EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Public Health and Risk Assessment
C7 - Risk assessment

Brussels, C7/VR/csteeop/musk ket ENV/080104 D(04)

SCIENTIFIC COMMITTEE ON TOXICITY, ECOTOXICITY AND THE ENVIRONMENT (CSTEE)

Opinion on the results of the Risk Assessment of:

MUSK KETONE
ENVIRONMENTAL PART

CAS No.: 81-14-1
EINECS No.: 201-328-9

Carried out in the framework of Council Regulation (EEC) 793/93 on the evaluation and control of the risks of existing substances[1]

Adopted by the CSTEE during the 41st plenary meeting of 8 January 2004

[1] Regulation 793/93 provides a systematic framework for the evaluation of the risks to human health and the environment of those substances if they are produced or imported into the Community in volumes above 10 tonnes per year. The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC)1488/94, which is supported by a technical guidance document.

SCIENTIFIC COMMITTEE ON TOXICITY, ECOTOXICITY AND THE ENVIRONMENT (CSTEE)

Opinion on the results of the Risk Assessment of:
MUSK KETONE
ENVIRONMENTAL PART
CAS No.: 81-14-1
EINECS No.: 201-328-9

Adopted by the CSTEE during the 41st plenary meeting
of 8 January 2004

Terms of Reference

In the context of Regulation 793/93 (Existing Substances Regulation), and on the basis of the examination of the Risk Assessment Report the CSTEE is invited to examine the following issues:

(1) Does the CSTEE agree with the conclusions of the Risk Assessment Report?

(2) If the CSTEE disagrees with such conclusions, the CSTEE is invited to elaborate on the reasons for this divergence of opinion.

According to the Technical Guidance Document on Risk Assessment – European Communities 2003:

- *conclusion i): There is a need for further information and/or testing;*
- *conclusion ii): There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already;*
- *conclusion iii): There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.*

GENERAL COMMENTS

The major emissions come from private use of the consumer products and waste water is the receiving medium. Musk ketone is partly metabolised in STPs to the corresponding monoamino derivatives. More information is needed on these compounds to be able to judge their possible effect in the environment, and **the CSTEE would therefore have preferred conclusion i) for the metabolites.**

The use volume of musk ketone varies between regions in the EU and that not all sewage water is treated in an STP. This may give higher than the predicted concentrations in some areas. Most of the measured concentrations are from countries that have restricted the use of musk xylene, and may thus not describe the situation in high consumption regions, and **CSTEE therefore recommend further exposure studies in such areas.**

There are several indications that larvae of fish and copepods are sensitive to musk ketone exposure, but these have not been taken into account by the assessor. The CSTEE suggests that additional chronic studies on plants and soil microorganisms are requested (conclusion i))

The predicted environmental concentrations for private use gives a PEC/PNEC slightly over 1 for fish-eating animals, and the situation may be worse in some regions with higher consumption and no STP. **The risk for secondary poisoning should therefore be further considered**.

The CSTEE supports the conclusion for the PBT assessment.

SPECIFIC COMMENTS

Background

Musk ketone (3,5-dinitro-2,6-dimethyl-4-tert-butylacetophenone) is a component in many fragrance compositions used in cosmetic products, detergents, fabric softeners and household cleaning products. The substance is not produced in the EU, and the import in 2000 is estimated to 35 tonnes per year. Repeated surveys of used volumes show that these have been decreasing over the period 1992 to 2000.

Exposure assessment

Musk ketone is not readily biodegradable in standard tests, but in the reductive phase in an STP at least one of the nitro groups are to some extent reduced to the corresponding amines. Due to the limited quantitative information about this reaction, it is not taken into account in the assessment of emissions from STPs, which is supported by the CSTEE. The bioconcentration in fish has been measured to values from 1100 to 1380 L/kg ww, and the assessor is using the higher value. In a recent study (Gatermann R, Biselli S, Huhnerfuss H, Rimkus GG, Hecker M, Karbe L. Synthetic musks in the environment. Part 1: Species-dependent bioaccumulation of polycyclic and nitro musk fragrances in freshwater fish and mussels. Arch Environ Contam Toxicol. 2002 May;42(4):437-46) bioaccumulation factors of up to 1300 in carp and eel were measured in a sewage water pond.

Discharges from fragrance compounding are small compared to the emissions from private use, where most of the musk ketone is ending up in the waste water. Using the EUSES, the assessor calculates a $PEClocal_{water}$ of 0.76 µg/L and a $PECregional_{water}$ of 0.11 µg/L. **The known differences in consumption volumes in different parts of the EU is not taken into account, which is surprising as this may increase these levels by almost a factor of 2 for some areas**. **Furthermore, as some waste water is not treated in STPs, the concentration may locally be still higher**.

Measured data for musk ketone in water are in agreement with predictions or lower, in some cases several orders of magnitude below the predictions. For the risk characterisation both predicted and measured concentrations are used. It has to be kept in mind that the measured data may represent mainly areas with a low consumption of musk ketone, but that also several of the results are from samples taken at a time when the consumption of the substance was higher than it is today. Measured concentrations in sludge are lower than predicted data. Also the concentrations found in fish are lower than the predicted values.

Effect assessment

Aquatic organisms

There are chronic toxicity tests for musk ketone available on algae (NOEC 88 µg/L), *Daphnia magna* (NOEC 170 µg/L) and rainbow trout (NOEC 63 µg/L), and assessment factor of 10 is used in accordance with the TGD to get a $PNEC_{water}$ of 6.3 µg/L. There is, however, a recent study on Zebra fish embryos, which indicate that the survival times for the larvae is significantly reduced already at 100 µg musk ketone/L, with a NOEC of 33 µg/L. The assessor argues that this test involves also starvation as a stressor is not using this endpoint for derivation of PNEC. In the same study several parameters

were studied in exposed newly fertilised Zebrafish eggs, and an inhibition of heartbeat frequency could be observed at 10 µg musk ketone/L. The CSTEE agrees with the assessors that it is not clear how this parameter influences the fish population. There is also a study on larval development rate of the marine copepod *Acartia tonsa*, indicating an EC_{10} of 10 µg/L, but the final report is not available yet. Also the larval development *Nitocra spinipes* seems to be sensitive to musk ketone, and a not yet published report gives a NOEC of 30 µg/L. **The CSTEE is of the opinion that the available information calls for further studies on reproduction toxicity in fish, and that such studies should be requested to make a proper risk assessment possible**.

Terrestrial organisms

Toxicity tests for musk ketone are available for springtail and earthworm, and the lowest NOEC leads to a $PNEC_{soil}$ value of 0.22 mg/kg dw using an assessment factor of 50. **As the tests available are conducted on organisms belonging to the same taxonomic group (soil dwelling invertebrates) the proper factor should have been 100. In addition, the PNEC based on the equilibrium portioning method should also have been estimated and the lowest PNEC should have been used in the assessment**.

Non compartment specific effects

There are no data on effects of musk ketone in predators, and an oral NOAEL for rat (2.5 mg/kg bw/d in a 28-days test) is used. A food conversion factor of 20 is applied, and an assessment factor of 150 is used instead of the factor of 300 suggested in the TGD. The reason for this reduction is that the effects at the next dose level was only marginal, and that other tests indicate higher NOAELs, although these tests do not fulfil all TGD requirements. The CSTEE support these conclusions.

Risk characterisation

The assessor calculates PEC/PNEC values for musk ketone below 1 in the aquatic compartment, that for private use being the highest at 0.1. These values would still become below 1 if the higher toxicity data had been taken into account. However, the use of the lowest toxicity values and an additional factor of 2 in the exposure assessment to cover the known differences in consumption volumes within the EU, would result in a PEC/PNEC value of 1.2.

The PEC/PNEC ratios for the terrestrial compartment will be larger than 1 if an assessment factor of 100 is used. **CSTEE suggests that additional chronic studies on plants and soil microorganisms are requested.(conclusion i)).**

For fish-eating predators the PEC/PNEC ratios for secondary poisoning are 1 for end product formulation and 1.8 for private use scenarios. In reality, the RAR suggest a risk for secondary poisoning downstream discharges of municipal effluents assuming that the municipal sewages goes to a STP and has a dilution factor of at least 20. In the EU, municipal discharges with no STP are still frequent and dilutions factors below 10 are also frequent is some areas and seasons, therefore as the risks are associated to a widely distributed private use **a high concern for secondary poisoning should be considered (conclusion i))**. For worm-eating animals the risk quotient is below one for all default scenarios.

Metabolites of musk ketone

The most common metabolite of musk ketone seems to be the 2-amino compound. It is found at comparable or higher levels as the mother substance in surface water. There are very limited data on effects of musk ketone metabolites, but they seem to interact with the estrogen receptor. According to the assessor, the limited data bases for both environmental concentrations for and the potency of the metabolites indicate that there is no reason for concern, and conclusion ii) is considered. **The CSTEE finds this conclusion based on a weak scientific basis, especially as the concentrations were measured in German rivers after the restrictions on nitro musks were introduced in that country, and would have preferred conclusion i).**

PBT assessment

Musk ketone does not fulfil the bioaccumulation criterion.