

# Opinion On Nitro Musk Compounds In Foods (Expressed On 13 June 1997)

## Terms of reference

The Committee is requested to evaluate the potential risk to human health arising from the presence of certain nitro musk compounds in foods.

## Background

Nitro musk compounds are used as fragrance substances in detergents, cleaning agents and cosmetic products. They are not easily biodegradable and accumulate in the environment. Reports of the presence of traces of nitro musk substances in a number of foodstuffs and in human milk and adipose tissue prompted the Federal Republic of Germany to request the Commission to consult the Scientific Committee for Food in the light of the reported levels of occurrence in foods and the toxicological evaluation of these substances made by the Scientific Committee for Cosmetology.

## Discussion

Nitro musk compounds have been found as contaminants in some foodstuffs, human milk and adipose tissue. Maximum concentrations of musk xylene, musk ketone and musk ambrette in farmed fish (mainly trout) and fish originating from rivers amount to about 90, 68 and 1 µg/kg fresh weight [ , , , ]. Human milk has been found to contain up to 1.2 mg musk xylene and 0.2 mg musk ketone/kg fat [ , ].

From the concentrations found in human adipose tissue and the elimination half-life of 63-107 days determined in volunteers, a total average daily intake of about 11 µg musk xylene was estimated [4]. The mean intake from fish or other contaminated foodstuffs, however, is much lower. It is quantitatively negligible in comparison with the contribution to body burden of cosmetic products and household detergents.

A long-term feeding study with musk xylene in mice for 80 weeks resulted in an increased incidence of liver adenomas in both sexes and liver carcinomas in males and harderian gland adenomas in males as compared to the controls at doses of 91 and 170 mg/kg b.w./day for males and 101 and 192 mg/kg b.w./day for females [ ]. Carcinogenicity data in rats are not available.

Ames test, chromosome aberration assay with CHO cells, mouse lymphoma assay and *in vitro* and *in vivo* UDS assays did not reveal genotoxicity of musk xylene [ ]. However, genotoxic intermediates such as aromatic amines can be formed *in vivo* since the nitrogroups of musk xylene are metabolically reduced to amino groups in rats [ ] and humans [ ].

Musk xylene induces cytochrome P 450 enzymes in rats, particularly those in the CYP 1A family [ , , ]. In mice, musk xylene causes generalised hepatic changes similar to classical CYP 2B inducers like phenobarbital. However, in contrast to phenobarbital, musk xylene is also a potent inhibitor of the CYP 2B enzymes such that there is no measurable increase in CYP 2B enzyme activity, even when CYP 2B protein levels are very high [ ].

Musk ambrette is neurotoxic and its use in cosmetic products has been banned in the EU. Furthermore it has been found to be mutagenic in *Salmonella typhimurium* in the presence of metabolic activation [ ]. Musk ketone, like musk xylene, is a strong inducer of toxifying liver enzymes [ , ]

## Conclusion

Musk xylene is carcinogenic in mice and given that number of tests did not reveal a genotoxic potential it is probably acting through a non-genotoxic mechanism in mice. On the other hand, it must be taken into account that musk xylene is metabolised in rats and humans to aromatic amines. In addition, musk xylene is an enzyme inducer and accumulates in body tissues because of its lipophilic nature. It is found in human milk and adipose tissue. The half-life in humans is extremely long in contrast to rats and mice. For these reasons, in the opinion of the Committee, contamination of food with musk xylene should be reduced as much as possible.

The toxicological data on musk ambrette, musk ketone, musk tibetene and musk moskene are insufficient to allow a reliable evaluation or to provide a basis for the setting of tolerable levels in food. These nitro musk compounds must also be expected to have a high tendency to accumulate. It is therefore the opinion of the Committee that, as a matter of prudence, contamination of food with these compounds should also be reduced as much as possible.