The European Agency for the Evaluation of Medicinal Products
Veterinary Medicines Evaluation Unit

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COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

POTASSIUM NITRATE

SUMMARY REPORT

1. Potassium nitrate (CAS 7757-79-1) is used as a diuretic in pigs, cattle and horses. It is administered by the oral route at doses up to 30 g per animal per day. The equivalent dose in mg/kg bw per day was not provided but can be estimated as approximately 167 mg/kg bw for a pig of 180 kg bodyweight or 60 mg/kg bw for horses and cattle of 500 kg body weight.

2. The potassium cation is an essential electrolyte that is important for the maintenance of intracellular osmotic pressure and for the maintenance of cell membrane potentials, particularly in electrically excitable tissues. It is a normal component of the diet and is particularly abundant in fruit and vegetables. The recommended daily intake varies from 350-1275 mg in children to 1875 and 5625 mg in adults. In the United Kingdom, the reference nutrient intake (RNI) is 3.5 g/day for adults.

3. The potassium ion itself possesses almost no toxicity; any toxicity of the salts is associated with the anion. Potassium nitrate is rapidly absorbed from the upper gastrointestinal tract of mammals and is excreted mostly unchanged. However a small percentage of the ingested dose is reduced by the microbial action of the gut to nitrite. Nitrites convert the haemoglobin in red blood cells into methaemoglobin.

4. Potassium nitrate was shown to be of low to moderate acute toxicity with acute oral LD_{50} values of 3750 and 1901 mg/kg bw in the rat and rabbit respectively. Repeated dose toxicity was investigated in rats given oral doses in the range 10-100 mg/kg bw per day for 4 months; bronchopneumonia, local haemorrhages and other circulatory disorders were observed in treated animals. Cattle were given oral doses of 345-450 mg/kg bw per day (expressed as nitrate) for several months; blood phosphate and magnesium were decreased and blood calcium, urinary magnesium and urea and milk urea were increased. It was not possible to draw any conclusions regarding NOELs from the brief summaries which were provided of the repeated-dose toxicity studies. Published papers reported that potassium nitrate was not teratogenic in the rat, guinea pig, pig, sheep or cow. Potassium nitrate gave negative results in an *in vitro* assay for gene mutation in *Salmonella typhimurium* TA98, TA100, TA1535, TA1537 and TA1538, in an *in vitro* rec. assay in *B. subtilis* and in an *in vivo* rat dominant lethal assay.

5. Nitrates are present at low concentrations as natural constituents of foods. Nitrates are also present in drinking water, chiefly as a consequence of fertiliser run-off from agricultural land. The Directive on Drinking Water Quality (80/778/EEC) stipulates a maximum admissible concentration of 50 mg/l for nitrates in drinking water.

6. Nitrates are also deliberately added to foods as preservatives, especially for cured meat and fish. Potassium nitrate is listed as a food additive (E 252) in part C of Annex III to Council Directive 95/2/EC. The residual amount, expressed as $NaNO_3$, should not exceed 250 mg/kg in cured and canned meat products, 50 mg/kg in cheese and 200 mg/kg in pickled herring and sprat. This group of preservatives has been specifically excluded from the general entry into Annex II of Council Regulation (EEC) 2377/90 for substances with an E-number.

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7. The Joint WHO/FAO Joint Expert Committee on Food Additives (JECFA) calculated a group Acceptable Daily Intake (ADI) of 5 mg/kg bw per day for sodium and potassium nitrate. In 1990, the EC Scientific Committee for Food calculated an ADI for the nitrate ion of 3.65 mg/kg bw (i.e. 219 mg for a 60 kg person). UK Government-sponsored surveys showed that dietary intake from all sources is around 53 mg/person/day in the United Kingdom.

8. No information was provided concerning the pharmacokinetics or residues depletion following administration of potassium nitrate to the target species. However, as potassium nitrate is administered to food producing animals by the oral route, it will be impossible to distinguish residues of potassium nitrate resulting from the treatment of animals and residues resulting from normal intake in the feed and drinking water.

Conclusions and recommendation:

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

- is a normal constituent of food and drinking water of humans and animals;
- is only used for treatment of individual animals;
- the animals are unlikely to be sent for slaughter during or immediately after treatment;

the Committee concludes that there is no need to establish an MRL for potassium nitrate and recommends its inclusion into Annex II of Council Regulation (EEC) No 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Animal species	Other provisions
Potassium nitrate	All food producing animals	