



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

SULFONAMIDES (1)

SUMMARY REPORT

1. The sulfonamides play an important role as effective chemotherapeutics of bacterial and protozoal diseases in veterinary medicine. They are frequently administered in combination with dihydrofolate reductase inhibitors of the group of diamino-pyrimidines. In food producing animals, residues deplete with widely variable velocity depending on many factors such as the nature of the compound, its formulation and route of administration, the treated animal species, genotypes etc.
2. The sulfonamide group includes a large number of very old compounds and adequate toxicological data meeting modern requirements for testing, together with carcinogenicity studies and mutagenicity data, are not available for the majority of these compounds.
3. From the overall picture, however, it is clear that the number of effects which are relevant for the assessment of low level exposure to residues are limited. Potential effects, which are not always related to dose, and which may be limited to predisposed humans, include allergic reactions.
4. Several Member States had previously adopted tolerances of 100 µg/kg, based on old data, as had certain third countries, and this tolerance was considered to provide a sufficient margin of safety.
5. In the case of sulfamethazine, however, additional studies have been undertaken, including recent carcinogenicity studies. Sulfamethazine has recently been evaluated by the 34th Joint WHO/FAO Expert Committee on Food Additives which concluded that the thyroid tumours in rodents were most likely due to a hormonal disturbance and that humans exposed to sulfamethazine below a threshold level would not be at carcinogenic risk. The JEFCA also established a maximum residue limit of 100 µg/kg for sulfamethazine in meat.
6. In these circumstances, the Committee for Veterinary Medicinal Products considers that an MRL of 100 µg/kg of the original drug substance should be applied to all compounds of the sulfonamide group.

Considering :

- Σ the available toxicological data, which suggest that the metabolites of the sulfanomides are within the same range of toxicity as the parent compounds;
- Σ the available pharmacokinetic studies;
- Σ the need to provide for simple analytical detection methods whenever possible;

the Committee does not consider it necessary to recommend the inclusion of any of the metabolites within this tolerance at present.

7. Residues of sulfonamides can be routinely monitored at or below the above required limits using, for example, High Performance Liquid Chromatography.
Reliable confirmatory or reference methods should be based on known procedures using gas chromatography/mass spectrometry.
8. In addition, the Committee recommends that the MRL of 100 µg/kg should be applied on a provisional basis to milk, pending additional information on residue depletion and analytical methods.