 minutes in a partially closed sea-cage.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Switchboard (44-20-7) 418 8400 Fax (44-20-7) 418 8447
E-mail: mail@emea.eudra.org http://www.eudra.org/emea.html

2. Two radiolabelled studies were conducted in Atlantic salmons.

   Groups of 2 atlantic salmons received a single intravenous administration of 0.25 mg/kg bw ^{14}C-deltamethrin. The levels of radioactivity in blood declined from 51.5 µg equivalents deltamethrin/kg, 4 hours after dosing to 48, 23.5, 7 and 2.5 µg/kg at 12, 48, 96 and 240 hours post dose. The elimination half-life of total radioactivity in blood was 54 hours. Four hours after the injection, the concentrations of total radioactivity were 4 and 20 µg equivalents deltamethrin/kg, in muscle and skin respectively. At 12 hours post injection they were 23.5 and 20 µg/kg for muscle and in skin respectively. At 48 hours post injection, they were 10.5 and 55 µg/kg in muscle and skin respectively and then they declined to 1 and 21 µg/kg at 240 hours post dosing. However, as only two animals were slaughtered per point, individual variations were important. Therefore, these results should be taken with caution.

   After a bath administration of 5 µg/l ^{14}C-deltamethrin in seawater at a temperature of 12°C for 30 minutes, it was shown by autoradiography that ^{14}C-deltamethrin was mainly absorbed from the seawater, through the gills**.** Deltamethrin is rapidly distributed to the all major organs and tissues with highest concentration of deltamethrin and its metabolites in bile, which constitutes the major route of excretion. The levels of radioactivity in the bile were were 2339, 2649, 1074, 841 µg equivalents deltamethrin /kg at 8, 24, 48 and 96 hours post dose, respectively. At 8 hours post dosing, the mean total radioactivity levels measured in groups of 10 atlantic salmons were 2.53, 13.19, 4.45 and 18.81 µg equivalents deltamethrin/kg in muscle, skin, kidney and liver, respectively. Then, they declined to 2.09, 7.36, 2.61 and 11.69 µg equivalents deltamethrin/kg at 24 hours post dosing and to 0.97, 4.65, 1.20 and 2.49 µg equivalents deltamethrin/kg at 96 hours in muscle, skin, kidney and liver, respectively.

3. Two radiometric depletion studies were conducted in Bluegills, which were exposed to a nominal concentration of 0.042 µg/l [^{14}C-benzyl]deltamethrin for 28 or 49 days, the water temperature being 17°C.

   In a first study, fish remained for 28 days in a bath of 0.042 µg/l [^{14}C-benzyl]deltamethrin. The concentrations of radioactivity in edible tissues ranged from 1.8 µg equivalents deltamethrin/kg on day 1 to 8.0 µg/kg on day 28. After the end of the treatment, the total residues declined from 5.1 µg equivalents deltamethrin/kg at 1 day after treatment to 3.6, 3.2 and 1.4 µg equivalents deltamethrin/kg at 3, 7 and 10 days after the end of the treatment.

   In a second study, during the 49 day period of exposure, the concentrations of radioactivity in muscle ranged from 2.28 µg equivalents deltamethrin/kg at day 10 of the treatment to 5.19 µg equivalents deltamethrin/kg at day 49. The ratio deltamethrin towards total radioactive residues was 0.78. However, as the dosage and the length of the treatment is far from that recommended for the target species, no firm conclusion about the ratio of deltamethrin towards total residues was reached for the target species.

4. Two non radiometric depletion studies were conducted in groups of 10 Atlantic salmons exposed to a bath treatment with a nominal deltamethrin concentration of 3 µg/l for 40 minutes in sea water at temperatures of 10°C or 5°C. No adverse effects were observed. Deltamethrin could not be detected (below the limit of detection, 5 µg/kg) in the samples of muscle plus skin in natural proportion at any time-point, the samples being collected from 2 hours to 240 hours after treatment.

5. According to the Note for guidance on the establishment of maximum residue limits for *salmonidae* and other fin fish, an extrapolation can be made as an MRL has already been established for muscle in several major mammalian species. Therefore, it may be applied to *salmonidae* and other fin fish as well and the parent compound is acceptable as a valid marker residue in *salmonidae* and other fin fish.

6. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) also assessed deltamethrin in 1999 and allocated the following MRLs for cattle, sheep, chicken and salmons: 30 µg/kg for muscle, 50 µg/kg for liver, 50 µg/kg for kidney, 500 µg/kg for fat or skin + fat, 30 µg/kg for milk and 30 µg/kg for eggs, based on the ADI established by Joint FAO/WHO Meeting on Pesticide Residues (JMPR).

7. An analytical GC/MS method was provided for monitoring residues of deltamethrin in muscle plus skin of fish. The limits of detection and quantification were stated to be at 2 and 5 µg/kg. However, additional data are requested to confirmed these figures. This analytical method was not fully validated according to the requirements of Volume VI of The Rules Governing Medicinal Products in the European Community.

Conclusions and recommendation

Having considered that:

- an ADI of 10 µg/kg bw (i.e. 600 µg/person) was established for deltamethrin,
- since deltamethrin is also widely employed as pesticide on plants used for human consumption, the portion of the ADI to be allocated to products of animal origin is 40%, i.e. 240 µg/day;
- the Note for guidance on the establishment of maximum residue limits for *salmonidae* and other fin fish can be applied,
- deltamethrin was identified as marker residue,
- an analytical method for monitoring residues is available but is not fully validated in accordance with Volume VI;

the Committee for Veterinary Medicinal Products recommended the inclusion of deltamethrin for fin fish in Annex III of Council Regulation (EEC) No 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs	Target tissue	Other provisions
Deltamethrin	Deltamethrin	Fin fish	10 µg/kg	Muscle and skin in natural proportions	Provisional MRL expire on the 1.1.2002

Based on these MRL values, the total daily intake including residues from the other animal derived foodstuffs (in particularly, eggs and milk) will represent about 8% of the ADI; this margin allows for total residue correction and is compatible with the Estimated Maximum Daily Intake (EMDI) and with the Theoretical Maximum Daily Intake (TDMI) of residues of deltamethrin from the pesticide use, which amount to 16% and 72%, respectively.

Before the Committee for Veterinary Medicinal Products can consider the inclusion of deltamethrin in annex I of Council Regulation (EEC) No 2377/90, the points included in the list of questions should be addressed.

LIST OF QUESTIONS

1. The applicant should provide a validated analytical method in accordance with the requirements of Volume VI of The Rules Governing Medicinal Products in the European Community. The values for the limit of detection and quantification should be confirmed. Additional data on specificity and stability are requested.