The European Agency for the Evaluation of Medicinal Products

EMEA/MRL/040/95

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

PHENOL

SUMMARY REPORT

1. Phenol is a preservative for pharmaceutical formulations. Clinically, it has limited use as a topical antiseptic at concentrations of up to 2%.

2. Phenol is active against vegetative Gram-positive and Gram-negative bacteria, some vegetative fungi and certain viruses.

3. Aqueous solutions of 0.2% to 1% are generally bacteriostatic while stronger solutions are bactericidal

4. The oral LD50 to rats is approximately 600 mg phenol/kg bodyweight. Phenol has equivocal mutagenicity potential, positive results have been observed with Salmonella TA 1538 in the presence of rat liver microsomal activation, but negative results were observed with four other strains. Phenol has been shown to induce genetic damage in human lymphocyte cultures in the presence of metabolic activators but was not mutagenic in Drosophila and in vivo mouse bone marrow test systems. It was concluded that there is no mutagenic risk associated with human exposure to phenol.

5. Teratogenic effects of phenol have not been observed in rats exposed to 100 to 1000 mg/l phenol for five generations and to 3000 to 5000 mg/l phenol for three generations.

   A study by the National Cancer Institute showed that phenol did not produce cancer in rats and mice when administered in the drinking water at levels up to 0.5%. Phenol is also not a cocarcinogen but did have a tumour promoting effect in albino mice given weekly skin applications of 20% phenol. Phenol does not appear to possess particularly strong sensitizing potential, although a 0.3% incidence of positive patch test reactions is reported.

6. Phenol is a normal constituent of animal and human tissues and occurs in the urine, faeces, saliva and sweat. Bacterial decomposition of proteins in the digestive tract give rise to the production of background levels of phenol. Medicinal preparations e.g. certain lozenges are a minor source of phenol in the human diet.

7. Phenol is metabolised principally by conjugation with glucuronic acid and sulphate and excreted in the urine. Approximately 77% of the administered sublethal dose was excreted in the urine of rabbits within 24 hours of dosing. In the rat, approximately 60% of the orally administered dose was metabolised by 4 hours after administration.

8. Because of its rapid metabolism, residues of phenol in animal produce will be insignificant and will not have an effect on human gut flora or starter cultures.

   Having considered the criteria laid down by the Committee for inclusion of substances into Annex II of the Council Regulation (EEC) No 2377/90 and that :

   - phenol is a natural component of the diet,

   - it is rapidly metabolised and eliminated.

   The Committee for Veterinary Medicinal Products concluded that maximum residue limits for tissues are not necessary to ensure consumer safety and recomments the inclusion of Phenol in Annex II of Council Regulation (EEC) No 2377/90. as indicated in the following table:

Pharmacological active substance(s)	Animal species	Other provisions
Phenol	All food producing species	

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Tel: (+44-171) 418 84 00 Fax: (+44-171) 418 84 16