



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

DELTAMETHRIN

(Extension to fin fish)

SUMMARY REPORT (4)

1. Deltamethrin, (S)- α -cyano-3-phenoxybenzyl, (1R)-cis-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane 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 used in Atlantic salmon and rainbow trout to treat sea lice (*Lepeophtheirus salmonis* and *Caligus elongatus*). The recommended bath dosages are 2 μ g deltamethrin/l for 30 minutes in a closed container or 3 μ g deltamethrin/l for 40 minutes in a partially closed sea-cage. It is also widely used as a pesticide on crops.

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

Currently, deltamethrin is included 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	Bovine	10 μ g/kg 50 μ g/kg 10 μ g/kg 10 μ g/kg 20 μ g/kg	Muscle Fat Liver Kidney Milk	Provisional MRL expire on 1.7.2001
		Ovine	10 μ g/kg 50 μ g/kg 10 μ g/kg 10 μ g/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 μ g/kg 50 μ g/kg 10 μ g/kg 10 μ g/kg 50 μ g/kg	Muscle Skin + fat Liver Kidney Eggs	Provisional MRL expire on 1.7.2001
		Fin fish	10 μ g/kg	Muscle and skin in natural proportion	Provisional MRL expire on the 1.1.2002

Recently the CVMP recommended the inclusion of deltamethrin MRLs for bovine and ovine species, at the above MRL-values in Annex I, and an extension of the Annex III-entry for chicken until 1.7.2003.

Additional data on the validation of the routine analytical method were provided in response to the list of questions further to the recommendation of provisional MRLs for deltamethrin in fin fish.

2. Two radiolabelled studies were conducted in Atlantic salmon.

Groups of 2 atlantic salmon 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 treatment to 48, 23.5, 7 and 2.5 $\mu\text{g}/\text{kg}$ at 12, 48, 96 and 240 hours post treatment. 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 treatment they were 23.5 and 20 $\mu\text{g}/\text{kg}$ for muscle and skin, respectively. At 48 hours post treatment, they were 10.5 and 55 $\mu\text{g}/\text{kg}$ in muscle and skin, respectively, and then they declined to 1 and 21 $\mu\text{g}/\text{kg}$ at 240 hours post treatment. However, as only two animals were slaughtered per time point, individual variations were important. Therefore, these results should be taken with caution.

After a bath administration of 5 $\mu\text{g}/\text{l}$ ^{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 2339, 2649, 1074, 841 μg equivalents deltamethrin/kg at 8, 24, 48 and 96 hours post treatment, respectively. At 8 hours post treatment, the mean total radioactivity levels measured in groups of 10 atlantic salmon 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 treatment 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 $\mu\text{g}/\text{l}$ [^{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 $\mu\text{g}/\text{l}$ [^{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 $\mu\text{g}/\text{kg}$ 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 salmon exposed to a bath treatment with a nominal deltamethrin concentration of 3 $\mu\text{g}/\text{l}$ 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 $\mu\text{g}/\text{kg}$) 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 (EMEA/CVMP/153b/97-FINAL), 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. MRLs in animal tissues and products were set at 50 µg/kg for fat, meat and for eggs by Council Directive 98/82/EC concerning the use of deltamethrin as pesticide. This level was indicated as the lower limit of analytical determination.
7. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) also assessed deltamethrin in 1999 and allocated the following MRLs at twice the limit of quantification of the analytical method for cattle, sheep, chicken and salmons as follows: 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 of 0.01 mg/kg bw established by Joint FAO/WHO Meeting on Pesticide Residues (JMPR). JECFA retained the sum of 3 isomers, cis-deltamethrin, trans-deltamethrin and alpha-R-deltamethrin as marker residue. This approach could not be followed by the CVMP as deltamethrin (synonym: cis-deltamethrin) is the only substance present in edible tissues and therefore retained by the CVMP as marker residue. As the expression of the marker residue is different, the CVMP could not retain similar MRLs to the ones adopted by JECFA.
8. An analytical GC/MS method was provided for monitoring residues of deltamethrin in muscle plus skin of fish, using ¹³C-permethrin as an internal standard. The limits of detection and quantification were 2 and 5 µg/kg, respectively. The method was fully validated according to the requirements of Volume VI of The Rules Governing Medicinal Products in the European Community and presented according to the ISO 78/2 format.

Conclusions and recommendation

Having considered that:

- an ADI of 10 µg/kg bw (i.e. 600 µg/person) was established for deltamethrin,
- in application of the Note for guidance on the establishment of maximum residue limits for *salmonidae* and other fin fish (EMEA/CVMP/153b/97-FINAL) deltamethrin was identified as marker residue,
- an analytical method for monitoring residues is available and is fully validated in accordance with Volume VI;

the Committee for Veterinary Medicinal Products recommends the inclusion of deltamethrin for fin fish in Annex I 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	

Based on this MRL value, also considering the other elements of the daily food basket for which MRLs have been established, i.e. eggs and milk, the maximum daily intake of residues will represent about 6 % of the ADI; this margin allows for total residue correction and is compatible with the Theoretical Maximum Daily Intake (TDMI) of residues of deltamethrin from the pesticide use, which amounts to 72%.