COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

NITROFURANS

SUMMARY REPORT

1. Nitrofurazone and furazolidone were discussed at the 40th JECFA and extensive data files were available for both compounds. In essence, JECFA concluded that nitrofurazone was carcinogenic but was not genotoxic whereas furazolidone was carcinogenic and genotoxic. In addition, nitrofurazone was observed to cause a severe arthropathy in experimental animals and a NOEL had not been observed. JECFA had not recommended further studies.

2. Since then, the Companies concerned have indicated their willingness to conduct further studies to support applications in order to have nitrofurans inserted in Annex I of Council Regulation (EEC) No 2377/90.

3. Extensive toxicological studies are required on both nitrofurazone and furazolidone before a decision on Annex I entry could be made; obviously, the outcome of these studies would need to be favourable. However, the companies are planning toxicological studies only for furazolidone; analytical studies are suggested for nitrofurazone. These analytical studies would be completely inadequate to address the JECFA and CVMP WGSR concerns. On the other hand, the companies are planning some investigative work on furaltadone for which there is no JECFA appraisal and no toxicological database. Hence there would be a need to construct and submit this to the Commission and for the WGSR and the CVMP to examine this.

4. The current entry for nitrofurans in Annex III of Council Regulation 2377/90 expires in July 1993. The provisional period for nitrofurans can be extended *for a maximum of 2 years* and this may be done *only once*. This has certain implications. The companies suggest that, depending on the results of some mutagenicity studies, they may have to conduct carcinogenicity studies. These will take a minimum of 4 years to conduct and possibly longer. There is therefore no prospect of these being conducted before the final expiry date (and even then the results may not be advantageous to the companies' efforts).

5. All of these considerations lead to certain conclusions :

   I There will be insufficient data to support Annex I entries for nitrofurazone and nitrofurantoin by July 1993 and even at the end of a 2 year extension.

   II There is no database for furaltadone, no assessment by JECFA of the CVMP and in consequence these will not be available by July 1993 or at the end of the 2 year extension.

   III Consequently, the only feasible destination for these 3 nitrofurans is Annex IV.

   IV Furazolidone is a candidate for further work and this work could be beneficial for Annex I entry were the results found to be favourable. The companies should be allowed to concentrate on this drug but there should be a strict timetable for the production of reports and they should be told that it is impossible to conduct carcinogenicity studies in the time available. It should be borne in mind that an extension is of a maximum period of 2 years and is not renewable for any further periods.

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V The current entry in Annex III should be changed from "nitrofurans" to "furazolidone", the provisional MRL retained, and the expiry date set at July 1995. The following data must be provided :

- mutagenicity data on the metabolite by March 1994;
- the results of the 3 months study by July 1994;
- any other data ro reassure the WGSR that the residues of furazolidone are not genotoxic and carcinogenic, by February 1995.

6. Unless good reasons are provided as to why delays have occurred, the Annex III entry for furazolidone would terminate and the drug would be placed in Annex IV. It should be noted that there will be insufficient time for further studies.

7. Other nitrofurans which may exist will not have Annex I, II or III entry and their use in food producing animals will eventually cease. Assuming Annex III entry for furazolidone, they will be covered by the term nitrofurans and the Annex IV entry could read "nitrofurans - except furazolidone, (see Annex III)".