The European Agency for the Evaluation of Medicinal Products
Veterinary Medicines Evaluation Unit

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

SODIUM DICHLOROISOCYANURATE

SUMMARY REPORT

1. Sodium dichloroisocyanurate as the candidate compound is used as a teat dip or spray prior to or after milking - it is applied topically. The dilution rate varies from 0.25 g/l to 5 g/l depending on use, the higher concentration being used for teat dipping.

2. Sodium dichloroisocyanurate is a well established disinfectant used for many purposes including wound cleansing, hospital use, sterilizing babies bottles, disinfection of water for human consumption and disinfection of swimming pools.

3. Sodium dichloroisocyanurate is poorly absorbed through the intact skin. Blood samples from rats exposed to high levels of radiolabelled compound were mainly negative for radioactivity.

4. Metabolism studies in rats and dogs following both oral and intravenous administration showed rapid absorption, distribution and excretion of unmetabolised sodium dichloroisocyanurate.

   Elimination half lives were:

Rat	intravenous or oral	5 mg/kg dose	32 - 43 minutes
Rat	oral	500 mg/kg dose	122-148 minutes.

   at 5 mg/kg excretion was mainly via the urine with less than 5% in faeces,

   at 500 mg/kg excretion 55-70% (rat) or 27-86% (dog) was excreted in the faeces.

   Radioactivity in tissues was less than or near the sensitivity of the method irrespective of dosage regime used.

5. Sodium dichloroisocyanurate has low oral or dermal toxicity in acute studies but high eye irritation toxicity.

   Following repeated administration, 13 weeks, in drinking water NOEL's were 896ppm (72 mg/kg/day) rat and 1792 ppm (522 mg/kg/day) mice.

   Major toxic change noted was irritation of the bladder lining and calculi in 2/25 mice and hyperplasia of the urinary bladder in male rats.

6. A three generation rat study did not induce significant fluctuations in reproductive or litter parameters, the NOEL was 5375 ppm.

7. There were no signs of terotogenicity, embryotoxicity or foetotoxicity in rats at doses of up to 5,000 mg/kg/day of monosodium cyanurate or in rabbits at doses of up to 200 mg/kg/day.

8. In a series of mutagenicity studies, Mouse Lymphoma cell, Rat Bone Marrow cytogenicity assay *in vivo*, CHO Assay (chromatid exchange) and Ames test all proved negative.

9. No oncogenic effects were noted in a 2-year rat study or in a 104-week mouse study involving doses of up to 5,375 ppm. The NOEL for toxic effects of significance [decreased survival and lesions secondary to the formation of calculi in the urinary tract (kidney and bladder) and heart were observed in males at doses of 5,375 ppm] was 2,400 ppm.

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10. The recommended WHO level for water purification is 10 ppm of residual available chlorine. On breakdown this is given by 17.4 mg/l. sodium dichloroisocyanurate, which also renders 12 ppm of sodium cyanurate. Since the maximum amount likely to be present in milk is 0.0048 mg/sodium cyanurate/l (assuming sodium dichloroisocyanurate present at just under limit of detection) the potential effect of sodium dichloroisocyanurate on the human gut flora at the levels likely to be present in milk is considered to be minimal.

11. Sodium dichloroisocyanurate and other chlorinated isocyanurates are well established as disinfectants being used for many purposes including wound cleansing, water disinfection for human consumption and swimming pool disinfection.

12. An ADI of 0.72 mg/kg bw/day is proposed based on a NOEL of 896 ppm in the 13 week rat study and using a safety factor of 100.

    The actual intake of sodium cyanurate, assuming maximum residue levels of 0.0048 mg/l would be 6,000 and 1,500 times less than the ADI for an adult (60 kg consuming 1.5 l milk/day) and a child (10 kg, consuming 1 l milk/day) respectively.

    From this it is concluded that an MRL is not required and that sodium dichloroisocyanurate should be entered into Annex II of Council Regulation (EEC) Nº 2377/90.