COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE

SODIUM NITRITE

SUMMARY REPORT

1. Sodium nitrite, CAS number: [7632-00-0], is an inorganic salt used as an antimicrobial agent, preservative and colour fixative. It is used in processed meats to slow or prevent growth of bacterial pathogens, in particular *Clostridium botulinum*. Sodium nitrite is a food additive (E250) approved in the European Union as a preservative for use in non-heat-treated, cured, dried meat products, canned meat products and foie gras with a maximum residual amount of 100 mg/kg (Part C of Annex III of Council Directive No 95/2/EC). In veterinary medicine the substance is intended for use as a disinfectant by topical application to the teats of dairy cows after milking in order to prevent mastitis. Considering the nature of the substance and its use as food additive the Committee for Medicinal Products for Veterinary Use agreed to accept an abridged MRL application consisting of evaluations of the safety data and a residue file.

2. No pharmacology, pharmacokinetics or toxicity studies were provided. A considerable number of studies (on absorption, distribution, biotransformation, excretion, repeated-dose toxicity, reproductive toxicity, genotoxicity and studies in humans) have been reviewed by various authorities on food safety such as the EU Scientific Committee for Food (SCF), the Joint WHO/FAO Expert Committee on Food Additives (JECFA) and the WHO; reports and summaries of those evaluations were made available.

The EU SCF established an ADI of 0-0.06 mg/kg bw, expressed as nitrite ion, based on the NOEL of 10 mg/kg bw/day potassium nitrite (equivalent to 5.4 mg/kg bw/day nitrite ion) for hypertrophy of the adrenal zona glomerulosa in the rat and an uncertainty factor of 100. JECFA originally established an ADI on the same basis, but following a review of the decision, established a slightly higher ADI of 0-0.07 mg/kg bw, expressed as nitrite ion, on the basis of the NOEL of 6.7 mg/kg bw/day for effects on the heart and lung in a 2-year study in rats and an uncertainty factor of 100.

3. Nitrite occurs naturally in the environment and is produced endogenously. It is a normal component of the diet of humans, both as a naturally occurring ingredient and following its use as food additive.

4. An intake assessment for nitrite (and nitrate) was performed and published by WHO (WHO Food Additive Series 50). Based on data from the United Kingdom (total diet studies) an intake of 70% of the ADI for nitrite (established by JECFA) was estimated, with major contributions from vegetables and beverages. A less representative study, performed in the Netherlands (short duration, low number of respondents), showed that in some cases the intake of nitrite may exceed the ADI. In summary, the results of the intake of nitrite from all dietary sources showed mean consumption below the ADI, although some consumers at high percentiles exceeded the ADI.

5. Because the original study reports were not provided, the CVMP could not establish an ADI. However the CVMP agreed with the conclusions of the evaluations carried out by the EU Scientific Committee for Food and the Joint WHO/Expert Committee on Food Additives, and in particular, the toxicological ADI of 0.07 mg/kg bw for nitrite ion (established by JECFA) which would correspond to approximately 0.09 mg/kg bw for sodium nitrite.
6. Residues of nitrite in milk from cows treated with the formulated product tended to be below the detection limit of 0.1 mg/l for the autoanalyzer colorimetric method. It was concluded that the amount of nitrite present in milk in practical and worst-case situations, would be negligible (also in comparison to some reported natural background levels). For this reason the potential effects of sodium nitrite on the microorganisms used for industrial food processing did not require further clarification.

7. Residues in milk at the limit of detection may be compared with the ADI of 0.07 mg/kg bw established by the Joint WHO/FAO Expert Committee on Food Additives, leading to the conclusion that the use of sodium nitrite as a teat dip, even on the basis of worst-case calculations, would represent a minor contribution to the total intake of European consumers and would not present a health risk to humans by consumption of milk from treated cows.

Conclusions and recommendation

Having considered the criteria laid down by the Committee for Medicinal Products for Veterinary Use for the inclusion of substances in Annex II of Council Regulation (EEC) No 2377/90 and in particular that:

- an ADI of 0.07 mg/kg bw for the nitrite ion was established by the Joint WHO/FAO Expert Committee on Food Additives, and this ADI was considerate appropriate by the CVMP,
- sodium nitrite is of endogenous origin and is a normal ingredient of the diet in humans (both as a naturally occurring component and following its use as a food additive),
- residues of nitrite in milk following topical application to the teats of cattle in practical and worst-case situations, are negligible;

the Committee for Medicinal Products for Veterinary Use concludes that there is no need to establish an MRL for sodium nitrite and recommends its inclusion in Annex II of Council Regulation (EEC) No 2377/90 in accordance with the following table:

<table>
<thead>
<tr>
<th>Pharmacologically active substance(s)</th>
<th>Target species</th>
<th>Other provisions</th>
</tr>
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<tbody>
<tr>
<td>Sodium nitrite</td>
<td>Bovine</td>
<td>For topical use only</td>
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