Annex to:

EFSA AHAW Panel (EFSA Panel on Animal Health and Welfare), More S, Bøtner A, Butterworth A, Calistri A, Depner K, Edwards S, Garin-Bastuji B, Good M, Gortázar Schmidt C, Michel V, Miranda MA, Nielsen SS, Raj M, Sihvonen L, Spoolder H, Thulke H-H, Velarde A, Willeberg P, Winckler P, Baldinelli F, Broglia A, Dhollander S, Beltrán-Beck B, Kohnle L and Dominique Bicout, 2017. Scientific Opinion on the assessment of listing and categorisation of animal diseases within the framework of the Animal Health Law (Regulation (EU) No 2016/429): Bovine viral diarrhoea (BVD). EFSA Journal 2017;15(8):4952, doi:10.2903/j.efsa.2017.4952

Annex A – Mapped fact-sheet used in the individual judgement on bovine viral diarrhoea (BVD)

Article 5

Question A(i)

Question A(i) scientific evidence indicate that the disease is transmissible **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(vi) the routes and speed of transmission of the disease between animals and, when relevant, between animals and humans	(a)(vi) 1 types of routes of transmission from animal to animal (horizontal, vertical)	Horizontal: direct (nose to nose) and airborne over short distances in buildings where persistently infected animals are present and indirect via contaminated equipment, facilities and personnel (Gunn, 1993). Spread of BVDV by ambient air or other vehicles involving transiently infected animals has never been demonstrated and is most to be of marginal significance (Lindberg and Houe, 2005). Virus may be shed in the semen of bulls (Rikula et al., 2008), but avoidance of transmission by this route during artificial insemination using semen collected in Member States can be achieved through compliance with the

		requirements for intra-community trade laid down in Council Directive 2003/43/EC or the OIE guidelines on collection and processing of bovine, small ruminant and porcine semen (OIE, 2016b). BVDV can also be transmitted by embryo transfer, but preliminary evidence indicates that the risk is negligible if in vivo embryos are collected and processed according to OIE guidelines (OIE, 2016a). Adventitious transmission by contaminated live vaccines has also been described (Løken, 1995). Virus has been recovered from biting and non-biting flies following exposure to PI animals in experimental studies, but with one exception onward transmission of the virus has not been demonstrated (Gunn, 1993; Rikula et al., 2008; OIE, 2016b). Vertical: transient infection of a naïve dam during the first third of pregnancy (up to approximately 125 days of gestation) will result in the birth of a persistently infected (PI) calf if the foetus is carried to term. All calves born to PI dams will also be PI.
	(a)(vi) 2 types of routes of transmission from animal to humans (direct, indirect)	Not relevant.

Question A(ii)

Question A(ii) animal species are either susceptible to the disease or vectors and reservoirs thereof exist in the Union Interpretation: indicate if animal species susceptible to the disease or vector or reservoir are present in the Union **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(i) animal species concerned by the disease	(a)(i) 1 naturally susceptible wildlife species	Evidence for natural susceptibility of wildlife species (Passler and Walz, 2010; Ridpath and Neill, 2016) comes mainly from serological surveys. While these have typically demonstrated the presence of antibodies capable of neutralising BVDV the possibility that they may in some cases indicate exposure to a different, but related, pestivirus cannot be excluded. Those species from which BVDV has been isolated (or viral antigen/RNA detected), confirming their susceptibility are underlined below; otherwise natural susceptibility is based on serological evidence. Where only serological evidence of infection exists, it is recognised that due to the cross-reactive nature of pestiviral antibodies it is possible that these are due to infection with other pestiviral species and do not provide definitive evidence of susceptibility to BVDV (Ridpath and Neill, 2016). **Order Artiodactyla** **Family Bovidae** African Buffalo (*Syncerus caffer*); American Bison (*Bison bison*) (Ridpath and Neill, 2016); Bighorn Sheep (*Ovis canidensis*) (Ridpath and Neill, 2016); Blue Wildebeest (*Connochaetes taurinus*); Bushbuck (*Tragelaphus scriptus*); Chamois (*Rupicapra pyrenaica pyrenaica*) (Ridpath and Neill, 2016); Defrassa Waterbuck (*Kobus ellipsiprymnus*); Duiker (*Sylvicapra grimmia*); Eland (*Taurotragus oryx*) (Passler and Walz, 2010); European Bison (*Bison bonasus*); Gemsbok (or Oryx) (*Oryx gazella*); Hartebeest (*Alcelaphus buselaphus*); Impala (*Aepyceros melampus*); Kudu (*Tragelaphus strepsiceros*); Lechwe (*Kobus leche*); Lichenstein's Hartebeest (*Alcelaphus lichtensteinii*); Mouflon (*Ovis orientalis*); Mountain goat (*Oreamnos americanus*) (Ridpath and Neill, 2016); Nilgai (*Boselaphus tragocamelus*) (Passler and Walz, 2010); Nyala (*Tragelaphus angasi*); Oryx (*Oryx gazelle*); Reedbuck (*Redunca arundinum*); Roan Antelope (*Hippotragus equinus*); Sable Antelope (*Hippotragus niger*); Springbok (*Antidorcas marsupialis*); Topi (*Damaliscus lunatus jimela*); Tsessebe (*Damaliscus lunatus*); Waterbuck (*Kobus ellipsiprymnus*); Wildebeest (*Connochaetes taurinus*) **Family Cervidae** Axis Deer (*Axis axis*) (Passler and Walz, 2010); Barasingha Deer (*Cervus duvaucelii*) (Passler and Walz, 2010); Caribou (*Rangifer tarandus caribou*); Chinese Water Deer (*Hydropotes inermis*) (Ridpath and Neill, 2016); Elk (*Cervus canadensis*); Fallow Deer (*Dama dama*); Grey Brocket Deer (*Mazama gouazoubira*); Moose (*Alces alces*); Mule Deer (*Odocoileus hemionus*) (Ridpath and Neill, 2016); Pampas Deer (*Ozotoceros bezoarticus celer*); Red Deer (*Cervus elephus*) (Ridpath and Neill, 2016); Reindeer (*Rangifer tarandus*); Roe Deer (*Capreolus capreolus*) (Ridpath and Neill, 2016); Sika Deer (*Cervus nippon*); White-Tailed Deer (*Odocoileus virginianus*) (Ridpath and Neill, 2016) **Family Giraffidae** Giraffe (*Giraffa camelopardalis*) (Ridpath and Neill, 2016)

		Family Antilocapridae Pronghorn (*Artilocapra americana*) (Ridpath and Neill, 2016) **Family Camelidae** Alpaca (*Vicugna pacos*) (Passler and Walz, 2010); Dromedary (*Camelus dromedarius*) (Passler and Walz, 2010); Guanaco (*Lama guanicoe*); Llama (*Lama glama*) (Passler and Walz, 2010); Vicuna (*Vicugna vicugna*) **Family Suidae** Wart Hog (*Phacochoerus africanus*); Wild Boar (*Sus scrofa*) (Ridpath and Neill, 2016) **Family Traguilidae** Mousedeer (*Tragulus javanicus*) (Grondahl et al., 2003) **Order Lagomorpha** Evidence of susceptibility of Leporidae (order Lagomorpha) has been published. A study in wild rabbits in Germany found low levels of neutralizing antibodies in 40/100 sera (Frölich and Streich, 1998), although attempts at virus isolation were unsuccessful. A survey in the United Kingdom reported a weak positive result by ELISA (and with high levels of non-specific binding) in 3/260 wild rabbits (Grant et al., 2015), with the authors concluding BVDV is not established as an endemic infection of rabbits in the regions of the UK where sampling was conducted (Bachofen et al., 2014; Grant et al., 2015). More recently, 34/94 sera from European hares were found to contain VN antibodies to a ruminant pestiviruses (Colom-Cadena et al., 2016) with none testing positive for viral RNA by real time RTPCR. **Family Leporidae** Rabbit (*Oryctolagus cuniculus*) (Frölich and Streich, 1998; Grant et al., 2015); European hare (*Lepus europaeus*) (Colom-Cadena et al., 2016)
	(a)(i) 2 naturally susceptible domestic species	BVD virus is predominantly a pathogen of cattle, but interspecies transmission can occur following contact with sheep, goats and pigs. In common with cattle, infection of sheep can result in the birth of viable PI lambs. In contrast, the birth of PI offspring appears to be a rare result of *in utero* infection in goats and pigs (Passler and Walz, 2010). **Order Artiodactyla** **Bovidae** Cattle; Sheep; Goats **Family Suidae (Pigs)** Pigs
	(a)(i) 3 experimentally susceptible wildlife species	**Family Leporidae** Rabbit *(Oryctolagus cuniculus)* Challenge of New Zealand White rabbits with BVDV by the intra-venous (IV) and oro-nasal (ON) routes, and via contaminated hay resulted in seroconversion in some or all rabbits in each group in the absence of clinically apparent disease (Bachofen et al., 2014). All whole blood samples collected from each group during serial bleeds were negative by real time RT-PCR, as were oral swabs (providing no evidence for shedding by this route). Tissue samples and buffy coat were collected from rabbits challenged by the IV and ON routes, with some positive results, particularly following IV challenge. Virus isolation was attempted on ileum collected following IV challenge, with positive results. IV challenge of pregnant rabbits did not result in clinical signs or increased rates of abortion or stillbirth (Grant et al., 2015). Relatively few offspring (21%) had evidence of infection by real time RT-PCR at the end of the experiment (maximum 10 days of age), with a proportion of these also seropositive by ELISA. Persistence of infection was therefore not demonstrated.
	(a)(i) 4 experimentally susceptible domestic species	With the exception of rabbits mentioned under (3) a range of non-arteriodactyls, including horses, cats, dogs, guinea pigs, mice and embryonated chicken eggs have previously been reported not to be susceptible to infection with BVDV (Baker et al., 1954), although recent work has suggested that mice can be infected when inoculated by oral and intra-nasal challenge (Seong et al., 2015; Seong et al., 2016).
	(a)(i) 5 wild reservoir species	Lack of strict host-species specificity raises the possibility of reservoir species, but it has been considered that natural infections in species other than cattle and sheep do not represent a disease problem for control programmes in domestic ruminants (Løken and Nyberg, 2013). Passler et al. (2016) propose 4 criteria that a potential wildlife reservoir must satisfy: (1) be susceptible to BVDV, (2) shed BVD (particularly through persistently infected animals), (3) maintain BVDV in the population, (4) have sufficient contact with cattle to allow spillback infections to occur. Applying these criteria to white-tailed deer (*Odocoileus virginiansis*) in the United States, where they have been intensively studied in relation to BVDV, they conclude that they represent a low risk as an important reservoir species in most environments. In general seroprevalence levels are much lower in wildlife (Passler and Walz, 2010) than in cattle in endemic situations, suggesting that the former are spillover hosts rather than true reservoir species. Evermann (2006) suggests three proposed population groups for pestiviral infections- cervid, camelid and domestic ruminants, with pestiviruses (which may be distinct from BVDV) circulating within and, under optimum conditions, between these clusters. While this may result in disease, the potential for limited intra-host spread in the new population is suggested to limit the possibility of this leading to

		an epidemic in the new population. In Europe a number of studies have also investigated the seroprevalence of BVDV in deer, typically to examine their epidemiological importance in the context of national eradication programmes. A sero-survey of free-living deer from regions of Denmark with a relatively high prevalence of cattle herds with a persistent BVD infection status prior to its eradication from cattle found a very low prevalence of cervid infection (Nielsen et al., 2000). The authors concluded that the positive animals were likely to have resulted from transmission from cattle to deer and that transmission among deer or from deer to cattle was highly unlikely and therefore that the possibility of free-living deer being a source of infection for cattle was remote. A serological survey in Norway between 1993 and 2000 found 12.3% roe deer to be seropositive to BVDV, with the authors concluding that pestivirus is endemic in this species (Lillehaug et al., 2003). While they noted the possibility of deer to cattle transmission impacting on eradication and surveillance within the Norwegian eradication programme, this has proven unfounded as demonstrated by the successful completion of the eradication programme (Løken and Nyberg, 2013). The role of wild ruminants, including red and roe deer, in the epidemiology of BVDV infections in domestic livestock in Switzerland was investigated (Casaubon et al., 2012). The authors found that despite regular interactions with farmed ruminants, infection in wild ruminants was sporadic with VN antibodies not found in any of 435 roe deer and detected in only 13/476 red deer (2.7%). They concluded that wildlife was an incidental spillover host rather than a reservoir host for BVDV and as such did not represent a threat to the Swiss national BVDV eradication programme in livestock (Presi and Heim, 2010). A recent study in Belgium (Tavernier et al., 2015) of wild roe deer found only 1.3% seropositive, despite an expanding population and regular contact with livestock, concluding that they do not play an important role in the epidemiology of infection in domestic animals. A similar study was conducted in the south of Spain (Paniagua et al., 2016) where wild ruminant populations have also increased substantially, resulting in the frequent sharing of habitats with domestic livestock. It found only 1 of 892 red deer to be seropositive and concluded that the deer were spillover hosts only and did not represent a risk for domestic ruminants. Another study of sympatric alpine populations of livestock and wild ruminants, including deer in north-west Spain generated similar findings (Fernández-Aguilar et al., 2016). Grant and others (Grant et al., 2015) consider that a wildlife reservoir in the rabbit (*Oryctolagus cuniculus*) poses a small but non-zero risk of re-infection for BVDV-free cattle herds. While this is unlikely to be of epidemiological relevance for most control scenarios it may theoretically play a role in the tail end of an eradication campaign. Detection of VN antibodies to pestiviruses, including BVDV, in European hares *(Lepus europaeus*) has led to the suggestion that they may be a wildlife reservoir, particularly in relation to the Pyrenean chamois (Colom-Cadena et al., 2016).
	(a)(i) 6 domestic reservoir species	Sheep and goats are susceptible to infection with BVDV. While both sheep and goats persistently infected (PI) with BVDV have been described, foetal death and non-viability of lambs are common sequelae of transplacental infection in sheep and viable PI kids are considered a rare result of *in utero* infection in goats, where reproductive failure or gross pathology of infected foetuses are the likely outcome (Løken, 1995; Bitsch et al., 2000; Krametter-Froetscher et al., 2010; Passler and Walz, 2010).

Question A(iii)

Question A(iii) disease causes negative effects on animal health OR poses a risk to public health due to its zoonotic character **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(ii) morbidity and mortality rates of the disease in animal populations	(a)(ii) 1 Prevalence/ incidence	A series of investigations aimed at assessing the prevalence of BVDV infection have been performed in Europe, from the late seventies and into the 21st century, and the results of these at both animal- (Table 1) and herd-levels (Table 2) have been reviewed within the position paper published by the EU Thematic network on control of bovine viral diarrhoea virus (BVDV) (2001). The general picture is that in many European countries without systematic control in place, or before such measures were implemented, the infection has been/is endemic at a high level with 60-80% of the animals being antibody positive and 1-2% being persistently infected. In many countries, surveys indicated that almost all herds had antibody carriers and approximately half of them had PI animals. However, a few countries had quite a different picture with much lower prevalences. This heterogeneity in the presence of BVDV infection in the absence of systematic control was considered likely to be a reflection of the distribution of risk factors for new BVDV infections and for persistence of the infection in the respective

<table>
<tr><td></td><td></td><td>countries.
Where a systematic approach has been adopted in MS, significant progress has been made. The Scandinavian MS Sweden, Finland, Denmark have completed eradication programmes (as has Norway) (Stahl and Alenius, 2012; Løken and Nyberg, 2013; Foddai et al., 2014; Norström et al., 2014), while national or regional programmes are under way and have reduced the prevalence of PI births in a number of other Member States, including Austria, Germany, Ireland, Austria, Scotland and Belgium (Rossmanith et al., 2010; Schirrmeier et al., 2012; Clegg et al., 2016; Duncan et al., 2016; Ribbens et al., 2016) and in Switzerland (Presi et al., 2011).
See Tables 1 and 2 at "Tables" section.</td></tr>
<tr><td></td><td>(a)(ii) 2 Case-morbidity rate (% clinically diseased animals out of infected ones)</td><td>The case morbidity rate for acute (transient) infections varies with a range of factors, including the age of the animal, its immune status and its reproductive state (Lanyon et al., 2014). The majority of acute infections are considered subclinical. However infection of a BVDV naïve animal results in a transient viraemia which can be associated with short-term leukopenia, lymphopenia and/or thrombocytopenia, apoptosis in the thymus, and pyrexia. The resultant immunosuppression, particularly in calves, can allow other infectious agents to become established, or allow the recrudescence of existing infections resulting in enteric or respiratory disease.
Infection of naïve breeding animals may have a range of negative outcomes depending on the stage of reproduction, including fertilisation failure, early embryonic death, abortion, congenital defects and the birth of persistently infected (PI) offspring which may be weak, undersized and ill-thrifty. Acute infection of sexually active bulls results in a reduction in sperm density and motility, plus an increase in sperm abnormalities (Lanyon et al., 2014).
Following the emergence of BVDV II in North America, much higher case morbidity rates (and mortality rates) were reported (Carman et al., 1998). The within-herd abortion rate was 44% (3-83%). The mortality rate was 53% (3-83%) for animals under two years of age and 9% (2-26%) for older animals. A recent study of BVDV type 2c in Germany reported a case-fatality rate of up to 60% and mortality in outbreak farms varied between 2.3 and 29.5% (Gethmann et al., 2015).
Persistent infections
PI animals have been shown to be significantly smaller than non-PI animals (Table 3). The annual incidence risk of dying or being slaughtered due to unthriftiness was calculated as 0.28 and 0.31 among 34 PI animals in 10 Danish dairy herds (Houe, 1993).
Observational studies on the impact of infection with BVDV on health and production parameters have been reviewed within the position paper of the EU Thematic network on control of bovine viral diarrhoea virus (BVDV) (2001) and the results are reproduced below (Table 3, see "Tables" section).</td></tr>
<tr><td></td><td>(a)(ii) 3 Case-fatality rate</td><td><table><tr><td></td><td>Case fatality rate/reference</td></tr><tr><td>Mucosal disease</td><td>100% (Lanyon et al., 2014)</td></tr><tr><td>Persistently infected animal</td><td>High (Lanyon et al., 2014)</td></tr><tr><td>Transiently infected animal</td><td>Low (but may be increased by secondary infections due to BVDV-induced immunosuppression) (Lanyon et al., 2014)</td></tr></table></td></tr>
<tr><td>(a)(iii) zoonotic character of the disease</td><td>(a)(iii) 1 report of zoonotic human cases</td><td>BVDV is not considered zoonotic, although the ability of BVDV to replicate in human cell lines has been reported in some studies and there are limited reports of detection of virus, viral RNA or antigen in human samples (Giangaspero et al., 1997; Walz et al., 2010; Bratcher et al., 2012).</td></tr>
<tr><td>(a)(iv) resistance to treatments, including antimicrobial resistance</td><td>(a)(iv) 1 resistant strain to any treatment even at laboratory level</td><td>Not applicable to viruses.</td></tr>
<tr><td rowspan="5">(b)(ii) Impact of the disease on human health</td><td>(b)(ii) 1 types of routes of transmission between animals and humans - see (a)(vi)2</td><td rowspan="5">Not applicable.</td></tr>
<tr><td>(b)(ii) 2 Incidence of zoonotic cases</td></tr>
<tr><td>(b)(ii) 3 Occasional or substantial?</td></tr>
<tr><td>(b)(ii) 4 Epidemic or pandemic?</td></tr>
<tr><td>(b)(ii) 5 DALY</td></tr>
<tr><td>(b)(iii) Impact of the disease on animal</td><td>(b)(iii) 1 severity of clinical signs at case</td><td>Clinical signs may vary from inapparent to death, depending on a variety of factors including whether the animal is acutely or persistently infected.</td></tr>
</table>

welfare	level and related level and duration of impairment	*Acute (transient) infections* Transient infection of naïve female breeding animals may have a range of negative outcomes depending on the stage of reproduction, including fertilisation failure, early embryonic death, abortion, congenital defects and the birth of persistently infected (PI) offspring which may be weak, undersized and ill-thrifty; infection of naïve bulls may result in decreased sperm motility and density and increase levels of sperm abnormalities (Lanyon et al., 2014). Other clinical signs associated with acute infection include pyrexia, diarrhoea, decreased milk yield, sudden death and haemorrhagic syndrome (Ridpath et al., 2013; Lanyon et al., 2014; Gethmann et al., 2015). However the majority of acute infections are considered subclinical, with seroconversion and recovery occurring 2-3 weeks post infection (Ridpath et al., 2013; Lanyon et al., 2014). Even in the absence of clinical signs infection of a BVDV naïve animal results in a transient viraemia which can be associated with short-term leukopenia, lymphopenia and/or thrombocytopenia, apoptosis in the thymus, and pyrexia. The resultant immunosuppression, particularly in calves, can allow other infectious agents to become established, or allow the recrudescence of existing infections resulting in enteric or respiratory disease which may be fatal. Recent work demonstrating a significant reduction in thymic size following challenge of calves with both low and high virulence BVDV strains, accompanied by a significant depletion of thymic cortex, suggests that transient infection of neonatal calves may have long-term immunosuppressive effects (Ridpath et al., 2013). Following the emergence of BVDV II in North America, much higher case morbidity rates (and mortality rates) associated with primary infection were reported (Carman et al., 1998). The within-herd abortion rate was 44% (3-83%). The mortality rate was 53% (3-83%) for animals under two years of age and 9% (2-26%) for older animals. A recent study of BVDV type 2c in Germany reported a case-fatality rate of up to 60% while mortality in outbreak farms varied between 2.3 and 29.5% (Gethmann et al., 2015). *Persistent infections* PI animals can be clinically healthy, but some may appear small, weak and ill-thrifty, showing decreased weight gain, stunted growth and chronic ill thrift. PI animals are considered more susceptible to secondary infections (Lanyon et al., 2014) leading to poor survivability of most PI animals. The annual incidence risk of dying or being slaughtered due to unthriftiness was calculated as 0.28 and 0.31 among 34 PI animals in 10 Danish dairy herds (Houe, 1993). In addition, PI animals are uniquely to susceptible to developing mucosal disease, which is inevitably fatal (Lanyon et al., 2014), with death occurring a few days to a few weeks following its onset.
(c) potential to generate a crisis situation and its potential use in bioterrorism	(c) 1 listed in OIE/CFSPH classification of pathogens	CFSPH (http://www.cfsph.iastate.edu/DiseaseInfo/) No OIE (http://www.oie.int/animal-health-in-the-world/oie-listed-diseases-2016/) Yes
	(c) 2 listed in the Encyclopedia of Bioterrorism Defense of Australia Group	(http://www.australiagroup.net/en/human_animal_pathogens.html) No
	(c) 3 included in any other list of potential bio-agro-terrorism agents	None identified.

Question A(iv)

Question A(iv) diagnostic tools are available for the disease Interpretation: diagnostic tools are available for the disease in the Union **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(viii) existence of diagnostic and disease control tools	(a)(viii) 1 Existence of diagnostic tools	A range of reliable diagnostic tools for detection of virus, viral antigens, RNA and antibodies are available **see (d)(i)(1):** A range of direct and indirect test methods for BVDV are described in OIE (2015), with these being further categorised according to the purpose of the test (Table 7). Within Europe availability of laboratories offering tests for both agent identification and detection of the immune response is high, with these commonly accredited to ISO 17025. Kits are readily available commercially. In some countries with eradication programmes underway, including: Germany (https://www.fli.de/en/services/licensing-authority/),

		Belgium (http://www.coda-cerva.be/index.php?option=com_content&view=article&id=376%3Acertifications-des-reactifs-de-diagnostiques&catid=194%3Acontrole-de-kits&Itemid=369&lang=en) and Ireland (https://www.agriculture.gov.ie/animalhealthwelfare/laboratoryservices/nationalreferencelaboratoriesother/bvdtestkitapproval/) protocols for kit approval are in place. See Table 7 at "Tables" section.
	(a)(viii) 2 Existence of disease control tools	Three central elements of systematic approaches to control and eradication of BVDV have been identified (Lindberg et al., 2006): a) biosecurity and possible use of vaccination (Lindberg et al., 2006) aimed at preventing re-introduction of the infection in free herds b) elimination of PI animals from infected herds c) surveillance to monitor the progress of interventions and to rapidly detect new infections. These have been applied in a number of European countries, with Scandinavia now considered free of infection. Compulsory national or regional programmes are currently underway in a number of other countries, including Austria, Belgium, Ireland, Northern Ireland, Germany, Scotland and Switzerland (Stahl and Alenius, 2012; Sarrazin et al., 2013).

Question A(v)

Question A(v) the risk-mitigating measures and, where relevant, surveillance of the disease are effective and proportionate to the risks posed by the disease in the Union **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(viii) existence of diagnostic and disease control tools	(a)(viii) 1 Existence of diagnostic tools	A range of reliable diagnostic tools for detection of virus, viral antigens, RNA and antibodies are available **see (d)(i)(1):** A range of direct and indirect test methods for BVDV are described in OIE (2015), with these being further categorised according to the purpose of the test (Table 7). Within Europe availability of laboratories offering tests for both agent identification and detection of the immune response is high, with these commonly accredited to ISO 17025. Kits are readily available commercially. In some countries with eradication programmes underway, including: Germany (https://www.fli.de/en/services/licensing-authority/), Belgium (http://www.coda-cerva.be/index.php?option=com_content&view=article&id=376%3Acertifications-des-reactifs-de-diagnostiques&catid=194%3Acontrole-de-kits&Itemid=369&lang=en) and Ireland (https://www.agriculture.gov.ie/animalhealthwelfare/laboratoryservices/nationalreferencelaboratoriesother/bvdtestkitapproval/) protocols for kit approval are in place. See Table 7 at "Tables" section.
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(b)(ii) Impact of the disease on human health	(b)(ii) 6 Availability of medical treatment and their effectiveness (therapeutic effect and any resistance)	Not applicable.
	(b)(ii) 7 Availability of vaccines and their effectiveness (reduced morbidity)	
(d)(i) feasibility,	(d)(i) 1 officially/internationally	A range of direct and indirect test methods for BVDV are described in OIE (2015), with these being further categorised according to the purpose of the test (Table 7). Within Europe availability of laboratories offering tests for both agent identification and detection of the

availability and effectiveness of diagnostic tools and capacities	recognised diagnostic tool, OIE certified	immune response is high, with these commonly accredited to ISO 17025. Kits are readily available commercially. In some countries with eradication programmes underway, including: Germany (https://www.fli.de/en/services/licensing-authority/), Belgium (http://www.coda-cerva.be/index.php?option=com_content&view=article&id=376%3Acertifications-des-reactifs-de-diagnostiques&catid=194%3Acontrole-de-kits&Itemid=369&lang=en) and Ireland (https://www.agriculture.gov.ie/animalhealthwelfare/laboratoryservices/nationalreferencelaboratoriesother/bvdtestkitapproval/) protocols for kit approval are in place. See Table 7 at "Tables" section.
	(d)(i) 2 Se and Sp of diagnostic test	See Table 8 ("Tables" section). It is important that all assays are appropriately validated before use, particularly in relation to their ability or otherwise to detect both BVDV 1 and 2 (and other related pestiviruses) (Bauermann et al., 2012).
	(d)(i) 3 type of sample matrix to be tested (blood, tissue, etc.)	See Table 8 ("Tables" section).
(d)(ii) feasibility, availability and effectiveness of vaccination	(d)(ii) 1 types of vaccines available on the market	Both live and dead (inactivated vaccines are available (see Table 9 at "Tables" section).
	(d)(ii) 2 availability / production capacity (per year)	A search of the websites of the European Medicines Agency (http://www.ema.europa.eu/ema) and the Health Products Regulatory Authority (http://www.hpra.ie/homepage/veterinary) on 15.10.16 provided details of three vaccines currently licenced for use in one or more Member states with datasheet claims relating to foetal protection (Table 9, see "Tables" section). No DIVA vaccines are currently licenced. All vaccines licenced in Member states with a claim relating to foetal protection must satisfy the requirements of the BVD Monograph of the European Pharmacopoeia. BVD vaccines are widely available in Europe and worldwide, but specific data on production capacities are lacking.
	(d)(ii) 3 Field protection as reduced morbidity (reduced susceptibility to infection and/or to disease)	All vaccines licenced in Member states with a claim relating to foetal protection must satisfy the requirements of the BVD Monograph of the European Pharmacopoeia. The role of vaccines in systematic control is as an additional biosecurity measure. In areas where the risk of introducing BVDV infection is known or perceived to be high, one option is to implement systematic vaccination in the initial stages of control/eradication programmes, after removal of PI animals. The need for including a vaccination regime will differ between countries/regions and it will also change over time, as the prevalence of infected herds decreases (EU Thematic network on control of bovine viral diarrhoea virus (BVDV), 2001). Even in this context, there are a number of additional factors that require consideration before using vaccines, including antigenic variation between vaccine and field strains, incorrect use of vaccines, lack of common understanding of the purpose of vaccination, the desirability of 100% efficacy of foetal protection, importance of complying with wider programme elements (not just vaccination), diagnostic confounding and the potential for live BVDV vaccines to be contaminated with adventitious viruses (Lindberg et al., 2006). There is little information available on the field efficacy of vaccines. A meta-analysis of the efficacy of BVDV vaccination to prevent reproductive disease measured by risk of foetal infection, abortion risk and pregnancy risk revealed significant decreases of nearly 45% in abortions and nearly 85% in foetal infection rate in vaccinated cattle compared with unvaccinated cohorts (Newcomer et al., 2015). When data relating to field challenge only were included, abortion risk was significantly reduced by 33%, while insufficient data were available for analysis regarding the risk of foetal infection. Additionally, pregnancy risk was increased by approximately 5% in field trials of BVDV vaccinates. It should be noted though that many of the vaccines used in this study are not licenced for use in the EU.
	(d)(ii) 4 Duration of protection	See Table 9 ("Tables" section).
	(d)(ii) 5 Way of administration	
(d)(iii) feasibility, availability and effectiveness of medical treatments	(d)(iii) 1 types of drugs available on the market and/or allowed by the EU regulatory system	No antiviral drugs are available for treating infection with BVDV.
	(d)(iii) 2 availability / production capacity (per year)	
	(d)(iii) 3	

	therapeutic effect in the field (effectiveness)	
	(d)(iii) 4 Way of administration	
(d)(iv) feasibility, availability and effectiveness of biosecurity measures	(d)(iv) 1 available biosecurity measures	Biosecurity measures seek to either: -Prevent introduction of PI animals and carriers OR -Prevent dams in early pregnancy from having direct or indirect contact with sources of BVD virus to avoid creation of PI calves. Lindberg and Alenius (1999) have reviewed risk factors for the introduction of BVDV into non-infected herds, evaluated the perceived need for control for each of these and proposed relevant control measures (Table 10).
	(d)(iv) 2 effectiveness of biosecurity measure	Overall the effectiveness of available biosecurity measures in preventing the entry of BVDV by direct or indirect routes is considered high when applied appropriately. One exception relates to the introduction of pregnant non-PI females carrying PI calves (referred to as Trojan animals). While movement controls can partially manage this risk there is currently no available diagnostic method to reliably identify this cohort of animals (Lanyon et al., 2014).
	(d)(iv) 3 feasibility of biosecurity measure	The biosecurity measures described are considered feasible, having been applied in the context of a number of eradication programmes.
(d)(v) feasibility, availability and effectiveness of restrictions on the movement of animals and products, as control measure	(d)(v) 1 available restriction movement measures	The key restriction measure relates to the movement of PI animals. This is readily available through prior testing. Identification of Trojan dams by diagnostic testing prior to movement is not available, but has been addressed in eradication programmes by applying restrictions at herd level for a period following removal of PI animals (EU Thematic network on control of bovine viral diarrhoea virus (BVDV), 2001). Movement of transiently infected animals is considered a much lower risk but is more difficult to address.
	(d)(v) 2 effectiveness of restriction of animal movement in preventing the between farm spread	Prevention of movement of PI animals is considered key to control. The effectiveness of movement controls are clearly dependent on the level of uptake/industry engagement, being most effective in the context of systematic control and least effective when participation/involvement is voluntary (Lindberg et al., 2006).
	(d)(v) 3 feasibility of restriction of animal movement	PI animals comprise a small percentage of the population (Houe, 1999) and therefore restricting their movement is feasible. Restricting movements of pregnant females from herds where BVDV has been identified until sufficient time has elapsed to minimize the possibility of the sale of pregnant animals carrying PI calves is also feasible, but is more disruptive to trade and will affect a larger proportion of animals. Measures to prevent movement of TI animals are likely to have a greater impact still, although the duration of the measure at herd level is likely to be much shorter.
(d)(vi) feasibility, availability and effectiveness of killing of animals	(d)(vi) 1 available killing of animal measures	PI animals are not excluded from the food chain subject to passing appropriate ante mortem and post mortem inspection. Therefore slaughter is normally carried out in abattoirs. Where juvenile PI animals are being culled there are typically one or a small number of animals per herd which can be slaughtered by veterinary practitioners or knackery operators.
	(d)(vi) 2 effectiveness of killing animals (at farm level or within the farm) for reducing /stopping spread of the disease	Identification and removal of PI animals is recognised to be key to stopping the spread of infection, both within and between farms.
	(d)(vi) 3 feasibility of killing animals	Disposal of small numbers of PI animals either through abattoirs or on farm is feasible (and already happening in eradication programmes).
(d)(vii) feasibility, availability and effectiveness of disposal of carcasses and other relevant animal by—products	(d)(vii) 1 disposal options available	Depending on the age and health of the animal, carcasses and by-products may be disposed of through the abattoir system or by rendering.
	(d)(vii) 2 effectiveness of disposal option	Currently available disposal options are considered effective.
	(d)(vii) 3 feasibility of disposal option	Disposal via abattoir or rendering is already routine.

Question B(i)

Question B(i) disease causes or could cause significant negative effects in the Union on animal health, OR poses or could pose a significant risk to public health due to its zoonotic character? **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(ii) morbidity and mortality rates of the disease in animal populations	(a)(ii) 1 Prevalence/ Incidence	A series of investigations aimed at assessing the prevalence of BVDV infection have been performed in Europe, from the late seventies and into the 21st century, and the results of these at both animal- (Table 1) and herd-levels (Table 2) have been reviewed within the position paper published by the EU Thematic network on control of bovine viral diarrhoea virus (BVDV) (2001). The general picture is that in many European countries without systematic control in place, or before such measures were implemented, the infection has been/is endemic at a high level with 60-80% of the animals being antibody positive and 1-2% being persistently infected. In many countries, surveys indicated that almost all herds had antibody carriers and approximately half of them had PI animals. However, a few countries had quite a different picture with much lower prevalences. This heterogeneity in the presence of BVDV infection in the absence of systematic control was considered likely to be a reflection of the distribution of risk factors for new BVDV infections and for persistence of the infection in the respective countries. Where a systematic approach has been adopted in MS, significant progress has been made. The Scandinavian MS Sweden, Finland, Denmark have completed eradication programmes (as has Norway) (Stahl and Alenius, 2012; Løken and Nyberg, 2013; Foddai et al., 2014; Norström et al., 2014), while national or regional programmes are under way and have reduced the prevalence of PI births in a number of other Member States, including Austria, Germany, Ireland, Austria, Scotland and Belgium (Rossmanith et al., 2010; Schirrmeier et al., 2012; Clegg et al., 2016; Duncan et al., 2016; Ribbens et al., 2016) and in Switzerland (Presi et al., 2011). See Tables 1 and 2 at "Tables" section.
	(a)(ii) 2 Case-morbidity rate (% clinically diseased animals out of infected ones)	The case morbidity rate for acute (transient) infections varies with a range of factors, including the age of the animal, its immune status and its reproductive state (Lanyon et al., 2014). The majority of acute infections are considered subclinical. However infection of a BVDV naïve animal results in a transient viraemia which can be associated with short-term leukopenia, lymphopenia and/or thrombocytopenia, apoptosis in the thymus, and pyrexia. The resultant immunosuppression, particularly in calves, can allow other infectious agents to become established, or allow the recrudescence of existing infections resulting in enteric or respiratory disease. Infection of naïve breeding animals may have a range of negative outcomes depending on the stage of reproduction, including fertilisation failure, early embryonic death, abortion, congenital defects and the birth of persistently infected (PI) offspring which may be weak, undersized and ill-thrifty. Acute infection of sexually active bulls results in a reduction in sperm density and motility, plus an increase in sperm abnormalities (Lanyon et al., 2014). Following the emergence of BVDV II in North America, much higher case morbidity rates (and mortality rates) were reported (Carman et al., 1998). The within-herd abortion rate was 44% (3-83%). The mortality rate was 53% (3-83%) for animals under two years of age and 9% (2-26%) for older animals. A recent study of BVDV type 2c in Germany reported a case-fatality rate of up to 60% and mortality in outbreak farms varied between 2.3 and 29.5% (Gethmann et al., 2015). *Persistent infections* PI animals have been shown to be significantly smaller than non-PI animals (Table 3). The annual incidence risk of dying or being slaughtered due to unthriftiness was calculated as 0.28 and 0.31 among 34 PI animals in 10 Danish dairy herds (Houe, 1993). Observational studies on the impact of infection with BVDV on health and production parameters have been reviewed within the position paper of the EU Thematic network on control of bovine viral diarrhoea virus (BVDV) (2001) and the results are reproduced below (Table 3, see "Tables" section).
	(a)(ii) 3 Case-fatality rate	<table><tr><td></td><td>Case fatality rate/reference</td></tr><tr><td>Mucosal disease</td><td>100% (Lanyon et al., 2014)</td></tr><tr><td>Persistently infected animal</td><td>High (Lanyon et al., 2014)</td></tr><tr><td>Transiently infected animal</td><td>Low (but may be increased by secondary infections due to BVDV-induced immunosuppression) (Lanyon et al., 2014)</td></tr></table>
(a)(iii) zoonotic	(a)(iii) 1 report of	BVDV is not considered zoonotic, although the ability of BVDV to replicate in

character of the disease	zoonotic human cases	human cell lines has been reported in some studies and there are limited reports of detection of virus, viral RNA or antigen in human samples (Giangaspero et al., 1997; Walz et al., 2010; Bratcher et al., 2012).
(a)(iv) resistance to treatments, including antimicrobial resistance	(a)(iv) 1 resistant strain to any treatment even at laboratory level	Not applicable to viruses.
(b)(ii) Impact of the disease on human health	(b)(ii) 1 types of routes of transmission between animals and humans - *see (a)(vi)2*	Not applicable.
	(b)(ii) 2 Incidence of zoonotic cases	
	(b)(ii) 3 Occasional or substantial?	
	(b)(ii) 4 Epidemic or pandemic?	
	(b)(ii) 5 DALY	

Question B(ii)

Question B(ii) disease agent has developed resistance to treatments WHICH poses a significant danger to public and/or animal health in the Union?
Interpretation: disease agent has developed resistance to treatments AND therefore poses a significant danger to public and/or animal health. If no treatment exists the answer should be na
Answer Y ☐ N ☐ na ☐

Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(iv) resistance to treatments, including antimicrobial resistance	(a)(iv)1 list of any resistant strain to any treatment even at laboratory level	Not applicable to viruses.

Question B(iii)

Question B(iii) disease causes or could cause a significant negative economic impact affecting agriculture or aquaculture production in the Union?
Interpretation: disease and/or infection causes or could cause a significant negative economic impact affecting agriculture or aquaculture production in the Union if no intervention is in place
Answer Y ☐ N ☐ na ☐

Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(ii) morbidity and mortality rates of the disease in animal populations	(a)(ii) 3 Case-fatality rate	<table><tr><td></td><td>Case fatality rate/reference</td></tr><tr><td>Mucosal disease</td><td>100% (Lanyon et al., 2014)</td></tr><tr><td>Persistently infected animal</td><td>High (Lanyon et al., 2014)</td></tr><tr><td>Transiently infected animal</td><td>Low (but may be increased by secondary infections due to BVDV-induced immunosuppression) (Lanyon et al., 2014)</td></tr></table>
(b)(i) the impact of the disease on agricultural and aquaculture production and other parts of the economy	(b)(i) 1 Number of MSs where the disease is present	As noted above in (a)(viii)1 (see Question A(iv)), a number of member states have eradication programmes underway. However currently only Denmark and Sweden have completed eradication and therefore the disease is considered still present in all other MS.
	(b)(i) 2 Proportion of production losses (%) by epidemic/endemic situation (milk, growth, semen, meat, etc.)	Health and production losses from observational studies are summarized in Table 3. Losses attributable to BVD arise from 3 main sources- reproductive losses, immunosuppression in calves and persistently infected animals (Gunn et al., 2004). Estimates of economic/financial losses due to BVDV associated with initial outbreaks, the average losses at herd level and at national livestock level have been reviewed in the Report on the EU Thematic Network on control of BVDV and the results are summarized in Tables 4, 5, and 6 (EU Thematic network on control of bovine viral diarrhoea virus (BVDV), 2001). More recent data are provided after each table where relevant. **Table 4:** Summary of financial-economic losses due to initial outbreaks of BVDV.<table><tr><td>Country</td><td>Herd type</td><td>Cost/cow (range)</td><td>Year</td></tr><tr><td>UK</td><td>Dairy</td><td>£137</td><td>1999</td></tr><tr><td>UK</td><td>Dairy</td><td>£39-92</td><td>1986</td></tr><tr><td>Netherlands</td><td>Dairy</td><td>€45</td><td>1998</td></tr></table>

Netherlands	Dairy	€19-130	1990
Denmark	Dairy	€30-89	1994
Canada	Dairy	€240-600	1998

Table 5: Summary of average financial-economic losses due at herd level due to BVDV.

Country	Herd type	Cost/cow (range)	Year
Canada	Dairy	€34	2002
UK	Dairy	£31	2000
UK	Beef	£32-43	2004
France	Dairy	€60-100	2004

The variation in the economic impact of BVDV at dairy farm level in a number of MS arising from uncontrolled output following introduction to a BVDV-naıve herd with in year 1 of a 10- year epidemic represented 22, 7, 8, 5, 8 and 20% of the BVDV-free annuity for the UK, Northern Portugal, Holland, Norway, Italy and Germany, respectively (Gunn et al., 2005).
Total loss attributable to infection with BVDV in New Zealand dairy herds was estimated at NZ$87 per cow and year in affected herds, and NZ$44.5 million per year overall, based on an estimated 14.6% affected herds (Heuer et al., 2007).
The maximum annual output losses per cow in 50-cow suckler (cow-calf) beef herds in Scotland where the herd was either initially BVDV-free or of unknown status were estimated at £38.71 and £28.22 respectively (Stott et al., 2012).
The average annuity equivalent of unchecked losses due to BVDV infection and re-infection in typical British hill suckler (cow-calf) enterprises over a 10 year disease ranged from almost £0/cow to approximately £40/cow/year, depending on the initial disease status of the herd, the initial source of virus, the probability and source of further infection, the probability of virus transmission within the herd and herd size (Gunn et al., 2004).

Table 6: Summary of financial-economic losses at the national livestock sector level.

Country	National loss	Cost/cow (range)	Year
UK	£5-30 Million		1999
UK	£40 Million		2003
Denmark	€20 Million/1M calvings		1993
Denmark	52 Million/1M calving (high virulence strain)		1993

Based on data for 1993, the annual financial loss due to BVD in Norway in the absence of control was estimated at approximately NOK 32.5 million (Valle et al., 2005).
The annual losses to the Irish cattle industry due to BVDV were estimated at €102 million (Stott et al., 2012).
Using an economic welfare model, the net discounted economic gain for Scotland of eradicating BVD from the Scottish dairy herd was estimated at £47 million over a 10-year eradication period (Weldegebriel et al., 2009).
The annual cost of BVDV in the Australian cattle population was estimated to be AUS $57.9 million (Lanyon and Reichel, 2014).

Question B(iv)

Question B(iv) disease has the potential to generate a crisis or the disease agent could be used for the purpose of bioterrorism
Answer Y ☐ N ☐ na ☐

Art. 7 criteria	Art. 7 parameters	Assessment of the Art. 7 parameters from the fact-sheet
(c) potential to generate a crisis situation and its potential use in bioterrorism	(c) 1 listed in OIE/CFSPH classification of pathogens	CFSPH (http://www.cfsph.iastate.edu/DiseaseInfo/) No OIE (http://www.oie.int/animal-health-in-the-world/oie-listed-diseases-2016/) Yes
	(c) 2 listed in the Encyclopaedia of Bioterrorism Defense of Australia Group	(http://www.australiagroup.net/en/human_animal_pathogens.html) No
	(c) 3 included in any other list of potential bio-agro-terrorism agents	None identified.

Question B(v)

Question B(v) disease has or could have a significant negative impact on the environment, including biodiversity, of the Union **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(b)(iv) impact of the disease on biodiversity and the environment	(b)(iv) 1 endangered wild species affected: listed species as in CITES and/or IUCN list	The CITES list contains a number of species in the Families Antilocapridae, Bovidae, Cervidae, Camelidae and Suidae, within the Order Arteriodactyla (https://www.cites.org/eng/app/appendices.php, accessed 17.10.2016). However there is no specific data confirming their susceptibility to infection with BVDV (although a related pestivirus has been isolated from pronghorn (Ridpath and Neill, 2016).
	(b)(iv) 2 mortality in wild species	Despite abundant evidence that pestiviruses currently circulate in wildlife populations, the full impact of exposure and prevalence of these infections are largely unknown (Ridpath and Neill, 2016).
	(b)(iv) 3 capacity of the pathogen to persist in the environment and cause mortality in wildlife	BVDV does not survive for extend periods in the environment (see (a)(v)4). Despite abundant evidence that pestiviruses currently circulate in wildlife populations, the full impact of exposure and prevalence of these infections are largely unknown (Ridpath and Neill, 2016).
(e)(iv) the impact of disease prevention and control measures, as regards the environment and biodiversity	(e)(iv) 2 Mortality in wild species	Control measures are not anticipated to result in mortality in wild species.

Article 9

Questions 1

Instruction to answer: The answer to the question 1CAq can be Y only for diseases affecting aquatic animal species, therefore do not assess this question for diseases affecting terrestrial animal species

Question 1A the disease is not present in the territory of the Union OR present only in exceptional cases (irregular introductions) OR present in only in a very limited part of the territory of the Union **Answer** Y ☐ N ☐ na ☐		
Question 1B the disease is present in the whole OR part of the Union territory with an endemic character AND (at the same time) several Member States or zones of the Union are free of the disease **Answer** Y ☐ N ☐ na ☐		
Question 1C the disease is present in the whole OR part of the Union territory with an endemic character **Answer** Y ☐ N ☐ na ☐		
Question 1CAq several Member States or zones of the Union are free of the disease **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(b)(i) the impact of the disease on agricultural and aquaculture production and other parts of the economy	(b)(i) 1 Number of MSs where the disease is present	As noted above in (a)(viii)1, a number of member states have eradication programmes underway. However currently only Denmark and Sweden have completed eradication and therefore the disease is considered still present in all other MS.

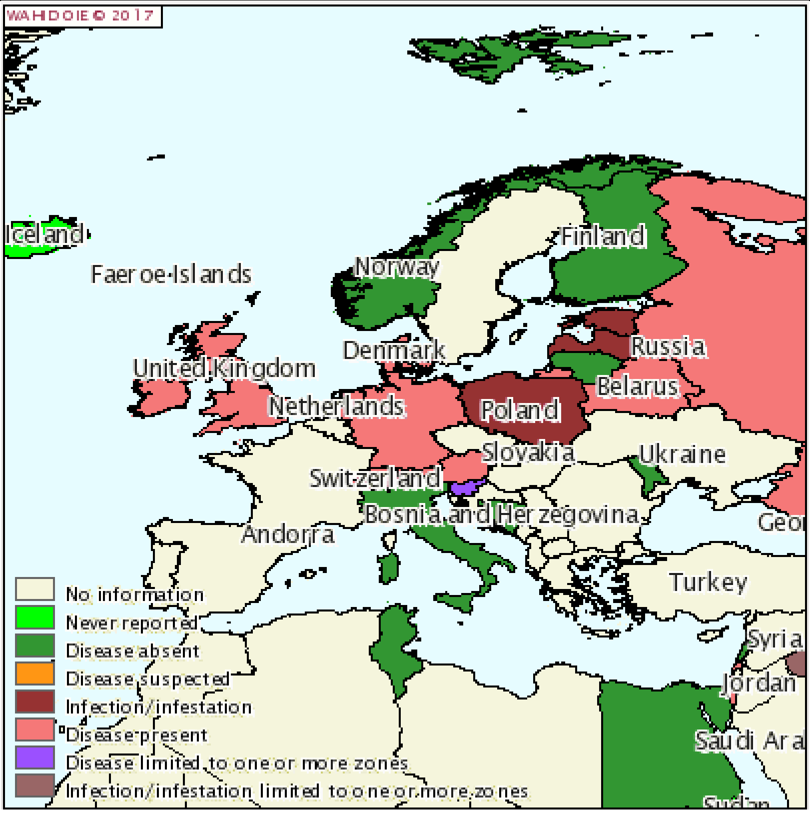
<table>
<tr>
<td rowspan="3">(a)(vii) the absence or presence and distribution of the disease in the Union, and, where the disease is not present in the Union, the risk of its introduction into the Union</td>
<td>(a)(vii) 1 Map of MSs where the disease is present</td>
<td>


Figure 1: Distribution of BVD in Europe in domestic and wild animal species from January to June 2016 *source*: OIE- WHAIS
</td>
</tr>
<tr>
<td>(a)(vii) 2 Type of epidemiological occurrence</td>
<td>The disease is considered endemic in all MS in the absence of systematic eradication programmes (Tables 1, 2).
Where a systematic approach has been adopted in MS, significant progress has been made. The Scandinavian countries Sweden, Finland, Denmark have completed eradication programmes (as has Norway) (Stahl and Alenius, 2012; Løken and Nyberg, 2013; Foddai et al., 2014; Norström et al., 2014), while national or regional programmes are under way and have reduced the prevalence of PI births in a number of other Member States, including Austria, Germany, Ireland, Austria, Scotland and Belgium (Rossmanith et al., 2010; Schirrmeier et al., 2012; Clegg et al., 2016; Duncan et al., 2016; Ribbens et al., 2016) and in Switzerland (Presi et al., 2011).</td>
</tr>
<tr>
<td>(a)(vii) 3, 4, 5, 6, 7, 8, Risk of introduction (all related parameters)</td>
<td>Infection is already present in EU.</td>
</tr>
</table>

Questions 2.1

Question 2.1A the disease is highly transmissible **Answer:** Y ☐ N ☐ na ☐
Question 2.1BC the disease is moderately to highly transmissible **Answer** Y ☐ N ☐ na ☐

<table>
<tr><th>Art. 7 criteria</th><th>Art. 7 parameters</th><th>Assessment of the Art. 7 parameters from the fact-sheet</th></tr>
<tr><td rowspan="2">(a)(vi) the routes and speed of transmission of the disease between animals and,
when relevant, between animals and humans</td><td>(a)(vi) 3 Incidence between animals and, when relevant, between animals and humans</td><td rowspan="2">R0 of 0.25 (95% CI 0.01; 1.95) and 0.24 (95% CI 0.01; 2.11) for transiently infected animals. R of +∞ (95% CI 1.88; +∞) for PI animals (Sarrazin et al., 2014).</td></tr>
<tr><td>(a)(vi) 4 Transmission rate (beta) (from R_0 and infectious period) between animals and, when relevant, between animals and humans</td></tr>
</table>

Question 2.2

Question 2.2AB there be possibilities of airborne or waterborne or vector-borne spread Interpretation: the disease or the infection can be transmitted via airborne or waterborne or vector-borne (mechanical or biological vector) spread

Answer Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(vi) the routes and speed of transmission of the disease between animals and, when relevant, between animals and humans	(a)(vi) 1 types of routes of transmission from animal to animal (horizontal, vertical)	Horizontal: direct (nose to nose) and airborne over short distances in buildings where persistently infected animals are present and indirect via contaminated equipment, facilities and personnel (Gunn, 1993). Spread of BVDV by ambient air or other vehicles involving transiently infected animals has never been demonstrated and is most to be of marginal significance (Lindberg and Houe, 2005). Virus may be shed in the semen of bulls (Rikula et al., 2008), but avoidance of transmission by this route during artificial insemination using semen collected in Member States can be achieved through compliance with the requirements for intra-community trade laid down in Council Directive 2003/43/EC or the OIE guidelines on collection and processing of bovine, small ruminant and porcine semen (OIE, 2016b). BVDV can also be transmitted by embryo transfer, but preliminary evidence indicates that the risk is negligible if in vivo embryos are collected and processed according to OIE guidelines (OIE, 2016a). Adventitious transmission by contaminated live vaccines has also been described (Løken, 1995). Virus has been recovered from biting and non-biting flies following exposure to PI animals in experimental studies, but with one exception onward transmission of the virus has not been demonstrated (Gunn, 1993; Rikula et al., 2008; OIE, 2016b). Vertical: transient infection of a naïve dam during the first third of pregnancy (up to approximately 125 days of gestation) will result in the birth of a persistently infected (PI) calf if the foetus is carried to term. All calves born to PI dams will also be PI.

Question 2.3

Question: 2.3A the disease affects multiple species of kept and wild animals OR single species of kept animals of economic importance **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(i) animal species concerned by the disease	(a)(i) 1 naturally susceptible wildlife species	Evidence for natural susceptibility of wildlife species (Passler and Walz, 2010; Ridpath and Neill, 2016) comes mainly from serological surveys. While these have typically demonstrated the presence of antibodies capable of neutralising BVDV the possibility that they may in some cases indicate exposure to a different, but related, pestivirus cannot be excluded. Those species from which BVDV has been isolated (or viral antigen/RNA detected), confirming their susceptibility are underlined below; otherwise natural susceptibility is based on serological evidence. Where only serological evidence of infection exists, it is recognised that due to the cross-reactive nature of pestiviral antibodies it is possible that these are due to infection with other pestiviral species and do not provide definitive evidence of susceptibility to BVDV (Ridpath and Neill, 2016). **Order Artiodactyla** **Family Bovidae** African Buffalo (*Syncerus caffer*); American Bison (*Bison bison*) (Ridpath and Neill, 2016); Bighorn Sheep (*Ovis canidensis*) (Ridpath and Neill, 2016); Blue Wildebeest (*Connochaetes taurinus*); Bushbuck (*Tragelaphus scriptus*); Chamois (*Rupicapra pyrenaica pyrenaica*) (Ridpath and Neill, 2016); Defrassa Waterbuck (*Kobus ellipsiprymnus*); Duiker (*Sylvicapra grimmia*); Eland (*Taurotragus oryx*) (Passler and Walz, 2010); European Bison (*Bison bonasus*); Gemsbok (or Oryx) (*Oryx gazella*); Hartebeest (*Alcelaphus buselaphus*); Impala (*Aepyceros melampus*); Kudu (*Tragelaphus strepsiceros*); Lechwe (*Kobus leche*); Lichenstein's Hartebeest (*Alcelaphus lichtensteinii*); Mouflon (*Ovis orientalis*); Mountain goat (*Oreamnos americanus*) (Ridpath and Neill, 2016); Nilgai (*Boselaphus tragocamelus*) (Passler and Walz, 2010); Nyala (*Tragelaphus angasi*); Oryx (*Oryx gazelle*); Reedbuck (*Redunca arundinum*); Roan Antelope (*Hippotragus equinus*); Sable Antelope (*Hippotragus niger*); Springbok (*Antidorcas marsupialis*); Topi (*Damaliscus lunatus jimela*); Tsessebe (*Damaliscus lunatus*); Waterbuck (*Kobus ellipsiprymnus*); Wildebeest (*Connochaetes taurinus*) **Family Cervidae** Axis Deer (*Axis axis*) (Passler and Walz, 2010); Barasingha Deer (*Cervus duvaucelii*) (Passler and Walz, 2010); Caribou (*Rangifer tarandus caribou*); Chinese Water Deer (*Hydropotes inermis*) (Ridpath and Neill, 2016); Elk (*Cervus canadensis*); Fallow Deer (*Dama dama*); Grey Brocket Deer (*Mazama gouazoubira*); Moose (*Alces alces*); Mule Deer (*Odocoileus hemionus*) (Ridpath and Neill, 2016); Pampas Deer (*Ozotoceros bezoarticus celer*); Red Deer (*Cervus elephus*) (Ridpath and Neill, 2016); Reindeer

		(*Rangifer tarandus*); Roe Deer (*Capreolus capreolus*) (Ridpath and Neill, 2016); Sika Deer (*Cervus nippon*); White-Tailed Deer (*Odocoileus virginianus*) (Ridpath and Neill, 2016) **Family Giraffidae** Giraffe (*Giraffa camelopardalis*) (Ridpath and Neill, 2016) **Family Antilocapridae** Pronghorn (*Artilocapra americana*) (Ridpath and Neill, 2016) **Family Camelidae** Alpaca (*Vicugna pacos*) (Passler and Walz, 2010); Dromedary (*Camelus dromedarius*) (Passler and Walz, 2010); Guanaco (*Lama guanicoe*); Llama (*Lama glama*) (Passler and Walz, 2010); Vicuna (*Vicugna vicugna*) **Family Suidae** Wart Hog (*Phacochoerus africanus*); Wild Boar (*Sus scrofa*) (Ridpath and Neill, 2016) **Family Traguilidae** Mousedeer (*Tragulus javanicus*) (Grondahl et al., 2003) **Order Lagomorpha** Evidence of susceptibility of Leporidae (order Lagomorpha) has been published. A study in wild rabbits in Germany found low levels of neutralizing antibodies in 40/100 sera (Frölich and Streich, 1998), although attempts at virus isolation were unsuccessful. A survey in the United Kingdom reported a weak positive result by ELISA (and with high levels of non-specific binding) in 3/260 wild rabbits (Grant et al., 2015), with the authors concluding BVDV is not established as an endemic infection of rabbits in the regions of the UK where sampling was conducted (Bachofen et al., 2014; Grant et al., 2015). More recently, 34/94 sera from European hares were found to contain VN antibodies to a ruminant pestiviruses (Colom-Cadena et al., 2016) with none testing positive for viral RNA by real time RTPCR. **Family Leporidae** Rabbit (*Oryctolagus cuniculus*) (Frölich and Streich, 1998; Grant et al., 2015); European hare *(Lepus europaeus*) (Colom-Cadena et al., 2016)
	(a)(i) 2 naturally susceptible domestic species	BVD virus is predominantly a pathogen of cattle, but interspecies transmission can occur following contact with sheep, goats and pigs. In common with cattle, infection of sheep can result in the birth of viable PI lambs. In contrast, the birth of PI offspring appears to be a rare result of *in utero* infection in goats and pigs (Passler and Walz, 2010). **Order Artiodactyla** **Bovidae** Cattle; Sheep; Goats **Family Suidae (Pigs)** Pigs
	(a)(i) 3 experimentally susceptible wildlife species	**Family Leporidae** Rabbit *(Oryctolagus cuniculus)* Challenge of New Zealand White rabbits with BVDV by the intra-venous (IV) and oro-nasal (ON) routes, and via contaminated hay resulted in seroconversion in some or all rabbits in each group in the absence of clinically apparent disease (Bachofen et al., 2014). All whole blood samples collected from each group during serial bleeds were negative by real time RT-PCR, as were oral swabs (providing no evidence for shedding by this route). Tissue samples and buffy coat were collected from rabbits challenged by the IV and ON routes, with some positive results, particularly following IV challenge. Virus isolation was attempted on ileum collected following IV challenge, with positive results. IV challenge of pregnant rabbits did not result in clinical signs or increased rates of abortion or stillbirth (Grant et al., 2015). Relatively few offspring (21%) had evidence of infection by real time RT-PCR at the end of the experiment (maximum 10 days of age), with a proportion of these also seropositive by ELISA. Persistence of infection was therefore not demonstrated.
	(a)(i) 4 experimentally susceptible domestic species	With the exception of rabbits mentioned under (3) a range of non-arteriodactyls, including horses, cats, dogs, guinea pigs, mice and embryonated chicken eggs have previously been reported not to be susceptible to infection with BVDV (Baker et al., 1954), although recent work has suggested that mice can be infected when inoculated by oral and intra-nasal challenge (Seong et al., 2015; Seong et al., 2016).
	(a)(i) 5 wild reservoir species	Lack of strict host-species specificity raises the possibility of reservoir species, but it has been considered that natural infections in species other than cattle and sheep do not represent a disease problem for control programmes in domestic ruminants (Løken and Nyberg, 2013). Passler et al. (2016) propose 4 criteria that a potential wildlife reservoir must satisfy: (1) be susceptible to BVDV, (2) shed BVD (particularly through persistently infected animals), (3) maintain BVDV in the population, (4) have sufficient contact with cattle to allow spillback infections to occur. Applying these criteria to white-tailed deer (*Odocoileus virginiansis*) in the United States, where they have been intensively studied in relation to BVDV, they conclude that they represent a low risk as an important reservoir species in most environments. In general seroprevalence levels are much lower in wildlife (Passler and Walz, 2010) than in cattle in endemic situations, suggesting that the former are spillover hosts rather than

		true reservoir species. Evermann (2006) suggests three proposed population groups for pestiviral infections- cervid, camelid and domestic ruminants, with pestiviruses (which may be distinct from BVDV) circulating within and, under optimum conditions, between these clusters. While this may result in disease, the potential for limited intra-host spread in the new population is suggested to limit the possibility of this leading to an epidemic in the new population. In Europe a number of studies have also investigated the seroprevalence of BVDV in deer, typically to examine their epidemiological importance in the context of national eradication programmes. A sero-survey of free-living deer from regions of Denmark with a relatively high prevalence of cattle herds with a persistent BVD infection status prior to its eradication from cattle found a very low prevalence of cervid infection (Nielsen et al., 2000). The authors concluded that the positive animals were likely to have resulted from transmission from cattle to deer and that transmission among deer or from deer to cattle was highly unlikely and therefore that the possibility of free-living deer being a source of infection for cattle was remote. A serological survey in Norway between 1993 and 2000 found 12.3% roe deer to be seropositive to BVDV, with the authors concluding that pestivirus is endemic in this species (Lillehaug et al., 2003). While they noted the possibility of deer to cattle transmission impacting on eradication and surveillance within the Norwegian eradication programme, this has proven unfounded as demonstrated by the successful completion of the eradication programme (Løken and Nyberg, 2013). The role of wild ruminants, including red and roe deer, in the epidemiology of BVDV infections in domestic livestock in Switzerland was investigated (Casaubon et al., 2012). The authors found that despite regular interactions with farmed ruminants, infection in wild ruminants was sporadic with VN antibodies not found in any of 435 roe deer and detected in only 13/476 red deer (2.7%). They concluded that wildlife was an incidental spillover host rather than a reservoir host for BVDV and as such did not represent a threat to the Swiss national BVDV eradication programme in livestock (Presi and Heim, 2010). A recent study in Belgium (Tavernier et al., 2015) of wild roe deer found only 1.3% seropositive, despite an expanding population and regular contact with livestock, concluding that they do not play an important role in the epidemiology of infection in domestic animals. A similar study was conducted in the south of Spain (Paniagua et al., 2016) where wild ruminant populations have also increased substantially, resulting in the frequent sharing of habitats with domestic livestock. It found only 1 of 892 red deer to be seropositive and concluded that the deer were spillover hosts only and did not represent a risk for domestic ruminants. Another study of sympatric alpine populations of livestock and wild ruminants, including deer in north-west Spain generated similar findings (Fernández-Aguilar et al., 2016). Grant and others (Grant et al., 2015) consider that a wildlife reservoir in the rabbit (*Oryctolagus cuniculus*) poses a small but non-zero risk of re-infection for BVDV-free cattle herds. While this is unlikely to be of epidemiological relevance for most control scenarios it may theoretically play a role in the tail end of an eradication campaign. Detection of VN antibodies to pestiviruses, including BVDV, in European hares *(Lepus europaeus*) has led to the suggestion that they may be a wildlife reservoir, particularly in relation to the Pyrenean chamois (Colom-Cadena et al., 2016).
	(a)(i) 6 domestic reservoir species	Sheep and goats are susceptible to infection with BVDV. While both sheep and goats persistently infected (PI) with BVDV have been described, foetal death and non-viability of lambs are common sequelae of transplacental infection in sheep and viable PI kids are considered a rare result of *in utero* infection in goats, where reproductive failure or gross pathology of infected foetuses are the likely outcome (Løken, 1995; Bitsch et al., 2000; Krametter-Froetscher et al., 2010; Passler and Walz, 2010).

Questions 2.4

Instruction to answer: The answer to the question 2.4CAq can be Y only for diseases affecting aquatic animal species, therefore do not assess this question for diseases affecting terrestrial animal species

Question 2.4A the disease may result in high morbidity and significant mortality rates **Answer** Y ☐ N ☐ na ☐
Question 2.4B the disease may result in high morbidity and in general low mortality **Answer** Y ☐ N ☐ na ☐
Question 2.4C the disease usually does not result in high morbidity and has negligible or no mortality AND often the most observed effect of the disease is production loss **Answer** Y ☐ N ☐ na ☐
Question 2.4CAq the disease may result in high morbidity and usually low mortality AND often the most observed effect of the disease is production loss **Answer** Y ☐ N ☐ na ☐

Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(ii) morbidity and mortality rates	(a)(ii) 1 Prevalence/ Incidence	A series of investigations aimed at assessing the prevalence of BVDV infection have been performed in Europe, from the late seventies and into

<table>
<tr>
<td>of the disease in animal populations</td>
<td></td>
<td>the 21st century, and the results of these at both animal- (Table 1) and herd-levels (Table 2) have been reviewed within the position paper published by the EU Thematic network on control of bovine viral diarrhoea virus (BVDV) (2001).
The general picture is that in many European countries without systematic control in place, or before such measures were implemented, the infection has been/is endemic at a high level with 60-80% of the animals being antibody positive and 1-2% being persistently infected. In many countries, surveys indicated that almost all herds had antibody carriers and approximately half of them had PI animals. However, a few countries had quite a different picture with much lower prevalences. This heterogeneity in the presence of BVDV infection in the absence of systematic control was considered likely to be a reflection of the distribution of risk factors for new BVDV infections and for persistence of the infection in the respective countries.
Where a systematic approach has been adopted in MS, significant progress has been made. The Scandinavian MS Sweden, Finland, Denmark have completed eradication programmes (as has Norway) (Stahl and Alenius, 2012; Løken and Nyberg, 2013; Foddai et al., 2014; Norström et al., 2014), while national or regional programmes are under way and have reduced the prevalence of PI births in a number of other Member States, including Austria, Germany, Ireland, Austria, Scotland and Belgium (Rossmanith et al., 2010; Schirrmeier et al., 2012; Clegg et al., 2016; Duncan et al., 2016; Ribbens et al., 2016) and in Switzerland (Presi et al., 2011).
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<td>(a)(ii) 2 Case-morbidity rate</td>
<td>The case morbidity rate for acute (transient) infections varies with a range of factors, including the age of the animal, its immune status and its reproductive state (Lanyon et al., 2014). The majority of acute infections are considered subclinical. However infection of a BVDV naïve animal results in a transient viraemia which can be associated with short-term leukopenia, lymphopenia and/or thrombocytopenia, apoptosis in the thymus, and pyrexia. The resultant immunosuppression, particularly in calves, can allow other infectious agents to become established, or allow the recrudescence of existing infections resulting in enteric or respiratory disease.
Infection of naïve breeding animals may have a range of negative outcomes depending on the stage of reproduction, including fertilisation failure, early embryonic death, abortion, congenital defects and the birth of persistently infected (PI) offspring which may be weak, undersized and ill-thrifty. Acute infection of sexually active bulls results in a reduction in sperm density and motility, plus an increase in sperm abnormalities (Lanyon et al., 2014).
Following the emergence of BVDV II in North America, much higher case morbidity rates (and mortality rates) were reported (Carman et al., 1998). The within-herd abortion rate was 44% (3-83%). The mortality rate was 53% (3-83%) for animals under two years of age and 9% (2-26%) for older animals. A recent study of BVDV type 2c in Germany reported a case-fatality rate of up to 60% and mortality in outbreak farms varied between 2.3 and 29.5% (Gethmann et al., 2015).
Persistent infections
PI animals have been shown to be significantly smaller than non-PI animals (Table 3). The annual incidence risk of dying or being slaughtered due to unthriftiness was calculated as 0.28 and 0.31 among 34 PI animals in 10 Danish dairy herds (Houe, 1993).
Observational studies on the impact of infection with BVDV on health and production parameters have been reviewed within the position paper of the EU Thematic network on control of bovine viral diarrhoea virus (BVDV) (2001) and the results are reproduced below (Table 3, see “Tables” section).</td>
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<tr>
<td>(b)(i) impact of the disease on agricultural and aquaculture</td>
<td>(b)(i) 1 Number of MSs where the disease is present</td>
<td>As noted above in (a)(viii)1 (see Question A(iv)), a number of member states have eradication programmes underway. However currently only Denmark and Sweden have completed eradication and therefore the disease is considered still present in all other MS.</td>
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<table>
<tr>
<td>production and other parts of the economy</td>
<td>(b)(i) 2 Proportion of production losses (%) by epidemic/endemic situation (milk, growth, semen, meat, etc.)</td>
<td>
Health and production losses from observational studies are summarized in Table 3. Losses attributable to BVD arise from 3 main sources- reproductive losses, immunosuppression in calves and persistently infected animals (Gunn et al., 2004). Estimates of economic/financial losses due to BVDV associated with initial outbreaks, the average losses at herd level and at national livestock level have been reviewed in the Report on the EU Thematic Network on control of BVDV and the results are summarized in Tables 4, 5, and 6 (EU Thematic network on control of bovine viral diarrhoea virus (BVDV), 2001). More recent data are provided after each table where relevant.
Table 4: Summary of financial-economic losses due to initial outbreaks of BVDV.
<table>
<tr><th>Country</th><th>Herd type</th><th>Cost/cow (range)</th><th>Year</th></tr>
<tr><td>UK</td><td>Dairy</td><td>£137</td><td>1999</td></tr>
<tr><td>UK</td><td>Dairy</td><td>£39-92</td><td>1986</td></tr>
<tr><td>Netherlands</td><td>Dairy</td><td>€45</td><td>1998</td></tr>
<tr><td>Netherlands</td><td>Dairy</td><td>€19-130</td><td>1990</td></tr>
<tr><td>Denmark</td><td>Dairy</td><td>€30-89</td><td>1994</td></tr>
<tr><td>Canada</td><td>Dairy</td><td>€240-600</td><td>1998</td></tr>
</table>
Table 5: Summary of average financial-economic losses due at herd level due to BVDV.
<table>
<tr><th>Country</th><th>Herd type</th><th>Cost/cow (range)</th><th>Year</th></tr>
<tr><td>Canada</td><td>Dairy</td><td>€34</td><td>2002</td></tr>
<tr><td>UK</td><td>Dairy</td><td>£31</td><td>2000</td></tr>
<tr><td>UK</td><td>Beef</td><td>£32-43</td><td>2004</td></tr>
<tr><td>France</td><td>Dairy</td><td>€60-100</td><td>2004</td></tr>
</table>
The variation in the economic impact of BVDV at dairy farm level in a number of MS arising from uncontrolled output following introduction to a BVDV-naıve herd with in year 1 of a 10- year epidemic represented 22, 7, 8, 5, 8 and 20% of the BVDV-free annuity for the UK, Northern Portugal, Holland, Norway, Italy and Germany, respectively (Gunn et al., 2005).
Total loss attributable to infection with BVDV in New Zealand dairy herds was estimated at NZ$87 per cow and year in affected herds, and NZ$44.5 million per year overall, based on an estimated 14.6% affected herds (Heuer et al., 2007).
The maximum annual output losses per cow in 50-cow suckler (cow-calf) beef herds in Scotland where the herd was either initially BVDV-free or of unknown status were estimated at £38.71 and £28.22 respectively (Stott et al., 2012).
The average annuity equivalent of unchecked losses due to BVDV infection and re-infection in typical British hill suckler (cow-calf) enterprises over a 10 year disease ranged from almost £0/cow to approximately £40/cow/year, depending on the initial disease status of the herd, the initial source of virus, the probability and source of further infection, the probability of virus transmission within the herd and herd size (Gunn et al., 2004).
Table 6: Summary of financial-economic losses at the national livestock sector level.
<table>
<tr><th>Country</th><th>National loss</th><th>Cost/cow (range)</th><th>Year</th></tr>
<tr><td>UK</td><td>£5-30 Million</td><td></td><td>1999</td></tr>
<tr><td>UK</td><td>£40 Million</td><td></td><td>2003</td></tr>
<tr><td>Denmark</td><td>€20 Million/1M calvings</td><td></td><td>1993</td></tr>
<tr><td>Denmark</td><td>52 Million/1M calving (high virulence strain)</td><td></td><td>1993</td></tr>
</table>
Based on data for 1993, the annual financial loss due to BVD in Norway in the absence of control was estimated at approximately NOK 32.5 million (Valle et al., 2005).
The annual losses to the Irish cattle industry due to BVDV were estimated at €102 million (Stott et al., 2012).
Using an economic welfare model, the net discounted economic gain for Scotland of eradicating BVD from the Scottish dairy herd was estimated at £47 million over a 10-year eradication period (Weldegebriel et al., 2009).
The annual cost of BVDV in the Australian cattle population was estimated to be AUS $57.9 million (Lanyon and Reichel, 2014).
</td>
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</table>

Questions 3

Question 3C the disease has a zoonotic potential with significant consequences for public health or possible

significant threats to food safety **Answer** Y ☐ N ☐ na ☐		
Question 3B the disease has a zoonotic potential with significant consequences on public health, including epidemic potential OR possible significant threats to food safety **Answer** Y ☐ N ☐ na ☐		
Question 3A the disease has a zoonotic potential with significant consequences on public health, including epidemic or pandemic potential OR possible significant threats to food safety **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(a)(iii) zoonotic character of the disease	(a)(iii) 1 report of zoonotic human cases	BVDV is not considered zoonotic, although the ability of BVDV to replicate in human cell lines has been reported in some studies and there are limited reports of detection of virus, viral RNA or antigen in human samples (Giangaspero et al., 1997; Walz et al., 2010; Bratcher et al., 2012).
(a)(vi) the routes and speed of transmission of the disease between animals and, when relevant, between animals and humans	(a)(vi) 2 types of routes of transmission between animals and humans (direct and indirect including foodborne)	Not relevant.
	(a)(vi) 3 Incidence between animals and, when relevant , between animals and humans	R0 of 0.25 (95% CI 0.01; 1.95) and 0.24 (95% CI 0.01; 2.11) for transiently infected animals. R of +∞ (95% CI 1.88; +∞) for PI animals (Sarrazin et al., 2014).
	(a)(vi) 4 Transmission rate (beta) (from R_0 and infectious period) between animals and, when relevant ,between animals and humans	
(b)(ii) Impact of the disease on human health	(b)(ii) 5 Disability-adjusted life year (DALY)	Not applicable.
	(b)(ii) 6 Availability of medical treatment and their effectiveness (therapeutical effect and any resistance)	
	(b)(ii) 7 Availability of vaccines and their effectiveness (reduced morbidity)	
(c) potential to generate a crisis situation and its potential use in bioterrorism	(c) 1 listed in OIE/CFSPH classification of pathogens	CFSPH (http://www.cfsph.iastate.edu/DiseaseInfo/) No OIE (http://www.oie.int/animal-health-in-the-world/oie-listed-diseases-2016/) Yes
	(c) 2 listed in the Encyclopaedia of Bioterrorism Defense of Australia Group	(http://www.australiagroup.net/en/human_animal_pathogens.html) No
	(c) 3 included in any other list of potential bio- agro-terrorism agents	None identified.

Questions 4

Question 4AB the disease in question has a significant impact on the economy of the Union, causing substantial costs, mainly related to its direct impact on the health and productivity of animals Interpretation: due to the substantial costs related to the disease's direct impact on the health and productivity of animals, the disease has a significant impact on the economy **Answer** Y ☐ N ☐ na ☐
Question 4C the disease has a significant impact on the economy of the Union, mainly related to its direct impact on certain types of animal production systems Interpretation: due to its direct impact on certain types of animal production systems, the disease has a significant impact on the economy **Answer** Y ☐ N ☐ na ☐

<table>
<tr><th>Art. 7 criteria</th><th>Art. 7 parameters</th><th>Assessment of the Art. 7 parameters from the fact-sheet</th></tr>
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<tr><td>(a)(ii) 2 Case-morbidity rate (% clinically diseased animals out of infected ones)</td><td>The case morbidity rate for acute (transient) infections varies with a range of factors, including the age of the animal, its immune status and its reproductive state (Lanyon et al., 2014). The majority of acute infections are considered subclinical. However infection of a BVDV naïve animal results in a transient viraemia which can be associated with short-term leukopenia, lymphopenia and/or thrombocytopenia, apoptosis in the thymus, and pyrexia. The resultant immunosuppression, particularly in calves, can allow other infectious agents to become established, or allow the recrudescence of existing infections resulting in enteric or respiratory disease.
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<tr><td rowspan="2">(b)(i) impact on agricultural and aquaculture production and other parts of the economy</td><td>(b)(i) 1 Number of MSs where the disease is present</td><td>As noted above in (a)(viii)1 (see Question A(iv)), a number of member states have eradication programmes underway. However currently only Denmark and Sweden have completed eradication and therefore the disease is considered still present in all other MS.</td></tr>
<tr><td>(b)(i) 2 Proportion of production losses (%) by</td><td>Health and production losses from observational studies are summarized in Table 3. Losses attributable to BVD arise from 3 main sources- reproductive</td></tr>
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	epidemic/endemic situation (milk, growth, semen, meat, etc.)	losses, immunosuppression in calves and persistently infected animals (Gunn et al., 2004). Estimates of economic/financial losses due to BVDV associated with initial outbreaks, the average losses at herd level and at national livestock level have been reviewed in the Report on the EU Thematic Network on control of BVDV and the results are summarized in Tables 4, 5, and 6 (EU Thematic network on control of bovine viral diarrhoea virus (BVDV), 2001). More recent data are provided after each table where relevant.

Table 4: Summary of financial-economic losses due to initial outbreaks of BVDV.

Country	Herd type	Cost/cow (range)	Year
UK	Dairy	£137	1999
UK	Dairy	£39-92	1986
Netherlands	Dairy	€45	1998
Netherlands	Dairy	€19-130	1990
Denmark	Dairy	€30-89	1994
Canada	Dairy	€240-600	1998

Table 5: Summary of average financial-economic losses due at herd level due to BVDV.

Country	Herd type	Cost/cow (range)	Year
Canada	Dairy	€34	2002
UK	Dairy	£31	2000
UK	Beef	£32-43	2004
France	Dairy	€60-100	2004

The variation in the economic impact of BVDV at dairy farm level in a number of MS arising from uncontrolled output following introduction to a BVDV-naıve herd with in year 1 of a 10- year epidemic represented 22, 7, 8, 5, 8 and 20% of the BVDV-free annuity for the UK, Northern Portugal, Holland, Norway, Italy and Germany, respectively (Gunn et al., 2005).
Total loss attributable to infection with BVDV in New Zealand dairy herds was estimated at NZ$87 per cow and year in affected herds, and NZ$44.5 million per year overall, based on an estimated 14.6% affected herds (Heuer et al., 2007).
The maximum annual output losses per cow in 50-cow suckler (cow-calf) beef herds in Scotland where the herd was either initially BVDV-free or of unknown status were estimated at £38.71 and £28.22 respectively (Stott et al., 2012).
The average annuity equivalent of unchecked losses due to BVDV infection and re-infection in typical British hill suckler (cow-calf) enterprises over a 10 year disease ranged from almost £0/cow to approximately £40/cow/year, depending on the initial disease status of the herd, the initial source of virus, the probability and source of further infection, the probability of virus transmission within the herd and herd size (Gunn et al., 2004).

Table 6: Summary of financial-economic losses at the national livestock sector level.

Country	National loss	Cost/cow (range)	Year
UK	£5-30 Million		1999
UK	£40 Million		2003
Denmark	€20 Million/1M calvings		1993
Denmark	52 Million/1M calving (high virulence strain)		1993

Based on data for 1993, the annual financial loss due to BVD in Norway in the absence of control was estimated at approximately NOK 32.5 million (Valle et al., 2005).
The annual losses to the Irish cattle industry due to BVDV were estimated at €102 million (Stott et al., 2012).
Using an economic welfare model, the net discounted economic gain for Scotland of eradicating BVD from the Scottish dairy herd was estimated at £47 million over a 10-year eradication period (Weldegebriel et al., 2009).
The annual cost of BVDV in the Australian cattle population was estimated to be AUS $57.9 million (Lanyon and Reichel, 2014).

Question 5a

Question 5a the disease has a significant impact on society, with in particular an impact on labour markets
Interpretation: the disease has a significant impact on society with (as the most important but not the only one) an impact on labour markets
Answer Y ☐ N ☐ na ☐

Art. 7 criteria	Art. 7 parameters	Assessment of the Art. 7 parameters from the fact-sheet

<table>
<tr>
<td rowspan="2">(b)(i) impact on agricultural and aquaculture production and other parts of the economy</td>
<td>(b)(i) 1 Number of MSs where the disease is present</td>
<td>As noted above in (a)(viii)1 (see Question A(iv)), a number of member states have eradication programmes underway. However currently only Denmark and Sweden have completed eradication and therefore the disease is considered still present in all other MS.</td>
</tr>
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<td>(b)(i) 2 Proportion of production losses (%) by epidemic/endemic situation (milk, growth, semen, meat, etc.)</td>
<td>Health and production losses from observational studies are summarized in Table 3. Losses attributable to BVD arise from 3 main sources- reproductive losses, immunosuppression in calves and persistently infected animals (Gunn et al., 2004). Estimates of economic/financial losses due to BVDV associated with initial outbreaks, the average losses at herd level and at national livestock level have been reviewed in the Report on the EU Thematic Network on control of BVDV and the results are summarized in Tables 4, 5, and 6 (EU Thematic network on control of bovine viral diarrhoea virus (BVDV), 2001). More recent data are provided after each table where relevant.
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Question 5b

Question 5b the disease has a significant impact on animal welfare, by causing suffering to large numbers of animals Interpretation: due to the suffering of large numbers of animals caused by the disease, the disease has a significant impact on animal welfare **Answer** Y ☐ N ☐ na ☐		
Art. 7 criteria	**Art. 7 parameters**	**Assessment of the Art. 7 parameters from the fact-sheet**
(b)(iii) impact of the disease on animal welfare	(b)(iii) 1 severity of clinical signs at case level and related level and duration of impairment	Clinical signs may vary from inapparent to death, depending on a variety of factors including whether the animal is acutely or persistently infected. *Acute (transient) infections* Transient infection of naïve female breeding animals may have a range of negative outcomes depending on the stage of reproduction, including fertilisation failure, early embryonic death, abortion, congenital defects and the birth of persistently infected (PI) offspring which may be weak, undersized and ill-thrifty; infection of naïve bulls may result in decreased sperm motility and density and increase levels of sperm abnormalities (Lanyon et al., 2014). Other clinical signs associated with acute infection include pyrexia, diarrhoea, decreased milk yield, sudden death and haemorrhagic syndrome (Ridpath et al., 2013; Lanyon et al., 2014; Gethmann et al., 2015). However the majority of acute infections are considered subclinical, with seroconversion and recovery occurring 2-3 weeks post infection (Ridpath et al., 2013; Lanyon et al., 2014). Even in the absence of clinical signs infection of a BVDV naïve animal results in a transient viraemia which can be associated with short-term leukopenia, lymphopenia and/or thrombocytopenia, apoptosis in the thymus, and pyrexia. The resultant immunosuppression, particularly in calves, can allow other infectious agents to become established, or allow the recrudescence of existing infections resulting in enteric or respiratory disease which may be fatal. Recent work demonstrating a significant reduction in thymic size following challenge of calves with both low and high virulence BVDV strains, accompanied by a significant depletion of thymic cortex, suggests that transient infection of neonatal calves may have long-term immunosuppressive effects (Ridpath et al., 2013). Following the emergence of BVDV II in North America, much higher case morbidity rates (and mortality rates) associated with primary infection were reported (Carman et al., 1998). The within-herd abortion rate was 44% (3-83%). The mortality rate was 53% (3-83%) for animals under two years of age and 9% (2-26%) for older animals. A recent study of BVDV type 2c in Germany reported a case-fatality rate of up to 60% while mortality in outbreak farms varied between 2.3 and 29.5% (Gethmann et al., 2015). *Persistent infections* PI animals can be clinically healthy, but some may appear small, weak and ill-thrifty, showing decreased weight gain, stunted growth and chronic ill thrift. PI animals are considered more susceptible to secondary infections (Lanyon et al., 2014) leading to poor survivability of most PI animals. The annual incidence risk of dying or being slaughtered due to unthriftiness was calculated as 0.28 and 0.31 among 34 PI animals in 10 Danish dairy herds (Houe, 1993). In addition, PI animals are uniquely to susceptible to developing mucosal disease, which is inevitably fatal (Lanyon et al., 2014), with death occurring a few days to a few weeks following its onset.
(a)(ii) morbidity and mortality rates of the disease in animal populations	(a)(ii) 2 Case-morbidity rate (% clinically diseased animals out of infected ones)	The case morbidity rate for acute (transient) infections varies with a range of factors, including the age of the animal, its immune status and its reproductive state (Lanyon et al., 2014). The majority of acute infections are considered subclinical. However infection of a BVDV naïve animal results in a transient viraemia which can be associated with short-term leukopenia, lymphopenia and/or thrombocytopenia, apoptosis in the thymus, and pyrexia. The resultant immunosuppression, particularly in calves, can allow other infectious agents to become established, or allow the recrudescence of existing infections resulting in enteric or respiratory disease. Infection of naïve breeding animals may have a range of negative outcomes depending on the stage of reproduction, including fertilisation failure, early embryonic death, abortion, congenital defects and the birth of persistently infected (PI) offspring which may be weak, undersized and ill-thrifty. Acute infection of sexually active bulls results in a reduction in sperm density and motility, plus an increase in sperm abnormalities (Lanyon et al., 2014). Following the emergence of BVDV II in North America, much higher case morbidity rates (and mortality rates) were reported (Carman et al., 1998). The within-herd abortion rate was 44% (3-83%). The mortality rate was 53% (3-83%) for animals under two years of age and 9% (2-26%) for older animals. A recent study of BVDV type 2c in Germany reported a case-fatality rate of up to 60% and mortality in outbreak farms varied between 2.3 and 29.5%

		(Gethmann et al., 2015). *Persistent infections* PI animals have been shown to be significantly smaller than non-PI animals (Table 3). The annual incidence risk of dying or being slaughtered due to unthriftiness was calculated as 0.28 and 0.31 among 34 PI animals in 10 Danish dairy herds (Houe, 1993). Observational studies on the impact of infection with BVDV on health and production parameters have been reviewed within the position paper of the EU Thematic network on control of bovine viral diarrhoea virus (BVDV) (2001) and the results are reproduced below (Table 3, see "Tables" section).

Question 5c

Question 5c the disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it

Interpretation: due to the direct impact of the disease OR to the impact of the measures taken to control it, the disease has a significant impact on the environment

Answer: Y ☐ N ☐ na ☐

Art. 7 criteria	Art. 7 parameters	Assessment of the Art. 7 parameters from the fact-sheet
(b)(iv) impact of the disease on biodiversity and the environment	(b)(iv) 1 endangered wild species affected: listed species as in CITES and/or IUCN list	The CITES list contains a number of species in the Families Antilocapridae, Bovidae, Cervidae, Camelidae and Suidae, within the Order Arteriodactyla (https://www.cites.org/eng/app/appendices.php, accessed 17.10.2016). However there is no specific data confirming their susceptibility to infection with BVDV (although a related pestivirus has been isolated from pronghorn (Ridpath and Neill, 2016).
	(b)(iv) 2 Mortality in wild species	Despite abundant evidence that pestiviruses currently circulate in wildlife populations, the full impact of exposure and prevalence of these infections are largely unknown (Ridpath and Neill, 2016).
(e)(iv) the impact of disease prevention and control measures	(e)(iv) 2 Mortality in wild species	Control measures are not anticipated to result in mortality in wild species.

Question 5d

Question 5d The disease has a significant impact on the long term on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds

Interpretation: the consequences of the impact of the disease can even lead to the possible disappearance or long-term damage of endangered species or breeds

Answer Y ☐ N ☐ na ☐

Art. 7 criteria	Art. 7 parameters	Assessment of the Art. 7 parameters from the fact-sheet
(b)(iv) impact of the disease on biodiversity and the environment	(b)(iv) 1 endangered wild species affected: listed species as in CITES and/or IUCN list	The CITES list contains a number of species in the Families Antilocapridae, Bovidae, Cervidae, Camelidae and Suidae, within the Order Arteriodactyla (https://www.cites.org/eng/app/appendices.php, accessed 17.10.2016). However there is no specific data confirming their susceptibility to infection with BVDV (although a related pestivirus has been isolated from pronghorn (Ridpath and Neill, 2016).
	(b)(iv) 2 Mortality in wild species	Despite abundant evidence that pestiviruses currently circulate in wildlife populations, the full impact of exposure and prevalence of these infections are largely unknown (Ridpath and Neill, 2016).
	(b)(iv) 3 Capacity of the pathogen to persist in the environment and cause mortality in wildlife	BVDV does not survive for extend periods in the environment (see (a)(v)4). Despite abundant evidence that pestiviruses currently circulate in wildlife populations, the full impact of exposure and prevalence of these infections are largely unknown (Ridpath and Neill, 2016).

Question D

Question D The risk posed by the disease in question can be effectively and proportionately mitigated by measures concerning movements of animals and products in order to prevent or limit its occurrence and spread

Answer Y ☐ N ☐ na ☐

Art. 7 criteria	Art. 7 parameters	Assessment of the Art. 7 parameters from the fact-sheet
(d)(v) feasibility, availability and effectiveness of restrictions on the movement of animals and products, as control measure	(d)(v) 1 available restriction movement measures	The key restriction measure relates to the movement of PI animals. This is readily available through prior testing. Identification of Trojan dams by diagnostic testing prior to movement is not available, but has been addressed in eradication programmes by applying restrictions at herd level for a period following removal of PI animals (EU Thematic network on control of bovine viral diarrhoea virus (BVDV), 2001). Movement of transiently infected animals is considered a much lower risk but is more

		difficult to address.
	(d)(v) 2 effectiveness of restriction of animal movement in preventing the between farm spread	Prevention of movement of PI animals is considered key to control. The effectiveness of movement controls are clearly dependent on the level of uptake/industry engagement, being most effective in the context of systematic control and least effective when participation/involvement is voluntary (Lindberg et al., 2006).
	(d)(v) 3 feasibility of restriction of animal movement	PI animals comprise a small percentage of the population (Houe, 1999) and therefore restricting their movement is feasible. Restricting movements of pregnant females from herds where BVDV has been identified until sufficient time has elapsed to minimize the possibility of the sale of pregnant animals carrying PI calves is also feasible, but is more disruptive to trade and will affect a larger proportion of animals. Measures to prevent movement of TI animals are likely to have a greater impact still, although the duration of the measure at herd level is likely to be much shorter.

Tables

Table 1: Animal-level prevalence of BVDV (seropositivity and persistent infection) in EU member states (reproduced from Table 6 of the EU Thematic network on control of bovine viral diarrhoea virus (BVDV) (2001))

Country /Region	Study Period	Sampling Frame	**Sampling Method**		**Sample Size**		**Prevalence (AB)**		**Prevalence (Virus)**		**Vaccination**	**Reference**
			Herds	**Animals**	**Herds**	**Animals**	**Herd Level Number (%)**	**Animal Level Number (%)**	**Herd Level Number (%)**	**Animal Level Number (%)**		
Belgium	...	S. Belgium, Belgium White Blue and Friesian Holstein	Some herds suspicious or had poor diagnosis (42.5%)	All animals in herd	61	9685	61 (100)	6344 (65.5)	27 (44.3)	73 (0.75)	Some vaccination (not considered important)	Schreiber et al. (1999)
Denmark	1988	Jutland in Denmark; Dairy herds	Representative NPE	All per farm	19	2570	19 (100)	1655 (64.4)	10 (52.6)	35/28 (1.4/1.1)	No Vaccination	Sarrazin et al. (2013)
Germany	...	N. Germany. Breeding animals	Exporting herds	Pregnant NPE	>1000	2317	-	-	-	21 (0.9 [viraemic])	...	Houe and Meyling (1991)
Germany	1993-94	Lower Saxony	NPE	Up to 3yrs	329	20,253	-	-	149 (45.3)	425 (2.1)	Some vaccination	Liess et al. (1987)
Lithuania	1997-2001	27 regions	Some suspect herds	Some suspect herds	147	3798	103 (70.1)	2211 (58.2)	-	-	No Vaccination	Frey et al. (1996)
Netherlands	...	9 herds participating in BHV1 vaccination trial. >100 involved in international trade	-	Random	>100	1798	-	1169 (65)	-	-	...	Szabára et al. (2016)
Norway	1984-86	Wide geographic representation. Norwegian	Representative NPE	Random, >2 yrs.	187	1133	52 (28)	210 (18.5)	-	-	No Vaccination	Cowley et al. (2012)

		Red cattle.										
Poland	…	Bulls at artificial insemination centres	-	> 6 months old	-	175	-	150 (86)	-	-	…	(Mockeliūnas et al., 2004)
Poland	…	Bulls at artificial insemination centres	-	> 6 months old	-	219	-	-	-	-5/2 (2.3 / 0.9)	…	(Kramps et al., 1999)
Scotland	1992-93	S.W. Scotland breeding bulls on dairy, beef or mixed farms (5 bulls from dealers)	-	Random	78	109	-	85 (78)	-	-	…	(Løken et al., 1991)
Slovakia	2000	6-12 mo. old	…	Random	45	1295	…	894 (69.0)	-	-	Animals not vaccinated	(Polak and Zmudzinski, 1999)
Slovakia	2000	6-12 mo. old	Herds with 70-98% seropositivity	Random	13	462***	-	-	…	6 (1.3)	Animals not vaccinated	(Polak and Zmudzinski, 1999)
Slovenia	1996	5 regions breeding herds	-	All animals in herd	274	6892	-	1144	-	-	…	Wernicki et al. (2015)
Spain	1997	Asturias region. Dairy herds	Random / stratified NPE	> 1 yr old. 20 herds; all animals. 8 herds; random.	28	529	24 (86)	112 (21.1 [CI: 17.8-24.6])	-	-	No vaccination	Lipowski (2014)
Sweden	1987	County of Kopparberg. Dairy herds	Random	All lactating cows	15	413	11 (73)	190 (46)	-	-	No Vaccination	McGowan and Murray (1999)
Switzerland	1994-95	Canton of St Gallen	Random	Cows and heifers (all)	95	2892	95	2421	-	-	…	Vilcek et al. (2003)
Switzerland	1995	Canton of St Gallen, 7 Alpine pastures. Swiss Braunvieh cattle. Dairy herds	Invited by cantonal veterinary officer	Animals prior to pasture; 98% were replacement cattle. NPE	149	990	-	627 (63.3)	-	9 (0.9)	…	Vilcek et al. (2003)
Switzerland	1993-94	Dairy herds	Random (at least 5 cows)	All cows	113	1635	112 (99.1)	1174 (72)	-	-	…	Grom and Barlic-Maganja (1999)
United Kingdom	1974-75	England and Wales	3 herds in each country	12 per herd representing a range of ages	133	1593	-	988 (62)	-	-	…	Mainar-Jaime et al. (2001)
United	198	…	…	Beef	-	924	-	-	-	7/4	…	Fernánde

Kingdom	0-85			calves 2-4 mo. old. Cows 2-3 yr old. Gnotobiotic calves. NPE						(0.8/0.4*)		z-Aguilar et al., 2016
United Kingdom	1985-86	England and Wales	-	Submissions of > 10 samples to CVL	-	18,759	-	12,175 (64.9)	-	-	…	Fernández-Aguilar et al., 2016
United Kingdom	1986	Central Veterinary Laboratory	-	Submissions of > 10 samples to CVL	-	3151	-	-	-	57 (1.8 viraemic)	…	Niskanen et al. (1991)

Note: Some numbers may have been calculated from percentages given in publications
General legends and abbreviations in tables:
- Information not measured or applicable
… Information not available in the paper
NPE No past evidence, meaning that herds were not selected based on past evidence of infection (unknown BVD status)
AI: Artificial insemination centres
BHV: Bovine herpes virus
*First number: Viraemic. Second number: Known to be PI
**Not all animals in each herd are tested (i.e. herd prevalence is underestimated)
*** Only 84 antibody negative tested

Table 2: Herd-level prevalence of BVDV (seropositivity and persistent infection) in EU member states (reproduced from Table 7 of the EU Thematic network on control of bovine viral diarrhoea virus (BVDV) (2001))

Country / Region	**Study Period**	**Sampling Frame**	**Sampling method**	**Sample size (Herds)**	**Sample**	**Herd prevalence AB Number (%)**	**Herd prevalence Virus/act. Inf Number (%)**	**Vaccination**	**Reference**
Austria	1996-98	Nieder-Osterreich. All breeding herds.	Stepwise: A; milk, B; Spot test, and C; All animals NPE	A: 5024 B: 512 C: 154	Milk Spot test All animals	-	50 (1.0) (PI animals were identified)	…	Rossmanith and Deinhofer (1998)
Denmark	1994	Dairy herds	All herds	16,113	Bulk milk	-	6284 (39) (suspected to have PI)	No vaccination	Bitsch and Rønsholt (1995)
Estonia	1993-95 1997-98 1999-00	Dairy cows with ≥20 cows	Representative random sample	328 363 351	Bulk milk and/or young stock test		152 (46) 65 (18) (suspected to have PI)	No vaccination	Viltrop et al. (2002)
Finland	1993	Dairy herds	All herds (>98%)	34,115	Bulk milk	342 (1)	-	No vaccination	Nuotio et al. (1999)
England and Wales	1996	9 regions. Dairy herds	Systemic random	1070	Bulk milk	1021 (95.4)	701 (65.5)	No vaccination	Paton et al. (1998)

		>40 cows							
Norther n Ireland	1999	Dairy herds	From the largest milk processor	929	Bulk milk	920 (99) (OD>0.04)	461 (49.6) OD>=0.55)	…	Graham et al. (2001)
Norway	1993	Dairy herds	All herds	26,430	Bulk milk	9779 (37) (OD>0.05)	1877 (7.1) OD>0.55	No vaccination	Waage et al. (1996)
Sweden	1993	Dairy herds	Majority of dairy herds	14,463	Bulk milk	-	7376 (51%) (OD>0.55)	No vaccination	Alenius et al. (1997)

*Note that the antibody detection methods vary between countries as do the cut offs when a herd is considered to have antibody carriers or PI animals. Prevalences are therefore just indicative of the level and not directly comparable between countries.

Table 3: Health and production effects of BVDV under different production settings in Europe (observational studies) (reproduced from Table 5 of the EU Thematic network on control of bovine viral diarrhoea virus (BVDV) (2001))

Country/region	Outcome variable	BVD condition (risk or exposure factor)	Measure	Number of animals/herd	Size of measure	Reference
Holland	Reduced milk yield with >10%	Seroconversion vs no seroconversion	OR	22 seroconverted 32 not seroconverted	11.5 (CI 3.0-43.5) for more than 10% reduction in milk yield *	Moerman et al. (1994)
Holland	Moderate or severe broncho-pneumonia	Receiving colostrum from AB negative dams (A) vs. AB positive dams (B).	Incidence risk	AB-neg colostrum: 44 calves AB-pos colostrum: 86 calves	A: 68.2% developed symptoms B: 40.7% developed symptoms	Moerman et al. (1994)
Sweden	Heart girth	PI calves vs. non-PI calves	Cm at 80 days Cm at 180 days	8 PI 13 non-PI	80 days: PI: 96.3 ±4.7cm; non-PI: 100.5 ±2.3cm PI: 123.3 ±8.8cm; non-PI: 130.2 ± 2.0cm	Larsson et al. (1994)
Sweden	Mastitis	Recent herd infection compared to low level of A in bulk ilk	OR	91 herds (7 with recent inf. And 84 without inf.)	1.8 (CI: 1.7-2.8)	Niskanen et al. (1995)
Sweden	Miscellaneous diseases	Recent herd infection compared to low level of A in bulk ilk	OR	91 herds (7 with recent inf. And 84 without inf.)	2.8 (CI: 1.7-4.4)	Niskanen et al. (1995)
Sweden	Retained placenta	Recent herd infection compared to low level of A in bulk ilk	OR	91 herds (7 with recent inf. And 84 without inf.)	2.8 (CI: 1.6-4.7)	Niskanen et al. (1995)
Sweden	Oestrus stimulating treatment	Long-term herd infection compared to low level of AB in	OR	142 herds (58 with inf. and 84 without)	1.8 (CI: 1.3-2.6)	Niskanen et al. (1995)

		bulk milk				
Sweden	Calving interval	Lomg-term herd infection compared to low level of AB in bulk milk	Days	142 herds (58 with inf. and 84 without)	Long-term inf.: 394 (389-398) Non-infected: 385 (381-389)	Niskanen et al. (1995)
Sweden	Average annual milk yield per cow	Herds with detection of virus vs. free herds	Kg ECM	319 case herds 2270 control herds	Interaction with herd size: 30 cows: -142kg (CI: -281 - -3) less in case herds 40 cows: -198kg (CI: -330 - -66) 50 cows: -254kg (-389 - -119)	Lindberg and Emanuelson (1997)
Sweden	Average bulk milk somatic cell count x 1000	Herds with detection of virus vs. free herds	Cells/ml	319 case herds 2270 control herds	10,300 (1,600 – 18,900) cells/ml more in case herds.	Lindberg and Emanuelson (1997)
Norway	Clinical mastitis	Herds with rise in bulk milk antibodies vs. herds with continuous low level	Incidence rate	300 exposed herds vs. 13,671 non-exposed	7.1% (CI: 0.2-11.4) increase in exposed herds	Waage (2000)
Switzerland	Foetal death (mid-term abortion)	Seroconversion vs. no seroconversion	OR oand PAF	62 cases 952 controls	3.10 (CI: 1.16-8.29), PAF 7% (CI: 2.4-14)	Rüfenacht et al. (2001)
France	Late return to service (after 25 days)	Past-infected-recently-recovered vs. Not recently infected	RR	150,854 AI 122,697 cows 6,149 herds	1.03 (CI: 1.01-1.05)	Robert et al. (2004)
France	Late return to service (after 25 days)	Past steadily infected vs. Not recently infected	RR	150,854 AI 122,697 cows 6,149 herds	1.11 (CI: 1.05-1.17)	Robert et al. (2004)
France	Late return to service (after 25 days)	Recently infected vs. Not recently infected	RR	150,854 AI 122,697 cows 6,149 herds	1.11 (CI: 1.02-1.22)	Robert et al. (2004)
Holland	Prevalence of animals with clinical signs	Transient infection	%	136 cattle (1 herd)	7 of all animals with transient infection showed clinical signs (5%)	Moerman et al. (1994)

Table 7: Test methods available for diagnosis of bovine viral diarrhoea and their purpose (reproduced from OIE (2015))

Method	Purpose					
	Population freedom from infection	Individual animal freedom from infection prior to movement	Contribution to eradiation policies	Confirmation of clinical cases	Prevalence of infection-surveillance	Immune status in individual animals or populations post-vaccination

	Agent identification					
Virus isolation	+	+++	++	+++	-	-
Antigen detection by ELISA	++	+++	+++	+++	+++	-
IHC	-	-	-	++	-	-
NA detection by real time RT-PCR	+++	+++	+++	+++	+++	-
	Detection of immune response					
ELISA	+++	++	+++	-	+++	+++
VN	+	+++	++	-	+	+++

Key: +++ = recommended method; ++ = suitable method; + = may be used in some situations, but cost, reliability, or other factors severely limits its application; - = not appropriate for this purpose. Although not all of the tests listed as category +++ or ++ have undergone formal validation, their routine nature and the fact that they have been used widely without dubious results, makes them acceptable.
IHC, immunohistochemistry; NA, nucleic acid; VN, virus neutralisation

Table 8: Performance characteristics for diagnostic tests and comments thereon

Method	Commonly tested matrices	Se	Sp	Comments
	Agent identification			
Virus isolation	Serum, buffy coat, leucocytes, whole blood, tissues, semen	100%	100%	• Historically considered the gold standard (Lanyon et al., 2014) but less commonly used now due to issues of time, cost and requirement for cell culture. • Toxicity to cell cultures can be an issue, especially with semen • Maternally derived antibodies (MDA) may interfere with isolation from serum in young calves
Antigen detection by ELISA	Serum, plasma, whole blood, tissues (including ear notch)	93.5-100% (Hilbe et al., 2007; Presi and Heim, 2010)	99-100% (Hilbe et al., 2007; Presi and Heim, 2010)	• Not intended for the detection of acutely infected animals, although may occasionally do so. • The Erns ELISA may be less effective in young calves in the presence of MDA when testing serum (Fux and Wolf, 2013). • The NS2-3 ELISA may be less effective in young calves in the presence of MDA when testing serum or tissue (Fux and Wolf, 2013).
Antigen detection by IHC	Tissue	100% (Cornish et al., 2016)	Not available	• Skin biopsies such as ear notch samples have been shown to be useful for *in vivo* detection of PI animals (Cornish et al., 2016) • While perceived as robust and suitable for large numbers of tissue samples, it is labour intensive, prone to technical error, relies on a subjective scoring system, requires experienced personnel to ensure accuracy and is unreliable for use on samples stored in formalin for >15 days (Lanyon et al., 2014)
NA detection by real time RTPCR	Serum, buffy coat, leucocytes, whole blood, tissues, semen, milk, bulk tank milk	97.1-100% (Hilbe et al., 2007; Presi and Heim, 2010)	99-100% (Hilbe et al., 2007; Presi and Heim, 2010)	• High analytical sensitivity allows pooled samples (ear notch, serum) and bulk tank milk to be tested • Detection of viral RNA does not imply *per se* that infective virus is present
	Detection of immune response			
ELISA	Serum, milk, bulk tank milk	Up to 98% (Presi and Heim, 2010)	Up to 99% (Presi and Heim, 2010)	• Both indirect and blocking assays are commercially available • Indirect more sensitive for bulk tank testing (Foddai et al., 2015)
VN	Serum	100%	100%	• Considered the gold standard test, but time-consuming and expensive to perform.

Table 9: Selected details of licenced BVD vaccines taken from their Summary of Product Characteristics.

Name of the Veterinary Medicinal Product	Type (live/dead) and strain(s)	Way of administration	Duration of immunity/booster interval	Manufacturer

Bovela lyophilisate and solvent for suspension for injection for cattle	modified live bovine viral diarrhoea virus type 1, non-cytopathic parent strain KE-9 and modified live bovine viral diarrhoea virus type 2, non-cytopathic parent strain NY-93	Intramuscular injection	1 year	Boehringer Ingelheim
Bovidec	Bovine Viral Diarrhoea (BVD) virus strain KY1203nc (inactivated)	Subcutaneous infection	A single annual booster dose is recommended	Novartis Animal Vaccines Ltd
Bovilis BVD Suspension for injection for cattle	Inactivated antigen of cytopathogenic BVDV strain C-86	Intramuscular injection	One vaccination every 6 months	MSD Animal Health