The European Agency for the Evaluation of Medicinal Products

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CONCEPT PAPER ON THE DEVELOPMENT OF A CVMP NOTE FOR GUIDANCE ON THE QUALITY ASPECTS OF PHARMACEUTICAL VETERINARY MEDICINES ADMINISTERED VIA DRINKING WATER

Introduction

A number of drugs, especially antimicrobial agents, are administered to animals via their drinking water. This route of administration is most commonly used in treating poultry and pigs housed in large production units, although it is also used in other species, such as cattle.

Scope

The types of dosage forms which are administered in drinking water include powders, solutions, suspensions and emulsions. The proposed guideline would cover all of these different dosage form types.

Pharmaceutical and immunological products are administered in drinking water. The proposed guideline would only cover pharmaceutical products due to the differences in quality data requirements between these product groups.

Discussion

There already exists a CVMP guideline on "Additional Quality Requirements for Products Intended for Incorporation into Animal Feedingstuffs (Medicated Premixes)". This guideline does not cover medicines administered in drinking water.

Medicines administered in drinking water present a number of different and sometimes difficult challenges in terms of development, in comparison with other types of medicines. The following are examples of the problems:

- The pH of the medicated drinking water can be influenced by the excipients in the formulation which in turn can impact upon bioavailability as well as stability.
- Ingredients should be freely soluble or of fine particle size, otherwise water supply systems could be blocked.
- The solubility of the active substance, over a range of temperatures and in different water qualities, must be understood so that suitable recommendations can be made. For example, it should be ensured that the addition of concentrated solutions to the header tank of automatic water supply systems does not cause precipitation in the water supply lines.
- In the case of powders, a reasonable dissolution time at relevant temperatures, must be ensured. The control of parameters such as particle size and density may be necessary.

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- Measuring devices to ensure that the correct dose is added to the water are often required. Their suitability must be proven. In the case of powders the control of bulk density is usually required where such measures are supplied to ensure accuracy of dosing.
- Stability in drinking water has to be demonstrated. Unusual aspects which have to be considered when designing such a study include: water quality (pH, temperature, hardness, salts), contact with metals (e.g., buckets and pipework), exposure to light.

There is currently no EU guidance available to industry or assessors on the quality requirements for veterinary medicines administered via drinking water. National Authorities are therefore likely to have developed internal guidelines which can result in differing data requirements and cause problems during decentralised procedures for such products.

Conclusion

The Quality Working Party consider that it would be helpful to develop a CVMP guideline which considers all aspects of the supporting quality data required for pharmaceutical veterinary medicines which are administered in drinking water.