Divergent position on a CVMP opinion on an Article 33(4) referral of Directive 2001/82/EC for

Deltanil 10 mg/ml Pour-on Solution for cattle and sheep and Deltanil 100 mg Spot-on Solution for cattle (EMEA/V/A/093)

Deltanil 10 mg/ml Pour-on solution for cattle and sheep and Deltanil 100 mg/ml Spot-on solution for cattle are intended for the treatment and prevention of infestations of lice and flies on cattle, ticks, lice, keds and established blowfly strike on sheep and lice and ticks on lambs. This referral under Article 33(4) of Directive 2001/82/EC was initiated because the environmental risk assessment cannot be finalised due to insufficient data on soil degradation and bioaccumulation. Based on these findings the PBT status of deltamethrin could not be assessed finally as well. Furthermore, it should be noted that the applicant included the report on the EQS (environmental quality standard) derivation for deltamethrin in the dossier but only used beneficial endpoints. They did not use the lowest toxicity values for Gammarus for deriving the PNEC. This resulted in a PNEC much higher than when using the most sensitive PNEC from the EQS. On basis of this it was concluded that deltamethrin poses 'no risk to the aquatic environment' which is considered debatable.

It is the opinion of the undersigned that the provided references on **degradation** in soil are not in accordance with the relevant OECD guideline 307 as required by VICH guideline 38. No study reports have been provided, only three scientific publications which are considered not to be of acceptable quality. The following points, in particular, have been noted:

In the key publication used by the applicant the transformation of deltamethrin was investigated in one soil only, which was not characterised sufficiently. According to OECD guideline 307 investigations on four soils are recommended to reflect soils with different properties and transformation rates. The reported DT_{50} value of 72 days at 20 °C reflects only the transformation of deltamethrin in the tested soil but is not necessarily representative for other soils. Furthermore, information on the soil properties is lacking, which might affect the transformation rate. Moreover, the validity criteria regarding the analytical recovery rate are not met.

The second reference is a short description of investigations on the fate of deltamethrin and other pyrethroids under field and indoor conditions. Neither details on material and methods nor the residue concentrations were given to verify the reported half-lives of 34 days and 48 days.

The results in the third reference are presented as graphs only and no substance concentrations were given. As a consequence no conclusion on the plausibility of the presented DT_{50} values can be made. Different degradation kinetic models were applied, however, as a detailed description is missing no conclusion can be made on the acceptability of the models used. Furthermore, the described experiments were mainly focused on the concentrations of the tested substances in the field, without assessing bound residues or transformation products.

Three references from the public domain on **bioaccumulation** were provided which are considered inappropriate regarding their quality and therefore not acceptable as outlined below:

The key publication used by the applicant shows major deviations from the respective OECD guideline 305 which render the publication unacceptable. First of all the validity criteria were not met due to an insufficient recovery of the radiolabeled deltamethrin (^{14}C) and a too high carbon content in the test system which might have led to an underestimation of the bioaccumulation in fish. Furthermore, the accumulation phase of 3 days instead of 28 days was too short and a separate test system for the 8-days depuration phase was used.

A second publication was provided which investigated the fate of deltamethrin in small outdoor ponds. The main aim was to assess the distribution of deltamethrin between the water phase and the sediment. Additionally, concentrations of deltamethrin in fathead minnows (*Pimephales promelas*) were determined which showed that the fish accumulated levels of deltamethrin 248-907-fold higher than concentrations in water at 24 hours post treatment. The design of the study is not comparable to that of a standard bioconcentration study according OECD 305. Therefore, it is considered that the results of this publication cannot be used in the ERA.

Further references from the public domain were provided which cite a bioconcentration factor (BCF) value of 1400 in fish, which originates from one and the same publication. The original study was not conducted according to OECD guideline 305 but to an older guideline from 1982 and has some major deficiencies (e.g. one concentration tested, lipid content of the fish not analysed, BCF not normalised to 5% lipid content, steady-state not reached, $BCF_{steady\ state}$ used instead of $BCF_{kinetic}$). According to the recommendations in the EU technical guidance document for the interpretation and handling of BCF data, the BCF should be normalised to 5% lipid content in fish. Lipid normalisation of the cited BCF of 1400 under the assumption of a fat content of 1.9 g for juvenile Bluegill sunfish (*Lepomis machrochirus)* would result in a BCF >2000. This would classify deltamethrin as 'bioaccumulative' according to the criteria of the PBT assessment. This is supported by the fact that during the test BCFs at some single time points (BCF_{day21}, BCF_{day24}) exceeded the BCF trigger of 2000. Hence, the use of a BCF of 1400 in the ERA is considered to underestimate the bioaccumulation of deltamethrin.

Based on the above arguments on the data on biodegradation in soil and bioaccumulation it is considered the **PBT assessment** needs to be re-evaluated regarding persistence and bioaccumulation. It has to be noted that in the PBT assessment all available data for all compartments (water, sediment and soil) should be considered:

P – Persistence: According to the EU TGD the degradation half-lives which have been determined in standard tests for different environmental compartments should be normalised for example to an average EU outdoor temperature of 12 °C. Two of the publications cited in the dossier have non-normalised DT_{50} values as endpoints. Normalisation of the DT_{50} of 72 day at 20 °C in the key soil degradation publication to 12 °C leads to a DT_{50} of 153 days, which clearly exceeds the criteria for persistence in soil of 120 days.

In the other reference non-normalised DT_{50} values of 45 and 141 days were determined in water/sediment system at 20 °C. Based on these values it can be concluded that the P criterion would be fulfilled using the maximal DT_{50} value derived from the water/sediment study.

B – Bioaccumulation: According to the repeatedly cited $BCF_{steady\ state}$ of 1400 and the respective $BCF_{kinetic}$ of 1800 deltamethrin can be classified as highly bioaccumulative according to the criteria of the Phase II ERA. Normalisation of this BCF to a lipid content of 5% (which was used by the applicant for other BCF calculations) leads to a value which clearly exceeds the B-criterion of BCF >2000. Therefore it is considered that deltamethrin potentially fulfils the B criterion.

A final conclusion on the PBT assessment of deltamethrin cannot be made at present as the presented data on degradation and bioaccumulation are based on published literature only which were not conducted in accordance with appropriate guidelines and show major deficiencies. Therefore the presented data are considered inconclusive.

However, if performing a PBT assessment as outlined in EU TGD on Risk Assessment in support of the Commission Directive 93/67/EEC on risk assessment for new notified substances and Commission Regulation (EC) 1488/94, based on the available data, deltamethrin can be classified as potentially PBT.

Risk management approaches are based on fate and effect data and can only be defined in a reasonable manner, only if sufficient data are presented and the proposed measures can be justified. The literature submitted indicates that deltamethrin is toxic to dung fauna. Depending on the results of Tier A, a Tier B risk assessment may also be necessary. Therefore, a clear risk characterisation based on OECD tests is required. In order to identify potential effective risk mitigation measures, the environmental impact assessment for deltamethrin needs to be completed based on data obtained from experimental studies. The argument of the applicant to use RMM from similar products cannot be followed because the NTA (DG ENTR/F2/JR (2009)) states "…It is also not possible for competent regulatory authorities to simply refer to ERA data of the original dossier, or to any other dossier for a similar product without consent of the company holding the marketing authorisation." Therefore, in the case of Deltanil, own data have to be provided in order to finalise the Phase II Tier A assessment.

As the data for the environmental risk and PBT assessment is considered incomplete for Deltanil 10 mg/ml Pour-on Solution for cattle and sheep and Deltanil 100 mg Spot-on Solution for cattle the risk to the environment and the PBT assessment cannot be finally assessed. Additionally concerns also remain that deltamethrin poses a potential serious risk for dung fauna. As deltamethrin shows long term effect to dung fauna it has to be pointed out that RMM will not be appropriate to mitigate the risk of deltamethrin. Furthermore the active ingredient deltamethrin is potentially a PBT substance.

Overall, the benefit-risk balance is considered inconclusive for Deltanil 10 mg/ml Pour-on solution for cattle and sheep and Deltanil 100 mg/ml Spot-on solution for cattle. A serious concern remains in relation to environmental risk for dung fauna and the potentially PBT status of deltamethrin which could not be solved by the applicant.

London, 17 July 2013

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