Veterinary Medicines Directorate

**United Kingdom**
**Veterinary Medicines Directorate**
**Woodham Lane**
**New Haw**
**Addlestone**
**Surrey KT15 3LS**

**NATIONAL PROCEDURE**

# PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

## Bovilis Cryptium Emulsion for Injection for Cattle

**Date Created: November 2024**

# MODULE 1

## PRODUCT SUMMARY

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|---|---|
| Name, strength and pharmaceutical form | Bovilis Cryptium Emulsion for Injection for Cattle |
| Applicant | MSD Animal Health UK Limited, Walton Manor, Walton, Milton Keynes, Buckinghamshire, MK7 7AJ |
| Active substance(s) | Inactivated *Cryptosporidium parvum* glycoprotein (Gp40) |
| ATC Vetcode | QI02AO02 |
| Target species | Cattle (pregnant heifers and cows) |
| Indication for use | For active immunisation of pregnant heifers and cows to raise antibodies in their colostrum against Gp40 of *Cryptosporidium parvum*, intended for passive immunisation of calves to reduce clinical signs (i.e., diarrhoea) caused by *C. parvum*.<br><br>Newborn calves:<br>Onset of immunity: Passive immunity commences from the start of colostrum feeding.<br>Duration of immunity: In calves that receive colostrum and transition milk as indicated and which were challenged at birth, passive immunity has been demonstrated until 2 weeks of age. |

# MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

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

# MODULE 3

## PUBLIC ASSESSMENT REPORT

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|---|---|
| Legal basis of original application | Full application in accordance with Article 8 of VMRs 2013 (Schedule 1, Part 1) as amended. |
| Date of conclusion of the procedure | 06/08/2024 |

## I. SCIENTIFIC OVERVIEW

This is a full application for Bovilis Cryptium Emulsion for Injection for Cattle submitted in accordance with Article 8 of Veterinary Medicine Regulations 2013 as amended.

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, any reactions observed are indicated in the SPC.[1] 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. The efficacy [2] of the product was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

## II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

### *II.A. Composition*

The product contains *Cryptosporidium parvum* Gp40 and the excipients montanide ISA70VG, aluminium hydroxide, HEPES, sodium chloride, thiomersal and water for injections.

The container/closure system consists of Type I hydrolytic glass vials or PET vials closed with bromobutyl or chlorobutyl rubber stoppers and sealed aluminium caps. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the adjuvant, vaccine strain, inactivating agent and presence of preservative are justified.

The inactivation process and the detection limit of the control of inactivation are correctly validated.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

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

### *II.B. Method of Preparation of the Product*

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

### *II.C. Control of Starting Materials*

The active substance is *Cryptosporidium parvum* Gp40, a novel active substance. The active substance is manufactured in accordance with the principles of good manufacturing practice.

Starting materials of non-biological origin used in production comply with Ph. Eur. All excipients comply with the relevant monographs or CoAs are provided.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines and are appropriately screened for the absence of extraneous agents according to the Ph. Eur. Guidelines; any deviation was adequately justified.

The master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline.

The packaging materials comply with the relevant monographs.

### *II.C.4. Substances of Biological Origin*

Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

### *II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process*

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

### *II.E. Control Tests on the Finished Product*

The tests performed on the final product conform to the relevant requirements; any deviation from these requirements is justified.
The demonstration of the batch to batch consistency is based on the results of 3 batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

### *II.F. Stability*

The active substance is fully tested to ensure compliance with its specification immediately prior to its use in manufacture of the product.

Stability data on the finished product have been provided in accordance with applicable regulatory guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

The in-use shelf-life of the broached vaccine is supported by the data provided.

### *G. Other Information*

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 28 days.
Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Protect from light.
After broaching and first use, store upright and refrigerated (2 °C – 8 °C) until the next use.

## III. SAFETY ASSESSMENT

### *Laboratory trials*

The safety of the administration of one dose, and the repeated administration of one dose in the target animal is demonstrated in laboratory studies. The investigation was performed according to the recommendations of VMRs 2013 as amended and the relevant guidelines.

Effects on reproductive performance were examined and it was determined that the administration of the vaccine via the subcutaneous route to pregnant heifers and cows is supported. A slight increase in temperature was noted.

There are no data suggesting that this product might adversely affect the immune system of the vaccinated animal or its progeny therefore a specific study was not carried out.

The vaccine is inactivated and thus the specific tests to be performed for live vaccines are not applicable.

The adjuvant and excipients used are included in the table of allowed substances with the entry ‘no MRL required’ or ‘out-of-scope’ list. Based on this information, no withdrawal period is proposed.

The interaction of the vaccine with Bovilis Rotavec Corona was studied. Safety and efficacy data are available which demonstrate that this vaccine can be administered on the same day but not mixed with Bovilis Rotavec Corona. The vaccines should be given at different sites. The product literature of Bovilis Rotavec Corona should be consulted before administration. Different routes of administration should be respected. No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product

except the product mentioned above. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case-by-case basis.

### *Field studies*

The safety of the administration of the recommended two-dose schedule on reproductive performance was evaluated in a GCP field safety study and two GCP combined safety and efficacy studies.

Control groups were administered saline and were included in each study but were not blinded. The vaccine was administered on two occasions, 4 to 5 weeks apart in the third trimester of pregnancy at least three weeks before calving.

The GCP safety study was a pivotal field safety study where a non-mixed intramuscular dose of Bovilis Rotavec Corona was administered at the same time as the first trial vaccine dose. Local reactions were recorded as adverse uncommon events.

### *Ecotoxicity*

The applicant provided a Phase 1 environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the product should avoid direct or indirect contact with the environment. No warnings regarding protection of the environment are therefore required.

## IV. CLINICAL ASSESSMENT (EFFICACY)

### *Clinical Studies*

### *Laboratory Trials*

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements.

A challenge model was conducted and six laboratory studies were provided. Four of these studies investigated efficacy in pregnant heifers and cows vaccinated accordingly to the primary dosing schedule. The other two studies investigated efficacy in dairy and beef calves fed colostrum from vaccinated cows and included a challenge phase.

The challenge strain was adequately described. The route of infection was oral, mimicking natural infection.

### *Onset of Immunity*

Five onset of immunity studies in pregnant heifers and cows or in calves were presented to support the claim of active immunisation to raise antibodies in their colostrum or to support the claim of passive protection from the start of colostrum feeding. These studies examined the antibody response in serum and

colostrum following the primary vaccination schedule, in the alternative injection sites and in the associated non-mixed use with Bovilis Rotavec Corona.

### *Duration of Immunity*

The duration of passive immunisation has been shown under field conditons. However, the proposed duration of immunity in calves was stated to be until they develop active immunity. Bibliographic data was provided.

### *Field Trials*

Two field studies were conducted, one in a dairy herd and one in a beef herd. Vaccination of the pregnant cows inducted colostrum antibody titres and calf serum antibody titres, of the same magnitude as seen in the laboratory studies.

## V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

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 of the product is favourable.

# MODULE 4

## 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.

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