Divergent position on a revised CVMP opinion on an Article 35 referral of Directive 2001/82/EC for

All long acting formulations for injection containing barium selenate for all food producing species (EMEA/V/A/077)

This referral under Article 35 of Directive 2001/82/EC was submitted due to concerns that long-acting formulations for injection containing barium selenate for all food producing species could pose a significant threat to human health. Having considered all the information presented, it is the opinion of the undersigned that a real risk to consumer safety has not been substantiated.

The following points, in particular, were noted:

- The CVMP assessed barium selenate previously in the context of an application for establishment of maximum residue limits under Regulation (EEC) No 2377/90. Following the CVMP recommendation (EMEA/MRL/580/99-FINAL, April 1999), barium selenate was included in Annex II of Regulation (EEC) No 2377/90 for bovine and ovine species, and, subsequent to the implementation of Regulation (EC) 470/2009 replacing Regulation 2377/90, is currently included in table 1 of the Annex to Regulation (EU) No 37/2010 and categorised as 'no MRL required'; that is, the substance is not considered to pose a safety risk to consumers under normal conditions of use.

- Limited new information to substantiate the risk to the consumer has been provided. CVMP, when adopting the MRL Opinion for barium selenate, was aware that ingestion of selenium is potentially toxic in man and that residues of barium selenate persist at the injection site with the potential for exposure to relatively large quantities from a single injection site. Notwithstanding, CVMP agreed that barium selenate be categorised as 'no MRL required' and, in respect of the injection site specifically, concluded "*Considering the very low oral bioavailability of barium selenate, the ingestion of residues of selenium and barium from the injection site is unlikely to present a health risk for the consumer....*".

  Regarding the extent of availability, in the revised referral opinion it is stated: "*Data has been provided to estimate the oral bioavailability of selenium following ingestion of residues of barium selenate. Based on data available at the time the decision on the MRL status was taken it was assumed that the available fraction would be very low. CVMP has now been presented with data from an in vitro study simulating conditions in the human gastrointestinal tract. This study indicates that at least 5 % to 10 % of ingested selenium from barium selenate is bioavailable when present in a normal food matrix. This figure is much higher than what was assumed by the time the MRL decision was taken.*" Further, it is stated that these *in vitro* data are "*supported by an in vivo study in sheep (Archer and Judson, 1994). This study showed that orally ingested barium selenate (doses of 100 mg or 250 mg per animal similar to those present at injection sites) was absorbed/bioavailable in the gastrointestinal tract.*" On this issue, the undersigned note that

  - from the MRL Summary Report, it is not possible to know what CVMP meant when it described bioavailability as 'very low';
  - the *in vivo* sheep data predate the adoption of the CVMP MRL Opinion for barium selenate (that is, are expected to have been available to CVMP at that time).

- Any potential risk to the consumer from the use of veterinary medicinal products containing barium selenate in cattle relates to the potential for ingestion of injection site residues. While this might represent a potential acute risk, it is clear that ingestion of injection site tissue is likely to be an infrequent event. Indeed, the products in question are for administration by the subcutaneous route and, in this case, it is not an unreasonable expectation that any residue remaining at the site of injection will be removed during the process of stripping the hide and trimming of the carcass.
- Barium selenate has been included as active substance in veterinary medicinal products authorised in the Community for more than 20 years. During that time, regulatory authorities have not been notified of any product-specific concerns relating to consumer safety (either documented cases of residues being indentified at slaughter or reports of adverse effects in humans caused by residues of such products in tissues of treated animals).

As acknowledged in the CVMP assessment report, long-acting formulations containing barium selenate fulfil a valuable role in the treatment and prevention of disease related to selenium deficiency. Although alternative products exist, their differing formulations prevent them from being suitable for all cases requiring treatment. Non-availability of the long acting formulation could therefore have implications for animal welfare.

Taking account of the potential benefits of barium selenate containing products and the absence of a real, substantiated consumer safety risk, the undersigned hold the opinion that the benefit-risk assessment for the long-acting formulations for injection containing barium selenate for all food producing species remains positive.

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