



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

IODINE

SUMMARY REPORT

1. Iodine is an essential micronutrient for all animal species. In humans, iodine deficiency may lead to thyroid enlargement (goitre) and cretinism. Excessive iodine intake is harmful and can produce hyperthyroidism or thyrotoxicosis.

Various iodine-containing compounds are used in veterinary medicine as antiseptics and sanitisers; these include the iodide and iodate salts, iodophors, polyvinylpyrrolidone-iodine complex (povidone) and iodoform. Iodine compounds are used in teat dips for the prevention and control of mastitis in cattle and in topical preparations for prevention of infections in wounds. Preparations for oral and parenteral administration are also available for the treatment of iodine-deficiency.

Iodine-containing salts are also permitted for inclusion in animal feedingstuffs, in accordance with the provisions of Council Directive 70/524/EEC.

2. The main pharmacodynamic activity of iodine concerns its role as a constituent of the thyroid hormones thyroxine (T_4) and triiodothyronine (T_3). In humans, iodine compounds are readily absorbed after oral administration and less well absorbed after topical administration. Circulation in the blood is as the iodide. Iodine concentrates in the thyroid gland and is incorporated into T_3 and T_4 . The secretion of T_3 and T_4 is controlled by a "feedback" mechanism. In the case of iodine deficiency, a recycling process in the alimentary tract conserves iodine by reabsorbing iodide in the intestine. Excess iodide is excreted by the kidneys. Smaller amounts of iodides are excreted in the faeces, saliva and sweat. Iodides cross the placenta and are excreted in breast milk. In the dairy cow, 70-80% of the orally-ingested iodine is absorbed in the rumen and 10% in the omasum.

The toxicity studies which had been carried out with iodine compounds in laboratory animals were very limited and no conclusions could be drawn regarding NOELs. In contrast, the data on the effects of iodine compounds in humans were extensive.

Most iodine compounds were of fairly low acute toxicity and the iodophors, the inorganic iodide and iodates were of considerably lower acute toxicity than iodine itself. Iodine was a strong irritant but formulations containing iodophors were only slightly irritating to skin and eyes.

Rabbits tolerated twice weekly oral doses of 1 mg/kg bw sodium iodate for periods of up to one year and also tolerated twice weekly oral doses of 10 mg/kg bw per day for 6 weeks. In a 12-month study in dogs, doses 30, 37.5 and 45 mg/kg bw caused no overt signs of toxicity though a slight fall in the red blood cell count together with reticulocytosis was found in most of the animals and haemosiderin deposits in Kupfer cells. The doses used in this study were excessively high when compared with the daily iodine requirement for dogs.

In laboratory animals, iodine compounds were not teratogenic and did not affect fertility. In humans, excessive iodine intake and the use of iodine containing drugs during pregnancy have resulted in cases of foetal goitre. Iodine deficiency has been cited as a cause of malformation in livestock.

Although povidone-iodine was mutagenic towards one strain of *Salmonella typhimurium* in an Ames test, negative results were obtained in three *in vivo* assays. Human epidemiology data indicated an inverse relationship between dietary iodine concentrations and the incidence of various cancers, particularly thyroid cancers.

The data on iodine were reviewed by JECFA in 1989. JECFA concluded that an iodine intake of up to 1 mg per day was safe for the majority of the population but would cause adverse effects in some individuals, particularly those with thyroid disorders (e.g. Graves Disease, Hashimoto's disease) and those who were sensitive to iodine. JECFA set a provisional maximum tolerable daily intake of 1.0 mg iodine/day (0.017 mg/kg bw) from all sources.

3. The microbiological action of iodine was non-specific and involved indiscriminate binding to membranes and inhibition of enzymes.
4. In some Member States, milk was the major source of human dietary iodine. The concentrations of iodine in milk were dependent on the iodine content of the animal feed, the iodine content of any teat dips or sprays, and the nature of the hygiene practices employed during milking. Iodine concentrations in meat were dependent on the iodine content of the animal feed and the proportion of blood removed from the carcass at slaughter. Only small increases in serum iodine concentration were found after teat dipping indicating that the procedure had a negligible effect on tissue iodine concentrations.
5. Iodine exists in milk mostly (80-90%) as the iodide. Most analytical methods for the determination of residues included a step to convert all forms of iodine to the iodide, by wet or dry ashing. The iodide was then assayed by a spectrophotometric method with a limit of detection of 45 µg/l. A range of other analytical methods were also available, including methods based on gas chromatography, in which the residues were converted to iodobutane; and X-ray fluorescence, in which the milk was freeze-dried and compressed into tablets before analysis.
6. It was agreed that it would be inappropriate to elaborate MRLs for iodine and that iodine should therefore be included in Annex II of Council Regulation (EEC) 2377/90.