I. INTRODUCTION

Equip $EHV_{1,4}$ is an activated, carbomer adjuvanted, liquid vaccine intended for use in horses. It is indicated for the active immunisation of horses to reduce clinical signs due to infection with Equine Herpesvirus (EHV) 1 and 4 and to reduce abortion caused by EHV-1 infection. The product is administered intramuscularly.

A single dose should be administered from five months of age followed by a second injection after an interval of four to six weeks. In the event of increased infection risk, for example when a foal had consumed insufficient colostrum or there is a risk of early exposure to field infections with EHV-1 or EHV-4, earlier vaccination may be given. In these circumstances, the foal should receive a single dose from 3 months of age followed by the above mentioned full primary vaccination course. Following completion of the primary course, a single booster dose should be administered every 6 months. To reduce abortion due to EHV-1 infection, pregnant mares should be vaccinated during the fifth, seventh and ninth month of pregnancy with a single 1.5 ml dose on each occasion.

This application was an extension application submitted in accordance with Annex II of commission regulation (EC) No. 1084/2003. A national Marketing Authorisation was issued in 1994.The EHV-1 antigen contained in Equip $EHV_{1,4}$ is produced on rabbit cell line RK-13, which is derived from rabbit kidney in the United Kingdom. The original Solvay/FDAH RK-13 material was obtained from the University of Melbourne and was used for the preparation of the RK-13 MCS and the EHV-1 MSV. The RK-13 MCS and EHV-1 MSV tested positive for Bovine Viral Diarrhoea Virus (BVDV) when they were tested initially during the seed testing. However, during the original assessment in 1994 these seeds were approved for the production of Equip $EHV_{1,4}$ because the vaccine is inactivated with BEI, no BVDV sequences could be found in the finished product, nor in the animals administered with the vaccine, and there were no viral safety concerns associated with such contamination. However, such contamination is not considered to be an acceptable situation. In order to overcome the contamination problem, while avoiding the need for a completely new product development, the applicant replaced the contaminated RK-13 cell stocks with BVDV-free cell stocks in order to fully comply with current legislation. The applicant has submitted a complete revised Part II of the dossier.

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 and the slight reactions observed are indicated in the SPC. The product is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy of the product was demonstrated according to the claims made in the SPC and the overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

Product Development and Composition

The product contains inactivated EHV_1, strain 438/77, not less than $10^{7.3}$ $TCID_{50}$[1] and inactivated EHV_4, strain 405/76, not less than $10^{7.3}$ $TCID_{50}$ as, as vaccine antigens. The adjuvant is carbopol 934P and the excipients are disodium hydrogen phosphate, sodium dihydrogen phosphate and water for injection.

[1] Tissue culture infective dose

The development of the product is adequately described in accordance with the relevant European guidelines.

Vaccine Antigen
The vaccine antigens are inactivated EHV_1, strain 438/77 and EHV_4, strain 405/76. Satisfactory details of the isolation, passaging and testing were provided.

Other Substances
Starting materials of non-biological origin used in production comply with the in-house specifications. Biological starting materials used were appropriately screened for the absence of extraneous agents. The master and working seeds of the viral antigen were produced as described in the relevant guideline.

Packaging Materials
The product is packaged in 1.5 ml Type 1 glass vials with chlorobutyl rubber stopper and sealed with colour coded aluminium caps. The certificates demonstrating compliance with Ph. Eur. for the Type I glass vials and rubber closures were provided. The packaging material complies with the requirements on the relevant Ph. Eur. monographs.

Manufacture of the Finished Product
The vaccine is manufactured according to Good Manufacturing Practice, using defined and reproducible procedures and including controls to verify the correct functioning of the system. The manufacturing process is fairly standard for this type of vaccine using cells grown in roller bottles, infection of monolayers and harvest of infected cultures when cytopathic effects have occurred. The description of the production method is sufficient, which together with all the validation tests, ensures that the product is sterile, and the antigen is safe and efficacious.

Finished Product Quality Control
The tests performed on the final product conform to the relevant requirements; any deviation from these requirements was justified.
Demonstration of batch-to-batch consistency was based on the results of three batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

Stability of the Product
Vaccine Antigen
Satisfactory stability data for storage of the bulk antigen were provided.

Finished Product
Based on the information provided, a shelf life of 2 years was approved when stored and transported in its original unopened undamaged packing in the dark at +2°C-+8°C.

CONCLUSIONS ON QUALITY
The quality of the vaccine produced with the BVDV-free RK-13 cell line is comparable to the original vaccine. The following storage precautions are included in the SPC:
The vaccine has to be stored and transported in its original unopened undamaged packing in the dark at +2°C-+8°C.
Exposure to heat and/or direct sunlight has to be avoided. Do not freeze

III. SAFETY ASPECTS

The safety of the vaccine produced with the BVDV-free RK-13 cell line is similar to the original vaccine produced with contaminated RK-13 cell stocks. The applicant has referred to the batch safety data and provided raw data for the respective safety tests indicating that body temperature of vaccinated horses remained normal after vaccination and that no local or systemic reactions were observed after vaccination. Considering animal welfare further specific safety studies are not required. This is considered acceptable.

CONCLUSIONS ON SAFETY AND RESIDUES

Conclusions on User Safety
The applicant has not submitted any new data. This is considered acceptable.

Conclusions on Consumer Safety
The applicant has not submitted any new data. This is considered acceptable.

Conclusions on Environmental Safety
The applicant has not submitted any new data. This is considered acceptable.

IV. EFFICACY ASPECTS

Laboratory Tests
The applicant conducted an efficacy study with vaccine produced with the BVDV-free RK-13 cell line for respiratory symptoms. A suitable number of animals were divided into different treatment groups. The challenge with the EHV-1 strain took place at day 42. The virus was used at a dilution of $10^{2.0}$ to give a pseudo-Master concentration of $10^{5.0}$ $TCID_{50}$/ml. Observations post-challenge were performed for 14 days (until day 56). Nasal swabs were collected daily post-challenge. The study concluded that the product reduces clinical signs caused by EHV1 and shedding of EHV1.

The applicant has not submitted any study with regards to abortion in pregnant mares with vaccine produced with the BVDV-free RK-13 cell line. This is considered acceptable.

Field Trials
No field trials were performed with vaccine produced with BVDV-free RK-13 cell line. This is considered acceptable.

CONCLUSIONS ON EFFICACY ASPECTS
The efficacy of the vaccine produced with the BVDV-free RK-13 cell line is similar to the original vaccine produced. An efficacy study with regards to the respiratory symptoms with vaccine produced with the BVDV-free RK-13 cell line was performed. No study was performed with regards to abortion in pregnant mares with vaccine produced with the BVDV-free RK-13 cell line. Considering animal welfare further specific efficacy studies are not required.

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.

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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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