I. INTRODUCTION

Baycox 50mg/ml oral suspension for Piglets, Calves and Lambs is authorised for use in pig, calves and sheep. The product is indicated:

- for the prevention of clinical signs of coccidiosis in neonatal piglets on farms with a confirmed history of coccidiosis caused by Isospora suis,
- for the prevention of clinical signs of coccidiosis and reduction of coccidia shedding in housed calves replacing cows producing milk for human consumption (dairy cows) on farms with a confirmed history of coccidiosis caused by *Eimeria bovis* or *Eimeria zuernii* and
- for the prevention of clinical signs of coccidiosis and reduction of coccidia shedding in lambs on farms with a confirmed history of coccidiosis caused by *Eimeria crandallis* and *Eimeria ovinoidalis*

The product is an oral suspension containing Toltrazuril 50 mg/ml as an active substance. This product is an extension from the product Baycox 50 mg/ml Suspension in which three currently authorised products were rolled into one. All three products were exactly the same formulation, but were indicated for different species. Since all the data have already been assessed and approved, and these products are already on the market, no additional data have been submitted.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released on the market. It has been shown that the product can be safely used in the target species. The product is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.

II. QUALITY ASPECTS

Product Development and Composition

The product contains the active substance toltrazuril which is highly insoluble in water. Excipients include sodium docusate, simethicone emulsion, sodium benzoate (E211), sodium propionate (E281), bentonite, xanthan gum, citric acid anhydrous, propylene glycol and purified water. The choice of the formulation and presence of preservatives are justified.

The product is presented in 100 ml, 250 ml or 1000 ml high density polyethylene bottles with a blue polypropylene screw cap for the 100 ml bottle, and a green one for the 250 ml bottle and 1000 ml bottle. Declarations have been provided indicating that the materials comply with European Pharmacopoeia requirements in respect of suitability for food and pharmaceutical use.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

Active Substance

No pharmacopoeial specification is available for toltrazuril, however the applicant provided an in-house specification. The batch analysis data on three batches were provided along with certificates of analysis for three further batches. All showed compliance with the specification and a consistent high degree of purity.

Other Substances

All excipients with the exception of simethicone emulsion are described in the European Pharmacopoeia. Simethicone emulsion is the subject of a monograph of the USP-NF. The applicant also provided certificates of analysis for each component.

Packaging Materials

The 100, 250 and 1000 ml containers for the product are fabricated in high density polyethylene certified suitable under European regulations for food and pharmaceutical use. A specimen certificate of analysis showing compliance has been presented for each component.

Manufacture of the Finished Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The applicant has provided details of the stages of and method of manufacture. In process controls have also been described. Process validation data on the product have been presented in accordance with the relevant European guidelines.

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

Finished Product Quality Control

The tests performed during production are described and the results of 2 consecutive runs, conforming to the specifications, are provided.

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product. Satisfactory validation data for the analytical methods have been provided.

Stability of the Product

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions. A shelf life of five years was justified, without restriction on the temperature of storage, and without a requirement for protection from light. Following withdrawal of the first dose, the product should be used within three months.

CONCLUSIONS ON QUALITY

The formulation of the product was satisfactory and the controls proposed are adequate and appropriate. Good physical and chemical stability has been demonstrated for the product in intact and broached containers. The shelf life and in-use shelf life were justified.

III. SAFETY ASPECTS

Pharmacology

As this product is an extension in which three currently authorised products were rolled into one, all the data have already been assessed and approved, and these products are already on the market, no additional data have been submitted.

User Safety

Warnings and precautions as listed on the SPC and product literature are adequate to ensure safety to users of the product. The following user warnings are listed on the SPC and product literature:

- Wash any splashes from skin or eyes immediately with water.

Residues

The applicant made reference to the residues data that were submitted previously for all three products. The following withdrawal periods are listed on the SPC and product literature:

Piglets
Meat and offal: 77 days
Calves
Meat and offal: 63 days
Not permitted for use in lactating animals producing milk for human consumption.
Lambs
Meat and offal: 42 days
Not permitted for use in lactating sheep producing milk for human consumption

Environmental Safety

Reference is made to the environmental risk assessments submitted previously for all three products. The following phrases relating to environmental safety are listed on the SPC:

4.3 Contraindications

For environmental reasons:
Do not use in calves weighing more than 80 kg bodyweight.
Do not use in fattening units such as veal or beef calves
For more details see sections 4.5, other precautions and section 5.3, environmental properties.

4.5 Other Precautions

The major metabolite of toltrazuril, toltrazuril sulfone (ponazuril), has been shown to be both persistent (half-life >1 year) and mobile in soil and to be toxic to plants.

For environmental reasons:

In order to prevent any adverse effects on plants and possible contamination of groundwater manure from treated calves must not be spread onto land without dilution with manure from untreated cows. Manure from treated calves must be diluted with at least 3 times the weight of manure from mature cows before it can be spread onto land.

Lambs kept throughout the whole life span indoors under an intensive rearing system must not be treated beyond the age of 6 weeks or body weight of more than 20 kg at treatment. Manure from these animals should only be applied to the same piece of land every third year.

CONCLUSIONS ON SAFETY AND RESIDUES

Conclusions on User Safety
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Conclusions on Consumer Safety
The meat withdrawal period for piglets, calves and lambs has been justified and is the same as the reference products.

Conclusions on Environmental Safety
Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

IV. CLINICAL ASPECTS

Clinical Pharmacology
As this formulation has already been approved for all three species, the data on this section is not required.

Tolerance in the Target Species
The formulation has previously been demonstrated to have adequate target animal safety in piglets, calves and lambs. Therefore, the data for this section is not required.

Resistance
As this formulation has already been approved for all three species, the data on this section has not been submitted.

Clinical Efficacy

The applicant has previously demonstrated the efficacy of the product in piglets, calves and lambs. Therefore, the data for this section is not required.

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CONCLUSIONS ON CLINICAL ASPECTS

The efficacy claims and target species safety for this product are equivalent to those of the reference products.

PART V. OVERALL CONCLUSION ON THE PRODUCT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the benefit-risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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