ANNEX I

NAME, PHARMACEUTICAL FORM, STRENGTH OF THE MEDICINAL PRODUCT, ANIMAL SPECIES, ROUTES OF ADMINISTRATION, AND MARKETING AUTHORISATION HOLDER

Member State	Applicant or Marketing Authorisation Holder	Product invented name	Pharmaceutical form	Strength	Animal species	Frequency and route of administration	Recommended dose
Austria	Intervet Deutschland GmbH Feldstrasse 1a DE-85716 Unterschleissheim Germany Tel: +49 (89) 310 062 59 Fax: +49 (89) 310 03 27	Bovilis BVD-MD	Suspension for injection	Per 2 ml dose: 50 ELISA units, inducing ≥ 4.6 log2 VN units	Cattle	Intramuscular injection. (Immunisation schedules are given in the product information.)	One dose = 2 ml
Belgium	Intervet Belgium Bedrijvenlaan 7 B-2800 Mechelen Belgium Tel: +32 (15) 436 728 Fax: +32 (15) 436 733	Bovilis BVD	As above	As above	As above	As above	As above
Bulgaria	Intervet Bulgaria EOOD 7, Iskarsko shoes blvd BG-1528 Sofia Bulgaria Tel: +359 (2) 970 1070 Fax: +359 (2) 971 0900	Bovilis BVD	As above	As above	As above	As above	As above
Cyprus	Medivet Suppliers Ltd 87c Aglandjias Avenue PO Box 20932 CY-1665 Nicosia Cyprus Tel: +357 223 366 05 Fax: +357 223 366 07	Bovilis BVD	As above	As above	As above	As above	As above

Member State	Applicant or Marketing Authorisation Holder	Product invented name	Pharmaceutical form	Strength	Animal species	Frequency and route of administration	Recommended dose
Czech Republic	Intervet s.r.o. Zlicin Business Centre Na Radosti 413 CZ-155 21 Prague 5 Czech Republic Tel: +420 (2) 333 440 25 Fax: +420 (2) 333 440 22	Bovilis BVD	As above	As above	As above	As above	As above
Denmark	Intervet Danmark AS PO Box 66 Literbuen 9 DK-2740 Skovlunde Denmark Tel: +45 (44) 546 900 Fax: +45 (44) 531 955	Bovilis BVD	As above	As above	As above	As above	As above
Estonia	Intervet Baltic States Vasario 16-osios 9-6A LT-Kauna 3000 Lithuania Tel: +370 373 216 60 Fax: +370 372 012 93	Bovilis BVD	As above	As above	As above	As above	As above
France	Intervet S.A. Rue Olivier de Serres Angers Technopole BP 17144 FR-49071 Beaucouzé Cedex France Tel: +33 (2) 412 283 83 Fax: +33 (2) 412 283 00	Bovilis BVD	As above	As above	As above	As above	As above

Member State	Applicant or Marketing Authorisation Holder	Product invented name	Pharmaceutical form	Strength	Animal species	Frequency and route of administration	Recommended dose
Germany	Intervet Deutschland GmbH Feldstrasse 1a DE-85716 Unterschleissheim Germany Tel: +49 (89) 310 062 59 Fax: +49 (89) 310 03 27	Bovilis BVD-MD	As above	As above	As above	As above	As above
Greece	Intervet Hellas S.A. 3, Paparigopoulou Street GR-152 32 Halandri Athens Greece Tel: +30 (210) 689 0411 Fax: +30 (210) 683 2523	Bovilis BVD	As above	As above	As above	As above	As above
Hungary	Intervet Hungaria Kft. Budapest 1095 HU-Boráros tér. 7/2. 7.e.13 Hungary Tel: +36 (1) 456 3090 Fax: +36 (1) 456 3099	Bovilis BVD	As above	As above	As above	As above	As above
Ireland	Intervet Ireland Ltd. Magna Drive Magna Business Park Citywest Road IR-Dublin 24 Ireland Tel: +353 (1) 463 7330 Fax: +353 (1) 451 1906	Bovilis BVD	As above	As above	As above	As above	As above

Member State	Applicant or Marketing Authorisation Holder	Product invented name	Pharmaceutical form	Strength	Animal species	Frequency and route of administration	Recommended dose
Italy	Intervet Italia S.r.l. Via W. Tobagi 7 IT-20068 Peschiera Borromeo – Milano Italy Tel: +39 (02) 516 861 Fax: +39 (02) 516 866 87	Bovilis BVD	As above	As above	As above	As above	As above
Latvia	Intervet Baltic States Vasario 16-osios 9-6A LT-Kauna 3000 Lithuania Tel: +370 373 216 60 Fax: +370 372 012 93	Bovilis BVD	As above	As above	As above	As above	As above
Lithuania	Intervet Baltic States Vasario 16-osios 9-6A LT-Kauna 3000 Lithuania Tel: +370 373 216 60 Fax: +370 372 012 93	Bovilis BVD	As above	As above	As above	As above	As above
Luxembourg	Intervet Belgium Bedrijvenlaan 7 B-2800 Mechelen Belgium Tel: +32 (15) 436 728 Fax: +32 (15) 436 733	Bovilis BVD	As above	As above	As above	As above	As above

Member State	Applicant or Marketing Authorisation Holder	Product invented name	Pharmaceutical form	Strength	Animal species	Frequency and route of administration	Recommended dose
The Netherlands	Intervet International B.V. Wim de Korverstraat 35 NL-5831 AN Boxmeer The Netherlands Tel: + 31 485 587 652 Fax: + 31 485 587 653	Bovilis BVD	As above	As above	As above	As above	As above
Poland	Intervet International BV Sp. z.o.o. Przedstawicielstwo w Polsce ul. Wybrzeze Gdynskie 6c PL-01-531 Warszawa Poland Tel: +48 (22) 620 1147 Fax: +48 (22) 620 2935	Bovilis BVD	As above	As above	As above	As above	As above
Portugal	Intervet Portuguesa Ltd. Estrada Nacional 249, Km 14,2 PT-2725-397 Mem Martins Codes Portugal Tel: +351 (21) 922 83 00 Fax: +351 (21) 920 22 31	Bovilis BVD	As above	As above	As above	As above	As above
Slovakia	Representative of Intervet in the Slovak Rep. Palarikova 16 SK-040 01 Kosice Slovak Republic Tel: +421 (55) 676 9405 Fax: +421 (55) 676 9873	Bovilis BVD	As above	As above	As above	As above	As above

Member State	Applicant or Marketing Authorisation Holder	Product invented name	Pharmaceutical form	Strength	Animal species	Frequency and route of administration	Recommended dose
Slovenia	Intervet International Podruznica Krizna 10 SI-1000 Ljubljana Slovenija Tel: +386 (15) 417 567 Fax: +386 (15) 233 567	Bovilis BVD	As above	As above	As above	As above	As above
Spain	Laboratorios Intervet S.A. Poligono Industrial “El Montalva” Apartado 3006 ES-37080 Salamanca Spain Tel: +34 (923) 190 345 Fax: +34 (923) 190 347	Bovilis BVD	As above	As above	As above	As above	As above
UK	Intervet UK Ltd. Walton Manor Walton Milton Keynes Buckinghamshire MK7 7AJ UK Tel: +44 (1908) 665 050 Fax: +44 (1908) 664 778	Bovilis BVD	As above	As above	As above	As above	As above

ANNEX II

SCIENTIFIC CONCLUSIONS

SCIENTIFIC CONCLUSIONS

1. Introduction and background

Bovilis BVD was first authorised in Germany on 6 May 1998 (as Bovilis BVD-MD). The initial mutual recognition procedure was finalised on 24 June 1999, and 11 other Member States authorised the product at this time. The first renewal procedure for the vaccine was finalised in June 2004.

In March 2006 Intervet then submitted an application for a marketing authorisation for this vaccine following a repeat use mutual recognition procedure, with Germany acting as Reference Member State, for Denmark, Poland, Slovakia and Slovenia. The application was made in accordance with Article 12.3 of Directive 2001/82/EC as a stand alone application. The procedure started on 13 March 2006.

At day 90 of the MRP, 2 August 2006, Denmark could not agree to the granting of a marketing authorization as they considered the product to present a potential serious risk for animal health. The matter was referred to the Co-ordination Group for Mutual Recognition and Decentralised Procedures, CMD(v), for a 60 day procedure in accordance with Article 33(1) of Directive 2001/82/EC, as amended. This procedure started on 21 August 2006 and ended on 20 October 2006. The CMD(v) could not reach an agreement by day 60 of this procedure, as to where Denmark maintained their concerns. Consequently Germany notified the EMEA, on 31 October 2006, that the CMD(v) failed to reach an agreement regarding Bovilis BVD. Pursuant to Article 33(4) of Council Directive 2001/82/EC, as amended, the matter has been referred to CVMP.

Denmark considers that the proposed testing regime to demonstrate freedom from extraneous agents is insufficient to ensure that Bovilis BVD would not interfere with their national eradication campaigns for certain animal diseases and that therefore the benefit: risk assessment for Bovilis BVD is negative and authorisation of the product would represent a potential serious risk to animal health.

During its meeting of November 2006, the CVMP started a referral procedure under Article 33(4) of Directive 2001/82/EC as amended for Bovilis BVD. The Marketing Authorisation Holder should provide all supporting data to justify a positive benefit-risk ratio for the treated animal.

2. Discussion

The benefits of Bovilis BVD vaccine are accepted. The risk of accidental contamination with FMDV, IBRV, BLV and BTV is concluded to be low; consequently the risk of seroconversion against the listed agents is also concluded to be low.

Although the consequences of an accidental seroconversion against the listed extraneous agents would damage the animal health status of a country free from the four specified diseases, the benefit: risk evaluation remains positive due to the low risk of contamination of the product.

It is worthy of note that the first EU marketing authorisation for Bovilis BVD was granted in 1998, and the vaccine is currently authorised in 14 EU Member States. There are many years of experience with the use of this vaccine, and there are no known adverse reactions associated with the vaccine.

There is always a small risk of extraneous agent contamination from a variety of sources. The factors which determine the safety of a product are the measures applied in the production and control procedures. With regard to the potential benefit or otherwise from conducting additional tests, it is known that the efficiency of final batch testing in revealing defects is highly variable, depending on the type of defect, and that it is preferable to build quality into the whole process rather than rely on end product testing. No scientific arguments are available concerning how the additional testing would minimise the risk of possible seroconversion induced by the vaccine. On the contrary it is known that extremely high numbers of samples must be tested in order to detect a low level of defects. Considering all the measures taken, it is very unlikely that any contamination of Bovilis BVD could

firstly occur, and secondly that such contamination would eventually lead to seroconversion, even in a small number of vaccinated animals. The probability that any such contamination would be identified in the test proposed by the Danish Medicines Agency is even smaller. The added value of retesting for this feature in inactivated viral vaccines is extremely small.

Based on the current requirements and the relevant safeguards (e.g., GMP) the CVMP concludes that the Applicant has taken adequate measures to guarantee the quality and safety of Bovilis BVD.

3. Conclusions and Recommendations

As the likelihood of contamination of Bovilis BVD vaccine, and the subsequent probability of seroconversion by such contaminants is extremely low, the advantage of additional final product testing for extraneous agents (serological method) is considered to be negligible.

The extra testing (which requires the use of animals) would therefore be a disproportionate measure when balanced against the positive effects which can be obtained for this vaccine.

Therefore the Danish testing requirement is considered to be unjustified.

Foot and Mouth virus is virtually exotic to Western Europe and Bluetongue, although of a recent change in status, is not ubiquitous or endemic in the majority of the EU, so for these 2 agents the practical risks should be lower. BLV and IBRV are more ubiquitous but the measures summarised below have generally been accepted in the majority of member states to be adequate to ensure negligible risk.

In general, the absence of extraneous agents in vaccines can be ensured by:
1. GMP compliance of the production system
2. Extraneous agents testing of raw materials
3. Extraneous agents testing of batches of finished product, if required.

The production and testing of Bovilis BVD vaccine are in accordance with the relevant requirements of Directive 2001/82/EC, the relevant EU guidelines and the relevant monographs of the Ph.Eur.

In conclusion, CVMP is of the opinion that:

- the production of Bovilis BVD vaccine is in compliance with GMP requirements
- extraneous agents testing of raw materials are carried out according to the relevant requirements
- extraneous agents testing of finished batches of Bovilis BVD for FMDV, BLV, BTV and IBRV is not required in the relevant monographs

Therefore the requested additional specified extraneous testing requirement is scientifically not justified for Bovilis BVD.

CVMP have noted the inconsistencies (with regard to extraneous agents testing) in the Ph.Eur. monographs for inactivated bovine vaccines and have written to the EDQM and asked them to address this.

The CVMP has concluded that the risk/benefit for Bovilis BVD is favourable.

ANNEX III

SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE INSERT

The valid Summary of Product Characteristics, labelling and package leaflet are the final versions achieved during the Coordination group procedure.