



## **COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS**

### **DIMETRIDAZOLE (1)**

#### **SUMMARY REPORT**

1. Dimetridazole is a veterinary medicinal product traditionally used for the prevention and treatment of histomoniasis in turkeys, the treatment of trichomoniasis in pigeons, genital trichomoniasis in cattle and the prevention and treatment of haemorrhagic enteritis in pigs.
2. The safety of nitroimidazole residues in food for human consumption has been assessed on the basis of the mutagenic and carcinogenic potential of these compounds.
3. Dimetridazole has shown mutagenic activity in all the bacterial tests carried out. However, it has been proved that this activity was linked to the enzyme activity of the nitroreductases of the bacteria used in the tests. Dimetridazole did not show any mutagenic activity in any of the numerous other tests carried out. It was inferred that dimetridazole was not a genotoxic compound.
4. The carcinogenesis studies carried out with dimetridazole have been found to be inadequate. The only complete study involved only one species of animal : the rat. It showed that dimetridazole produces an increase in the incidence of benign mammary tumors. This effect occurs in males at a dose of 2000 ppm and in females at doses of 2000 and 400 ppm. Doses of 10 and 100 ppm have no effect. However, a high level of spontaneous benign mammary tumors was observed in the female controls.
5. Previous studies of metabolism do not provide all the information necessary for making a proper qualitative and quantitative assessment of the metabolites produced by the breakdown of dimetridazole in treated animals.

The information available, although it has been obtained from previous studies carried out using insufficiently sensitive methods of analysis, nevertheless indicates considerable metabolisation of dimetridazole and rapid elimination of the metabolites produced.

6. On the basis of the information available, a provisional MRL of 10 µg/kg is proposed for extractable residues including dimetridazole and metabolites which retain the nitroimidazole structure.
7. Additional information is requested before 1 January 1994 regarding the following :
  - Mechanics of the carcinogenic effect observed;
  - Metabolic studies carried out on pigs and turkeys using appropriate analytical methods and providing information on the quantity of bound residues;
  - Proposed marker metabolite and the reasons for choosing it.