



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL
Directorate C - Public Health and Risk Assessment
C7 - Risk assessment

Brussels, C7/VR/csteep/musk xyl ENV/080104D(04)

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

Opinion on the results of the Risk Assessment of:

**MUSK XYLENE
ENVIRONMENTAL PART**

**CAS No.: 81-15-2
EINECS No.: 201-329-4**

**Carried out in the framework of Council Regulation (EEC) 793/93 on
the evaluation and control of the risks of existing substances¹**

**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.

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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 consumer products and waste water is the receiving medium. Musk xylene seems to be 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 facts that the use volume of musk xylene varies between regions in the EU and that not all sewage water is treated in an STP may give higher than 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.**

The PEC/PNEC ratio for the aquatic compartment is close to 1, and taking into account the possibility for higher than predicted concentrations in some areas, and the effect on survival time of Zebra fish embryos, the **CSTEE recommend further studies on reproduction toxicity in fish.**

Both terrestrial and non compartment specific scenarios based on predicted data give PEC/PNEC ratios higher than 1. The use of a few measured concentrations in the terrestrial environment for excluding the risk is not acceptable. **Toxicity studies on soil dwelling organisms should be required.**

The predicted environmental concentrations for private use gives a PEC/PNEC slightly over 1 for worm-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 CSTEЕ supports the conclusion i) for the PBT assessment.

SPECIFIC COMMENTS

Background

Musk xylene (1-tert-butyl-3,5-dimethyl-2,4,6-trinitrobenzene) is a component in many fragrance compositions used in cosmetics, detergents, fabric softeners and household cleaning products. The substance is not produced in the EU, and the import in 2000 is estimated to 67 tonnes per year. Repeated surveys of used volumes show that these have been decreasing over the period 1992 to 2000

Exposure assessment

Musk xylene is not readily biodegradable in standard tests, but in the reductive phase in an STP one or several of the nitro groups are reduced to form the corresponding amines. Due to the limited quantitative information about this reaction, it is not taken into account in the assessment of musk xylene emissions from STPs, which is supported by the CSTEЕ. The bioconcentration in fish has been measured to values from 1,400 to 6,740, and the assessor is using 4,400 L/kg ww. 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 40,000 in eel were measured in a sewage water pond. In most of the species analysed in this study the 4-amino metabolite was found at a higher level than the musk xylene itself.

Discharges from both fragrance compounding and end product formulation are small compared to the emissions from private use, where most of the musk xylene is ending up in the waste water. Using the EUSES, the assessor calculates a $PEC_{local,water}$ of 0.98 $\mu\text{g/L}$ and a $PEC_{regional,water}$ of 0.18 $\mu\text{g/L}$. **The known differences in consumption volumes in different parts of the EU is not taken into account, which is surprising as this would have increased 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 in surface waters 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 xylene, 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.

The predicted concentrations in fish are also higher than the measured levels. This may also be explained by metabolism of the musk xylene.

Effect assessment

Aquatic organisms

There are long-term tests for musk xylene available on algae (NOEC > 560 µg/L) and *daphnia magna* (NOEC 56 µg/L), and assessment factor of 50 is used in accordance with the TGD to get a PNEC_{water} of 1.1 µg/L. An assessment factor of 100 for a 14 day fish study gives similar result. There is, however, a recent study on Zebra fish, which indicate that the survival times for the larvae is significantly reduced already at 33 µg musk xylene/L, with a NOEC of 10 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 xylene/L. The CSTEE agrees with the assessors that it is not clear how these parameters influence the fish population.

Terrestrial organisms

Earthworms showed no effect at the highest tested level (50 mg/kg dw) of musk xylene (OECD TG 207), and PNEC_{soil} was derived using the equilibrium partitioning theory, leading to a value of 0.26 mg/kg dw.

Non compartment specific effects

There are no data on effects of musk xylene in predators, and a NOAEL for rat (7.5 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 below 1 for the aquatic compartment, that for private use being the highest at 0.9. **As the environmental concentrations in some regions may be higher than those predicted, and in light of the observations in Zebra fish, the CSTEE had preferred to see a request for a reproduction toxicity study in fish.**

The PEC/PNEC ratios for the terrestrial compartment are below 1 for all scenarios but private use (1.7) when the predicted exposure values are used. Using measured data for sludge concentrations of musk xylene (two studies, at least one of them of good quality) all ratios become below 0.1. **The CSTEE is, however, of the opinion that toxicity studies on soil dwelling organisms are needed.**

For fish, the PEC/PNEC ratios for secondary poisoning are all above 1, private use scenario being as high as 5. In reality, the assessor suggests 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 in 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..** For worm-eating animals the risk quotient is below one for all default scenarios except private use, which becomes 1.1., and conclusion ii) can be accepted due to the fact that some of the musk xylene is metabolised in the STP.

Metabolites of musk xylene

The most common metabolite of musk xylene seems to be the 4-amino compound. (The metabolite names at page 25 are wrong, they should be 1-tert-butyl-3,5-dimethyl-4-amino-2,6-dinitrobenzene and 1-tert-butyl-3,5-dimethyl-2-amino-4,6-dinitrobenzene, respectively). It is found at comparable levels as the mother substance in fish, and up to 3-10 times higher concentrations in surface water. The 2-amino compound has also been found, but at lower levels. 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

All three PBT properties are on the borderline to fulfil the criteria given in the TGD, and the assessor recommends further testing. The biodegradation tests used are based on oxygen consumption or carbon dioxide formation, but as the musk xylene is being reduced these parameters will not disclose the metabolism. However, the CSTEE support further testing were the concentration of the substance is followed. The metabolites should also be including in the testing.