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Publisher's PDF, also known as Version of record

Link to published version (if available):
10.2903/j.efsa.2017.4951

Link to publication record in Explore Bristol Research
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Assessment of listing and categorisation of animal diseases within the framework of the Animal Health Law (Regulation (EU) No 2016/429): Borna disease

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Abstract

Borna disease has been assessed according to the criteria of the Animal Health Law (AHL), in particular criteria of Article 7 on disease profile and impacts, Article 5 on the eligibility of Borna disease to be listed, Article 9 for the categorisation of Borna disease according to disease prevention and control rules as in Annex IV and Article 8 on the list of animal species related to Borna disease. The assessment has been performed following a methodology composed of information collection and compilation, expert judgement on each criterion at individual and, if no consensus was reached before, also at collective level. The output is composed of the categorical answer, and for the questions where no consensus was reached, the different supporting views are reported. Details on the methodology used for this assessment are explained in a separate opinion. According to the assessment performed, Borna disease cannot be considered eligible to be listed for Union intervention as laid down in Article 5 (3) of the AHL because there was no compliance on criterion 5 A(v). Consequently, the assessment on compliance of Borna disease with the criteria as in Annex IV of the AHL, for the application of the disease prevention and control rules referred to in Article 9(1) is not applicable, as well as which animal species can be considered to be listed for Borna disease according to Article 8(3) of the AHL.

The EFSA Journal is a publication of the European Food Safety Authority, an agency of the European Union.

Table of contents

1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

The background and Terms of Reference (ToR) as provided by the European Commission for the present document are reported in Section 1.2 of the scientific opinion on the ad hoc methodology followed for the assessment of the disease to be listed and categorised according to the criteria of Article 5, Annex IV according to Article 9, and 8 within the Animal Health Law (AHL) framework (EFSA AHAW Panel, 2017).

1.2. Interpretation of the Terms of Reference

The interpretation of the ToR is as in Section 1.2 of the scientific opinion on the ad hoc methodology followed for the assessment of the disease to be listed and categorised according to the criteria of Article 5, Annex IV according to Article 9, and 8 within the AHL framework (EFSA AHAW Panel, 2017).

The present document reports the results of assessment on Borna disease (BD) according to the criteria of the AHL articles as follows:

- Article 7: Borna disease profile and impacts
- Article 5: eligibility of Borna disease to be listed
- Article 9: categorisation of Borna disease according to disease prevention and control rules as in Annex IV
- Article 8: list of animal species related to Borna disease.

2. Data and methodologies

The methodology applied in this opinion is described in detail in a dedicated document about the ad hoc method developed for assessing any animal disease for the listing and categorisation of diseases within the AHL framework (EFSA AHAW Panel, 2017).

3. Assessment

3.1. Assessment according to Article 7 criteria

This section presents the assessment of BD according to the Article 7 criteria of the AHL and related parameters (see Table 2 of the opinion on methodology (EFSA AHAW Panel, 2017)), based on the information contained in the fact-sheet as drafted by the selected disease scientist (see Section 2.1 of the scientific opinion on the ad hoc methodology) and amended by the AHAW Panel.

3.1.1. Article 7(a) Disease Profile

Borna disease is a fatal neurological disorder first described in horses and sheep and the name of the disease is due to devastating epidemics in the end of the 19th century in horses in Borna, a town in Saxony, Germany. The viral aetiology was already detected around 1925 and the underlying T-cell mediated immunopathology was confirmed in the 1980s. The family Bornaviridae belongs to the order Mononegavirales, along with rhabdoviruses, filoviruses and paramyxoviruses, which comprise single stranded negative stranded and non-segmented RNA viruses. Within the family Bornaviridae, there is only one genus *Bornavirus* and recent taxonomic classification indicates at least five virus species. Knowledge on *Bornavirus* infections has increased remarkably over the last decade and many phylogenetically different viruses were detected using novel molecular methods. For instance, a variety of novel bornaviruses was discovered in various avian and even reptile species and a novel virus with proven zoonotic capacity was found in certain squirrel species. Moreover, integrated endogenous sequences with homology to *Bornavirus* genes have been detected in several species and might indicate a so far unknown innate antiviral strategy.

If necessary, data are split up according to the new taxonomic reorganisation of the family Bornaviridae, order Mononegavirales, genus *Bornavirus* into at least five species (*Mammalian 1 bornavirus, Mammalian 2 bornavirus, Psittacine 1 bornavirus, Psittacine 2 bornavirus, Passeriform 1 bornavirus, Waterbird 1 bornavirus, Passeriform 2 bornavirus,* unassigned bornaviruses, *Elapid 1 bornavirus*, unclassified bornaviruses). For clarity, data for mammals, birds and other animals such as reptiles are summed up whenever possible.

3.1.1.1. Article 7(a)(i) Animal species concerned by the disease

Susceptible animal species

There are many reports on endogenous Bornavirus-like (EBL) sequences in many different animal classes: (e.g. birds, mammals, reptiles, fishes, insects and arachnids), infraclasses (e.g. marsupials) superorders and orders (e.g. primates, rodents, chiroptera, carnivores and afrotheria), suborders (e.g. serpents) or families (for instance, elephants, lemurs, squirrels and primates). Their role still remains to be clarified but might be associated with a novel type of antiviral immunity such as protection against further *Bornavirus* infections (Belyi et al., 2010; Horie et al., 2010; Horie et al., 2013; Fujino et al., 2014; Honda et al., 2016).

Reports on natural infection are based on varying detection methods, e.g. histological lesions, presence of viral antigen and RNA or virus-specific serum antibodies and/or viral RNA only.

Parameter 1 – Naturally susceptible wildlife species (or family/orders)

Mammalian bornaviruses (*Mammalian 1* and *2 bornavirus*): Reservoir bicoloured white-toothed shrew, zoo animals (alpacas (*Vicugna pacos*), sloth (Bradypodidae, Megalonychidae), vari monkeys (*Varecia*), hippopotamus (*Hippopotamus amphibius*)), animals kept in husbandries (variegated squirrels (*Sciurus variegatoides*), Prevost's squirrels (*Callosciurus prevostii*), one report on lynx (unspecified) deer (unspecified) (Dürrwald and Ludwig, 1997; Dürrwald et al., 2006; Kinnunen et al., 2007; Richt et al., 2007; Herden et al., 2013). Reports on naturally infected raccoons (*Procyon lotor*) and macaques based on virus-specific serum antibodies and viral RNA detection in the brain only also exist (Hagiwara et al., 2008; Hagiwara et al., 2009). Other wildlife species, e.g. foxes (*Vulpes vulpes*), badgers (*Meles meles*) and small mammals can display also virus-specific serum antibodies but no other signs of infection (Kinnunen et al., 2007; Bourg et al., 2013; Bourg et al., 2016).

Avian bornaviruses (*Psittacine bornavirus 1* and *2*, *Passeriform bornavirus 1* and *2*, *waterbird 1 bornavirus*, unclassified bornaviruses): Animals kept in husbandry: psittacine birds (e.g. order Psittaciformes at least 34 genera), canaries, finches (e.g. munia, estrildid finches), pheasant (one case), wild birds: psittacines, waterbirds (e.g. Canada goose (*Branta canadensis*), trumpeter swan (*Cygnus buccinator*), mute swan (*Cygnus olor*), gulls, wild ducks (e.g. northern pintail (*Anas acuta*), gadwall (*Anas strepera*), mallard (*Anas plytyrhynchos*), bald eagle (*Haliaeetus lecuocephalus*) (Staeheli et al., 2010; Heffels-Redmann et al., 2011; Payne et al., 2012; Delnatte et al., 2013; Herden et al., 2013; Rubbenstroth et al., 2013; Delnatte et al., 2014b; Encinas-Nagel et al., 2014; Guo et al., 2014; Rubbenstroth et al., 2014b; Bourque et al., 2015; Kuhn et al., 2015). For ducks, cranes, gulls, haliaeetus and emberiza data on natural infection based on detection of viral RNA only also exist (Sassa et al., 2015).

Bornaviruses in reptiles (only sequences reported so far): Loveridge's garter snake (*Elapsoidea loveridgei*), Gaboon viper (*Bitis gabonica*) (Stenglein et al., 2014; Kuhn et al., 2015).

Parameter 2 – Naturally susceptible domestic species (or family/orders)

Mammalian bornaviruses (*Mammalian 1 bornavirus*): Main natural hosts (or accidental hosts) are horses and sheep. Natural infections have also been described in other Equidae, farm animals (cattle, goats), rabbits, and very rarely in companion animals (dog, cat) (Rott and Becht, 1995; Staeheli et al., 2000; Dürrwald et al., 2006; Kinnunen et al., 2007; Herden et al., 2013).

Parameter 3 – Experimentally susceptible wildlife species (or family/orders)

Mammalian bornaviruses: so far shown for bank voles (*Myodes glareolus*) (Kinnunen et al., 2011).

Parameter 4 – Experimentally susceptible domestic species (or family/orders)

Mammalian bornaviruses (*Mammalian 1 bornavirus*): Very broad host range for experimental infections ranging from chicken up to non-human primates (e.g. tree shrew, rhesus monkey, chicken, rat, mouse, hamster, gerbil, rabbit, guinea pig (Heinig, 1969; Rott and Becht, 1995; Staeheli et al., 2000; Herden et al., 2013). Experimental Infection of ferrets, pigeons, dogs, and hamsters did not result in clinical disease but usually persistent infection (Danner, 1982; Rott and Becht, 1995).

Avian bornaviruses (*Psittacine bornavirus 1 and 2*, *Passeriform 1 bornavirus*): psittacines, e.g. cockatiels, african grey parrots, patagonian conures as well as canaries; failed in ducks

in one study (Gancz et al., 2009; Gray et al., 2010; Staeheli et al., 2010; Piepenbring et al., 2012; Rubbenstroth et al., 2013; Piepenbring et al., 2016).

Reservoir animal species

Parameter 5 – Wild reservoir species (or family/orders)

Mammalian bornavirus (*Mammalian 1 bornavirus*): bicoloured white-toothed shrew (Hilbe et al., 2006; Bourg et al., 2013; Dürrwald et al., 2014; Nobach et al., 2015). It needs to be further investigated whether variegated squirrels or Prevost's squirrels serve as reservoir for the novel variegated squirrel 1 bornavirus (VSBV-1).

Avian bornaviruses: Unknown whether susceptible wild animals serve as reservoir, especially wild birds.

Parameter 6 – Domestic reservoir species (or family/orders)

Mammalian bornavirus (*Mammalian 1 bornavirus*): unknown
Avian bornaviruses: unknown

3.1.1.2. Article 7(a)(ii) The morbidity and mortality rates of the disease in animal populations

Morbidity

Parameter 1 – Prevalence/incidence

Mammalian bornaviruses (*Mammalian 1 bornavirus*): most data are available for horses with some data also on cattle and sheep. Clinical neurological disease occurs typically in endemic areas in Germany, Switzerland, Austria and Liechtenstein. Due to reports on clinical disease in other countries, possible other clinical signs associated with infection and detection of virus-specific serum antibodies as well as/or viral RNA, within Europe and outside Europe, e.g. France, Sweden, Finland, Italy, Turkey, Israel, Japan, Iran, China, Australia and the USA, a more widespread distribution has been discussed but still awaits final proof or disproof by detailed epidemiological and phylogenetic studies (Herden et al., 2013). For instance, a case of BD in a horse in Great Britain could be traced back to infection in a German endemic area (Jacobsen et al., 2010). However, the continuous detection of novel Bornaviruses or related viral sequences might contribute to assess the geographical distribution of different bornaviruses in the future.

BD was epidemic at the end of the 19th century, but the incidence decreased significantly up to the 1990s. The great majority of infections is characterised by a clinically inapparent course, and disease incidence is typically low despite the higher seroprevalence in horses, even in endemic areas. In endemic areas in Germany (Bavaria), the incidence dropped down to about 0.02–0.04% in the 1990s (Herden et al., 2013). Thus, the incidence of clinical BD is relatively low, with less than 100 affected horses or sheep per year in endemic areas (Herzog et al., 1994; Dürrwald and Ludwig, 1997; Caplazi et al., 1999; Staeheli et al., 2000; Muller-Doblies et al., 2004; Dürrwald et al., 2006; Richt et al., 2007; Kistler et al., 2010). Seasonally, there is an increase of clinical cases in spring and early summer and secular rhythm has also been observed with disease peaks every 3–5 years. Species wise, the highest incidence of clinical disease is in horses and donkeys (less than 0.1.% of horse population in second half of 20th century), lower in sheep (with less than 0.01% of sheep population in second half of 20th century), even lower in new world camelids, other herbivores and rare in carnivores, e.g. dogs (Staeheli et al., 2000; Dürrwald et al., 2006).

It should be noted that seroepidemiological surveys from Germany indicate that infections in horses and sheep can be inapparent. Clinically healthy horses in Germany display an average seroprevalence of 11.5% (Herzog et al., 1994). However, seroprevalence increases in endemic areas up to 50% in stables where clinically diseased horses had been detected (Grabner et al., 2002). Occurrence of clinical disease is higher in stables with lower hygiene standards and mixed equine, bovine and ovine population (Staeheli et al., 2000; Dürrwald et al., 2006).

Thus, there is a great difference between seroprevalence and the low incidence of clinical cases. It has been speculated that various host and viral factors influence the outcome of the infection, e.g. age, immune status and genetic background, virus strain and dose of infection (Herden et al., 2013). Current expanding knowledge on the potential role of the endogenous bornaviral elements (see above) might suggest additional mechanisms.

Avian bornaviruses (*Psittacine bornavirus 1* and *2*, *Passeriform 1* and *2 bornavirus*, *waterbird 1 bornavirus*): Many different studies indicate that avian bornavirus (ABV) infections occur worldwide (e.g. various European countries, e.g. Germany, Austria, Switzerland, Hungary, Spain, Italy, the UK, Denmark, Canada, USA, Australia, Brazil, Japan) (Staeheli et al., 2010; Payne et al., 2011a; Herden et al., 2013; Sassa et al., 2013; Encinas-Nagel et al., 2014; Guo et al., 2014; Philadelpho et al., 2014; Sassa et al., 2015).

The typical clinical disease, proventricular dilatation disease (PDD) is associated with detection of ABV infection in 60–100% of cases depending on the respective study but infection can also be found in apparently clinically healthy animals (Herden et al., 2013).

Due to the large number of studies investigating the presence of ABV infections in captive and wild birds, only selected data are further detailed.

In a study employing 1,442 live and 73 dead birds of 54 genera of psittaciformes from different European countries (Germany, Spain, Italy, the UK, Denmark), ABV infection was detected in 22.8% of animals with a coincidence of virus-specific serum antibodies and viral RNA in cloacal and crop swabs in only 20% (Heffels-Redmann et al., 2012). This was confirmed by a study testing 112 pet psittacines in Brazil with a presence of 28.6% positive animals (Philadelpho et al., 2014). This coincides with a study investigating 86 wild psittacines in Brazil with a detection rate of 30.2% (Encinas-Nagel et al., 2014). A wide distribution of avian bornaviruses was also found in canary flocks in a percentage of 40% (12/30 flocks) and 22% of canaries tested, whereas the presence was lower in captive finches (3/286 samples positive) (Rubbenstroth et al., 2013; Rubbenstroth et al., 2014b). In contrast, in Japan in 2,078 samples from wild birds (1,908 waterfowl), only in 0.9% viral RNA was found (Sassa et al., 2015) and in 4/93 (4.3%) of the investigated pet birds (Sassa et al., 2013). In waterfowl, distinct avian bornaviruses (aquatic bird bornavirus 1) are widespread in North America and Canada in a percentage ranging between 10% and 30%, reported as high as 50% in few studies, e.g. in Canada geese, trumpeter and mute swans and ducks. They have been found in apparently healthy animals but also in birds from Canada and North America (Payne et al., 2011a; Delnatte et al., 2013; Delnatte et al., 2014b; Guo et al., 2014) with typical clinical or histopathological lesions. For instance, 24/409 (5.9%) geese samples were positive for viral RNA and in 51/995 (5.1%) geese necropsy cases from Canada viral RNA was detected or in 78–88% of retrospectively selected cases based on clinical history suggestive of avian borna virus infection (Payne et al., 2011a; Delnatte et al., 2013). Recently, aquatic bird bornavirus (ABBV-1) was detected in 7/333 (2.1%) brains of apparently healthy geese originating from Denmark (Thomsen et al., 2015).

<u>Parameter 2 – Case-morbidity rate (% clinically diseased animals out of infected ones)</u>

Mammalian bornaviruses (*Mammalian 1 bornavirus*): Typically, in case of development of clinical disease, natural Borna disease virus (BDV) infection in horses cause death 1–4 weeks after onset of signs in 80–90% of animals (Schmidt, 1952; Grabner and Fischer, 1991; Dürrwald and Ludwig, 1997; Grabner et al., 2002; Richt et al., 2007). In 72% of horse herds with BD cases, only individual animals develop clinical manifest BD. In cattle and sheep, death occurs after 1–6 weeks or 1–3 weeks in more than 50% of animals, respectively (Richt et al., 1997b; Bode et al., 2001). In sheep flocks, it has been reported that large animal numbers can be affected. In horse stables, repeated outbreaks of BD can occur, typically some time ranging from 2 months up to several years after the initial BD cases.

Avian bornaviruses (*Psittacine bornavirus 1*, *Passeriform 1* and *2 bornavirus*, *waterbird 1 bornavirus*): Many studies have shown that infection with ABV can run many different clinical courses and infection status, either in natural or experimental infections. Signs might range from typical PDD with gastrointestinal and/or neurological signs, sudden death, clinically inconspicuous so that the morbidity rate is difficult to assess (Herden et al., 2013). Thus, only few examples are given.

In a field study monitoring 63 psittacines over a period of 1 year, four different groups of infected and one group consisting of non-infected birds were classified. Only one group comprised clinical 6/63 (9.5%) PDD cases with various courses of virus infection whereas all other animals were subclinically infected and were grouped together according to the presence of serum antibodies and/or viral RNA (Heffels-Redmann et al., 2012). In experimental trials with cockatiels 5/18 (27.8%) or 12/18 (66.7%), birds developed clinical signs depending on the viral genotype used (Piepenbring et al., 2012; Piepenbring et al., 2016). Canaries and wild birds can also be infected without clinical signs or could present typical clinical disease or histological lesions (Weissenböck et al., 2009; Payne et al., 2011a; Payne et al., 2012; Delnatte et al., 2013; Rubbenstroth et al., 2013; Guo et al., 2014).

Mortality

Parameter 3 – Case-fatality rate

Mammalian bornaviruses (*Mammalian 1 bornavirus*): Typically, natural BDV infection in horses that develop clinical signs leads to death 1–4 weeks after onset of signs in 80–90% of animals (Schmidt, 1952; Grabner and Fischer, 1991; Dürrwald and Ludwig, 1997; Richt et al., 1997b; Grabner et al., 2002). In cattle and sheep, death was noted after 1–6 weeks or 1–3 weeks in more than 50% of animals, respectively (Bode et al., 1994; Richt et al., 1997b).

Avian bornaviruses (*Psittacine bornavirus 1, Passeriform 1* and *2 bornavirus, waterbird 1 bornavirus*): For variability of clinical course and outcome of infection, refer to as case morbidity rate. After ABV infection, sudden death might occur. The clinical picture of PDD has been described long before the virus was detected so that former reports on PDD exist describing a mortality rate of 100% (R-Gregory et al., 1994). In most cases, animals with overt clinical disease affected birds die due to energy deficiency or have to be euthanised (Hoppes et al., 2010; Lierz et al., 2010; Herden et al., 2013).

3.1.1.3. Article 7(a)(iii) The zoonotic character of the disease

Presence

Parameter 1 – Report of zoonotic human cases (anywhere)

Mammalian bornaviruses (*Mammalian 2 bornavirus*): There are three confirmed human deaths between 2011 and 2013 in breeders of variegated squirrels (*Sciurus variegatoides*) infected with novel bornavirus variegated squirrel 1 bornavirus (VSBV 1) belonging to the new species mammalian 2 bornavirus (Hoffmann et al., 2015; Schlottau et al., 2017), technical note 2016.

Mammalian bornaviruses (*Mammalian 1 bornavirus*): There was a long and controversial discussion whether the classical mammalian bornavirus BoDV-1 has to be regarded as zoonotic or not and might be involved in certain human psychiatric syndromes, including e.g. major depressive disorder, bipolar disorder, schizophrenia and autism. Some reports also described an association with chronic fatigue syndrome, AIDS encephalopathy, multiple sclerosis, motor neuron disease and brain tumours or the detection of viral RNA in peripheral blood mononuclear cells (PBMCs) and brain (Herden et al., 2013). Sequence homology of the human BoDV-sequences with BoDV laboratory strains or field isolates handled in the respective laboratories could argue for potential cross-contamination at laboratory level (Richt et al., 1997a; Schwemmle et al., 1999; Dürrwald et al., 2007). A recent large cohort study in the USA also did not provide any evidence for bornavirus infection in psychiatric patients (Hornig et al., 2012). However, it has been shown that psychiatric patients can exhibit virus specific antibodies, but typically with low titres and avidity (Bechter et al., 1996; Billich et al., 2002; Schwemmle and Billich, 2004).

Thus, it has to be emphasised that the VSBV-1 infection in humans was clearly different from the data on an association of the classical BoDV with human diseases. In all three patients, high VSBV-1 RNA and antigen loads and serum titers were present substantiating that VSBV-1 is a quite different novel zoonotic pathogen (Hoffmann et al., 2015).

Avian bornaviruses (*Psittacine bornavirus 1, Passeriform 1 and 2 bornavirus, waterbird 1 bornavirus*): There are no indications that avian bornaviruses are zoonotic in nature.

3.1.1.4. Article 7(a)(iv) The resistance to treatments, including antimicrobial resistance

Parameter 1 – Resistant strain to any treatment even at laboratory level

Mammalian bornaviruses (*Mammalian 1 bornavirus*): As current knowledge, no resistant strain to laboratory antiviral strategies has been reported. In this respect it should be noted that no curative treatment exists so far, but many studies tried antiviral treatments *in vitro* or *in vivo* and could show either reduction in viral loads, inhibition of viral spread.

Thus no curative treatment is available to date.

Avian bornaviruses: No resistant strain described so far.

3.1.1.5. Article 7(a)(v) The persistence of the disease in an animal population or the environment

Animal population

As of current knowledge, mammalian and avian bornaviruses are able to cause persistent non-cytolytic infection in their respective hosts and cell culture systems. However, virus distribution can

differ with widespread viral dissemination in nearly every organ system in reservoir species, variegated squirrels or neonatally immune incompetent or immunocompromised rats. Virus distribution can be highly variable in infected birds with similar widespread dissemination or more pronounced tropism to the nervous system and gastrointestinal tract (Herden et al., 2013). In end hosts/accidental hosts, typically a persistent infection with neurotropism occurs affecting the nervous system only.

Parameter 1 – Duration of infectious period in animals

Mammalian bornaviruses (*Mammalian 1 bornavirus*): Unknown for naturally infected animals, for bicoloured white-toothed shrews viral shedding has been shown over 600 days in husbandry (Nobach et al., 2015). Neonatally persistently infected rats also shed virus in urine, nasal and lacrimal secretions (Narayan et al., 1983a,b; Sauder and Staeheli, 2003). The incubation period for natural BD is unknown but a period ranging from 2 weeks to several months was proposed (Schmidt, 1912, 1952; Ludwig et al., 1985; Rott and Becht, 1995).This was underscored by naturally infected animals, a horse in the UK and an alpaca in Germany which both had been infected in endemic areas before being transported to the new region where they developed clinical signs, approximately 3–4 months later (Jacobsen et al., 2010; Priestnall et al., 2011). Experimentally, in rats, persistent infection has also been shown over long periods for more than 210 days (Narayan et al., 1983a,b).

Avian bornaviruses (*Psittacine bornavirus 1, Passeriform bornavirus 1*): Only few examples illustrating the situation are given.

In experimentally infected cockatiels either with PaBV2 oder PaBV4 infection was persistent until the end of the investigation, e.g. up to 231 dpi (Gancz et al., 2009; Gray et al., 2010; Kistler et al., 2010; Mirhosseini et al., 2011; Piepenbring et al., 2012; Piepenbring et al., 2016; Olbert et al., 2016). In canaries, experimental infection was also persistent over 5 months (Rubbenstroth et al., 2013). The reported incubation period of ABV infections is variable, ranging between approximately 20–60 days up to 200 days (Gancz et al., 2009; Gray et al., 2010; Payne et al., 2011b; Piepenbring et al., 2012; Piepenbring et al., 2016) in experimental trials.

Parameter 2 – Presence and duration of latent infection period

No data on latent infection, only subclinical courses have been described for ABV infections, e.g. detailed in (Heffels-Redmann et al., 2011).

Parameter 3 – Presence and duration of the pathogen in healthy carriers

Mammalian bornaviruses (*Mammalian 1 bornavirus*): See also under susceptible animal species, reservoir species.

So far known reservoir species bicoloured white-toothed shrew (*Crocidura leucodon*) for classical mammalian virus BoDV-1 appear clinically inconspicuous (Nobach et al., 2015). Interestingly, variegated squirrels (*Sciurus variegatoides*) infected with the novel VSBV-1 also do not show clinical signs (Schlottau et al., 2017). Data from seroepidemiological surveys also indicates that infection can be inapparent in horses and sheep (see also under prevalence/incidence).

Avian bornaviruses (*Psittacine bornavirus 1, Passeriform bornavirus 1*): Clinically apparently healthy birds have been described for natural infection and after experimental inoculation of psittacines and canaries and also for the panel of susceptible water birds, e.g. geese, swans, ducks, gulls (see also Section 3.1.1.1) (Staeheli et al., 2010; Heffels-Redmann et al., 2011; Heffels-Redmann et al., 2012; Payne et al., 2012; Herden et al., 2013; Rubbenstroth et al., 2013). Moreover, clinically healthy animals with continuous or intermittent shedding of viral RNA occur.

Environment

Parameter 4 – Length of survival (dpi) of the agent and/or detection of DNA in selected matrices (soil, water, air) from the environment (scenarios: high and low T)

Most data are available for the classical mammalian Bornavirus BoDV-1.

Mammalian bornaviruses (*Mammalian 1 bornavirus*): Incubation at 37°C or storage in serum for 24 h reduces infectivity only slightly. By storage at 4°C, BDV infectivity has been shown to be stable for more than 3 months. Viral infectivity is more preserved in tissues and cell free virus preparations than in cell culture extracts. Virus suspension stored at −80°C for 25 years was successfully used for experimental infections. Dried preparations retain their infectivity also very long, at room temperature for more than 2 month and under vacuum also for several years (Zwick, 1939; Ludwig et al., 1973; Ludwig et al., 1988; Danner and Mayr, 1979; Herden et al., 2013).

The virus resists acidic and alkaline milieu but neutral pH the best (Elford and Galloway, 1933; Heinig, 1955; Danner and Mayr, 1979).

Virus inactivation can be achieved by heating to 56°C for longer than 3 h and the virus is labile at pH 3. Since BoDV is an enveloped virus, common disinfection procedures for enveloped viruses can be applied, e.g. UV light, acidic settings with a pH below 4 as well as lipid solvents such as ether, chloroform or acetone or detergents (Danner, 1982; Herden et al., 2013).

3.1.1.6. Article 7(a)(vi) The routes and speed of transmission of the disease between animals, and, when relevant, between animals and humans

Routes of transmission

Parameter 1 – Types of routes of transmission from animal to animal (horizontal, vertical)

Mammalian bornaviruses (*Mammalian 1* and *2 bornavirus*): For natural infection of end hosts/accidental hosts, intranasal infection via the olfactory pathway was assumed as the most likely route of entry for a long time (Morales et al., 1988; Bilzer et al., 1995; Sauder and Staeheli, 2003; Herden et al., 2013). Neonatally infected rats develop a disseminated virus infection with shedding of infectious virus via secretions, urine and faeces (Morales et al., 1988; Bilzer et al., 1995; Sauder and Staeheli, 2003). This resembles closely the situation in the naturally infected reservoir, the bicoloured white-toothed shrew where infectious virus was also detected in secretions, excretions and skin (Nobach et al., 2015). For the novel bornavirus, VSBV-1 a similar viral distribution was found (Hoffmann et al., 2015; Schlottau et al., 2017). It can therefore be assumed that these ways of shedding can serve as most likely transmission matrix. For transmission of virus from shrew to horses contaminated food was also considered (Bourg et al., 2013).

Experimentally, various infection routes were successfully applied in rats, e.g. intranasal, intracerebral, intraocular, intraperitoneal, foot pad infection, but not intravenous (Carbone et al., 1987; Morales et al., 1988; Herden et al., 2013). The distance of the inoculation site to the central nervous system (CNS) delayed onset of clinical disease (Carbone et al., 1987). Detection of viral RNA in PBMCs has been reported but questioned by others (Herden et al., 2013) but viremia seem not to be involved in viral spread which is substantiated that intravenous inoculation was not successful.

Only few data exist on potential vertical transmission in horses (Hagiwara et al., 2000) or in mice (Okamoto et al., 2003).

Avian bornaviruses (*Psittacine bornavirus 1*, *Passeriform bornvirus 1*): For natural infection, the horizontal orofaecal route has been assumed as most likely way of entry due to detection of ABV RNA in faeces, cloacal and crop swabs. This has yet not been proven by respective experimental trials. Experimentally infection was successful via various routes, e.g. intracerebral, intravenous, subcutaneous, intramuscular or combination thereof but so far not oronasally (Gancz et al., 2009; Gray et al., 2010; Kistler et al., 2010; Mirhosseini et al., 2011; Rubbenstroth et al., 2013; Rubbenstroth et al., 2014a; Olbert et al., 2016; Piepenbring et al., 2016; Heckmann et al., 2017). Recent phylogenetic data indicate that horizontal inter species transmission seem to be relatively frequent as shown for PaBV2 and PaBV4 (Rubbenstroth et al., 2016). Horizontal transmission after hatch has also been discussed as mode of transmission (Kerski et al., 2012).

ABV antigen has been detected in testes and ovaries of infected parrots (Raghav et al., 2010) so that potential vertical transmission was assumed. To date, viral RNA was found in eggs, embryos hatchlings of, e.g. different psittacine species, canaries, geese originating from infected parents (Lierz et al., 2011; Kerski et al., 2012; Monaco et al., 2012; Rubbenstroth et al., 2013; Delnatte et al., 2014a). It was speculated that ABV reach eggs either from penetration of the shell after egg contamination, or contamination of oviduct secretions or ABV infection of ova or sperm (Monaco et al., 2012). However, productive viral replication has not been demonstrated from eggs or embryos so far.

Parameter 2 – Types of routes of transmission between animals and humans (direct, indirect, including food-borne)

Mammalian bornaviruses (*Mammalian 1 and 2 bornavirus*): To date, the classical mammalian bornavirus has not been considered as a proven zoonotic pathogen.

The route of transmission from the variegated squirrels infected with VSBV-1 to the three human cases remains to be elucidated but possibilities of intranasal infection, bites or scratches have been hypothesised (Hoffmann et al., 2015).

Avian Bornaviruses: There are yet no indications that avian bornaviruses are zoonotic in nature.

Speed of transmission

Parameter 3 – Incidence between animals and, when relevant, between animals and humans

Mammalian bornaviruses (*Mammalian 1 and 2 bornavirus*): No data on the incidence and speed of transmission are yet available for the currently known reservoir population, the bicoloured white-toothed shrews. Incidence of transmission from shrew to accidental/end hosts such as horses is also unknown, the discrepancy between seroprevalence and clinical manifest disease which occur only in single animals is detailed under morbidity. Data on the presence of viral antigen or RNA in peripheral organs or secretions of end/accidental hosts are contradictory (Bilzer et al., 1995; Lebelt and Hagenau, 1996; Schmahl et al., 1999) but transmission between end/accidental hosts does not seem to play an important role. This can be substantiated by the occurrence of only single diseased animals in one flock despite a high seroprevalence in stables with clinical manifest BD. See Section 3.1.1.2 Parameter 2.

Avian bornaviruses (*Psittacine bornavirus 1, Passeriform bornvirus 1*): By experimental trials, in sentinel birds viral RNA might be detected or no contact transmission was noted (Piepenbring et al., 2012; Rubbenstroth et al., 2013; Rubbenstroth et al., 2014a; Piepenbring et al., 2016). It has been assumed that asymptomatic carriers might contribute to the perpetuation of ABV infections. Interestingly, birds might not become infected despite close contact to ABV-infected birds (Raghav et al., 2010; Heffels-Redmann et al., 2012; Rubbenstroth et al., 2014a).

Parameter 4 – Transmission rate (beta) (from R_0 and infectious period) between animals and, when relevant, between animals and humans

Assessment of R_0 for infection either with mammalian bornaviruses or avian bornaviruses has not been possible to date. The infection runs a completely different course in reservoir species or immunocompromised/immune incompetent animals or accidental hosts. Variety of clinical signs and infection are even more variable for avian bornaviruses, e.g. close-contact animals are not necessarily infected (Rubbenstroth et al., 2014a; Bourque et al., 2015).

3.1.1.7. Article 7(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

Presence and distribution

Parameter 2 – Type of epidemiological occurrence (sporadic, epidemic, endemic) at MS level

Mammalian bornaviruses (*Mammalian 1 bornavirus*): There are endemic areas in Germany, Austria, Switzerland and Liechtenstein (Dürrwald and Ludwig, 1997; Staeheli et al., 2000; Kolodziejek et al., 2005; Dürrwald et al., 2006) where clinically diseased end hosts occur. For the classical BoDV-1, endemic viral clusters with a strong geographical association have been reported being related to the occurrence of the viral reservoir (Kolodziejek et al., 2005; Dürrwald et al., 2006; Hilbe et al., 2006; Bourg et al., 2013; Dürrwald et al., 2014).

For seasonality and open questions on geographical distribution, see also under Section 3.1.1.2 Parameter 2.

Avian bornaviruses (*Psittacine bornavirus 1, Passeriform bornavirus 1*): Due to the variability of courses of ABV infections (e.g. clinically healthy, PDD, sudden death, feather pecking) and lack of association between presence of clinical signs and detection of ABV, the type of epidemiological occurrence cannot be properly assessed.

Risk of introduction

Parameter 3 – Routes of possible introduction

Mammalian bornaviruses (*Mammalian 1 bornavirus*): Spread occurs most likely from reservoir (white-toothed bicoloured shrews) to end/accidental host (e.g. horses) probably via contaminated food and intranasal infection (Bourg et al., 2013; Dürrwald et al., 2014; Nobach et al., 2015).

Avian bornaviruses (*Psittacine bornavirus 1 and 2, Passeriform bornavirus 1 and 2, waterbird 1 bornavirus, unclassified bornaviruses*): For captive animals, trade or introduction of new animals into husbandry without proper testing might contribute to viral introduction. Recently, a lack of geographical association of viral sequences from captive psittacines might argue for assumed

worldwide viral distribution by trade in the past (Rubbenstroth et al., 2016). In this respect, especially clinically inconspicuous animals can represent potential risk factors (Herden et al., 2013). Whether or how an introduction from wild birds to captive birds play a role remains yet unknown (Rubbenstroth et al., 2016). For waterbirds, distinct geographical clusters of ABBV-1 in North America and Europe have been described but dispersal areas are larger (Payne et al., 2012; Delnatte et al., 2013; Thomsen et al., 2015; Rubbenstroth et al., 2016).

Parameter 4 – Number of animal moving and/or shipment size

Not applicable.

Parameter 5 – Duration of infectious period in animal and/or commodity

See under Section 3.1.1.5.

Parameter 6 – List of control measures at border (testing, quarantine, etc.)

There are no control measures in place so far.

Parameter 7 – Presence and duration of latent infection and/or carrier status

See under Section 3.1.1.5 Parameter 2.

3.1.1.8. Article 7(a)(viii) The existence of diagnostic and disease control tools

Diagnostic tools

Parameter 1 – Existence of diagnostic tools

Mammalian bornaviruses (*Mammalian 1 and 2 bornavirus*): Most studies concerning diagnostic tools exist for the classical mammalian bornavirus BoDV-1.

Diagnostic tools can either be applied for intra vitam or post-mortem diagnostics (Herden et al., 2013). Viral infection can be diagnosed by the presence of virus specific antibodies in the serum and/or cerebrospinal fluid (CSF) (Grabner and Fischer, 1991; Grabner et al., 2002) and/or infectious virus, viral antigens or RNA in the CNS post-mortem. Established test systems for serology are Western blot analysis (Herzog et al., 1994; Herzog et al., 2008), enzyme-linked immunosorbent assay (ELISA) or indirect immunofluorescence assay (IFA) (Herzog and Rott, 1980; Grabner and Fischer, 1991; Herzog et al., 1994; Grabner et al., 2002; Herzog et al., 2008; Bode et al., 2001). The IFA has been proven as test system with a high sensitivity and specificity (Herzog et al., 2008). It should be mentioned that titres do not correlate with the clinical course of the infection (Grabner et al., 2002; Herzog et al., 2008). Liquor cerebrospinalis (CSF) investigation is also possible, e.g. cell count, biochemical analysis. There was a debate on the presence of viral RNA or antigen in PBMC or leukocytes or even circulating immune complexes (Nakamura et al., 1995; Bode et al., 2001; Dieckhöfer, 2008) because the data could not be reproduced in other studies (Grabner et al., 2002; Wolff et al., 2006; Herzog et al., 2008). However, viral RNA might be detected from cells of the CSF.

Reliable intra vitam results in an animal displaying neurological signs are presence of virus specific antibodies in the serum and/or CSF, CSF pleocytosis or seroconversion. However, it should be mentioned that false negative serological results can occur in peracute or very early stages of acute BD or also after treatment with corticosteroids (Grabner et al., 2002), and that clinically healthy horses can be seropositive, usually without antibodies in the CSF (Herzog et al., 1994; Grabner et al., 2002). In such cases and cases with viral specific serum antibodies, a post-mortem investigation is required for a final diagnosis (Herzog et al., 2008).

Post-mortem diagnosis of bornavirus infection is possible by various methods, e.g. histopathology, demonstration of viral antigens or RNA by morphological methods (immunohistochemistry (IHC), *in situ* hybridisation (ISH)), western blot (WB), various reverse transcription polymerase chain reaction (RT-PCR) and real time RT approaches (Bilzer et al., 1996; Herden et al., 1999; Grabner et al., 2002; Porombka et al., 2008; Werner-Keiss et al., 2008; Herden and Richt, 2009; Herden et al., 2013; Bourg et al., 2016). There was a 100% overlap for histopathological lesions (non-purulent meningoencephalitis), IHC, WB and nested RT-PCR in equine cases of acute BD using more than 150 horses with or without BD (Herden et al., 1999; Grabner et al., 2002). With fresh tissue material, isolation of infectious virus is also possible (Herden et al., 1999; Herden et al., 2000; Nobach et al., 2015).

For the novel VSBV-1, also reliable methods have been established comparable to the ones used for BoDV-1, e.g. IFA, IHC, RT-PCR and real time RT PCR assays and isolation of infectious virus (Hoffmann et al., 2015; Schlottau et al., 2017).

Avian bornaviruses (*Psittacine bornavirus 1* and *2*, *Passeriform bornavirus 1* and *2*, *waterbird 1 bornavirus*, unclassified bornaviruses): Diagnostic tools can either be applied for intra vitam or post-mortem diagnostics (Herden et al., 2013).

Intra vitam PDD can be diagnosed by imaging of the gastrointestinal tract (Dennison et al., 2008) and pathohistological examination of upper gastrointestinal tract biopsies since clinical signs are not specific enough and allow many differential diagnoses. Biopsy interpretation is difficult due to the inconsistent distribution of lesion and only confirmative in case of presence of non-purulent inflammation of ganglia and/or nerves. One study reported false negative results in approximately 24% (Gregory et al., 1996). Serology for the detection virus specific antibodies is possible by WB, ELISA and IFA (de Kloet and Dorrestein, 2009; Lierz et al., 2009; Gray et al., 2010; Herzog et al., 2010; Villanueva et al., 2010). For IFA, a high sensitivity and specificity for detection of ABV- specific serum antibodies was shown. For virus detection, various RT-PCR assays had to be established due to the heterogeneity of the viral genotypes/species. Faeces, swabs of crop and cloaca, blood and feather calami can be used (Lierz et al., 2009; Rinder et al., 2009; Gray et al., 2010; Kistler et al., 2010; de Kloet et al., 2011). Since shedding of viral RNA can be intermittent and variable organ-wise and the possible presence of only ABV RNA or ABV–specific antibodies or both, even in apparently healthy virus carriers, testing should be repeated and serology and viral RNA detection should be carried out in parallel (de Kloet and Dorrestein, 2009; Lierz et al., 2009; Herzog et al., 2010; Kistler et al., 2010; Villanueva et al., 2010; Heffels-Redmann et al., 2012).

Post-mortem, non-purulent (peri)ganglionitis, neuritis mainly in the gastrointestinal tract but also in other organs, e.g. heart, adrenal gland and encephalitis is quite typical for PDD (Herden et al., 2013). Viral antigen can be visualised by IHC (Ouyang et al., 2009; Rinder et al., 2009; Herzog et al., 2010; Raghav et al., 2010; Weissenböck et al., 2010; Wunschmann et al., 2011; Piepenbring et al., 2012; Piepenbring et al., 2016). Viral RNA can be demonstrated by ISH or various RT-PCR assays (see above) (Honkavuori et al., 2008; Kistler et al., 2008; Rinder et al., 2009; Weissenböck et al., 2009; Gray et al., 2010; Kistler et al., 2010; Lierz et al., 2009; Raghav et al., 2010; Villanueva et al., 2010; Wunschmann et al., 2011). It should be mentioned, that in birds with PDD, similar presence of histopathological lesions, viral antigen and RNA can reach up to 100% specificity and sensitivity (Ouyang et al., 2009; Weissenböck et al., 2009; Raghav et al., 2010; Weissenböck et al., 2010; Herzog et al., 2010; Heffels-Redmann et al., 2011; Wunschmann et al., 2011). Infectious virus can be isolated using avian cell lines, e.g. quail fibroblasts or skeletal muscles or duck embryo fibroblasts (Rinder et al., 2009; Gray et al., 2010; Herzog et al., 2010).

Control tools

Parameter 2 – Existence of control tools

There are no official disease control tools for mammalian or avian bornaviruses.

Mammalian bornaviruses (*Mammalian 1 bornavirus*): Until 2011, there was obligation to report on cases of Borna disease due to classical infection with BoDV in Germany. However, this was cancelled in 2011.

3.1.2. Article 7(b) The impact of diseases

3.1.2.1. Article 7(b)(i) The impact of the disease on agricultural and aquaculture production and other parts of the economy

The level of presence of the disease in the Union

Parameter 1 – Number of MSs where the disease is present

Mammalian bornaviruses (*Mammalian 1 bornavirus*): Confirmed disease in end hosts such as horses and sheep have been reported in at least 5 countries (Germany from earliest reports on around 1890s to date, Switzerland, Austria, Liechtenstein – all since 1970s, the UK (2008) (Dürrwald et al., 2006; Priestnall et al., 2011).

Avian Bornaviruses (*Psittacine bornavirus 1* and *2*, *Passeriform bornavirus 1* and *2*, *waterbird 1 bornavirus*, unclassified bornaviruses): Presumably present in all Member States (MS), although no data from all MS are available.

The loss of production due to the disease

Parameter 2 – Proportion of production losses (%) by epidemic/endemic situation

Mammalian bornaviruses (*Mammalian 1 bornavirus*): In contrast to the seroprevalence in end/accidental hosts such as horses and sheep, the disease incidence rate is low (see under Section 3.1.1.2 Parameter 2).

Avian bornaviruses (*Psittacine bornavirus 1* and *2*, *Passeriform bornavirus 1* and *2*, *waterbird 1 bornavirus*, unclassified bornaviruses): Avian bornaviruses have mainly been described in birds not used for animal production so far.

3.1.2.2. Article 7(b)(ii) The impact of the disease on human health

Transmissibility between animals and humans

Parameter 1 – Types of routes of transmission between animals and humans

Mammalian bornaviruses (*Mammalian 2 bornavirus*): Unknown so far (see also under Section 3.1.2.2).

Avian bornaviruses (*Psittacine bornavirus 1 and 2*, *Passeriform bornavirus 1 and 2*, *waterbird 1 bornavirus*, unclassified bornaviruses): Current knowledge does not indicate zoonotic potential.

Transmissibility between humans

Parameter 3 – Human to human transmission is sufficient to sustain sporadic cases or community-level outbreak

Mammalian bornaviruses (*Mammalian 2 bornavirus*): There is no current evidence on human to human transmission for the novel zoonotic VSBV-1. In humans the infection was neurotropic which can argue against a possibility of human- human transmission. This resemble closely situation in naturally infected and diseased end/accidental hosts such as horses (see also under Section 3.1.2.2) where transmission between horses does not play an important role. However, it should be emphasised that current knowledge on this novel virus is still sparse.

Parameter 4 – Sporadic, endemic, epidemic, or pandemic potential

Mammalian bornaviruses (*Mammalian 2 bornavirus*): So far only three documented human cases infected with the novel bornavirus VSBV-1 exist (Hoffmann et al., 2015).

The severity of human forms of the disease

Parameter 5 – Disability-adjusted life year (DALY)

Mammalian bornaviruses (*Mammalian 2 bornavirus*): No data.

The availability of effective prevention or medical treatment in humans

Parameter 6 – Availability of medical treatment and their effectiveness (therapeutic effect and any resistance)

Mammalian bornaviruses (*Mammalian 2 bornavirus*): There is no curative medical treatment and treatment was only symptomatic in the three human patients, but treatment was not successful (Hoffmann et al., 2015).

Parameter 7 – Availability of vaccines and their effectiveness (reduced morbidity)

Mammalian bornaviruses (*Mammalian 1 bornavirus*): For the classical mammalian bornavirus, a live vaccine for animals existed but was abandoned in 1992, because its efficacy was questionable (Herden et al., 2013). Moreover, there were concerns on potential viral shedding after vaccination and establishment of a persistent virus reservoir. Due to the underlying immunopathogenesis of the clinical disease in end/accidental host, routine vaccination strategies were even more questionable (Herden et al., 2013). Thus, to date, there is no commercial vaccine available neither for BoDV nor the novel VSBV-1.

3.1.2.3. Article 7(b)(iii) The impact of the disease on animal welfare

Parameter 1 – Severity of clinical signs at case level and related level and duration of impairment

Mammalian bornaviruses (*Mammalian 1* and *2 bornavirus*): For the classical mammalian bornavirus BoDV-1, typically clinical signs progressively worsen within the course of disease of approximately 1–4 weeks. The case-fatality rate reaches up to 90% in horses (Schmidt, 1952; Grabner and Fischer, 1991; Dürrwald and Ludwig, 1997; Grabner et al., 2002; Richt et al., 2007). In 72% of flocks with BD cases, only individual animals develop clinical manifest BD. In cattle and sheep, death was reported to occur after 1–6 weeks or 1–3 weeks in more than 50% of animals, respectively (Bode et al., 1994; Richt et al., 1997b).

See also under Section 3.1.1.2 Parameter 2.

Avian bornaviruses (*Psittacine bornavirus 1* and *2, Passeriform bornavirus 1* and *2, waterbird 1 bornavirus*, unclassified bornaviruses): As detailed under morbidity, clinical signs in captive psittacines and non-psittacine birds can vary remarkably with variation in the virus detection and spread. Severity can range from apparently healthy birds up to sudden death and typical PDD signs such as gastrointestinal dysfunction and associated wasting with or without neurological signs (Gregory et al., 1996; Hoppes et al., 2010; Staeheli et al., 2010; Payne et al., 2012; Herden et al., 2013). In clinical manifest, PDD decreased motility, anorexia, lethargy, undigested seeds in the faeces, regurgitation, diarrhoea, weight loss resulting in cachexia and vomiting was observed. In cases exhibiting only neurological signs depression, ataxia, tremor, seizures and motor or proprioceptive deficits occur. Blindness might occur rarely. Also, in wild birds as shown for example geese, animals that appear clinically inconspicuous and animals with typical histological lesions can be found (Payne et al., 2012; Delnatte et al., 2013; Herden et al., 2013).

See also under Section 3.1.1.2 Parameter 2.

3.1.2.4. Article 7(b)(iv) The impact of the disease on biodiversity and the environment

Biodiversity

Parameter 1 – Endangered wild species affected: listed species as in CITES and/or IUCN list

Mammalian bornaviruses (*Mammalian 1* and *2 bornavirus*): Not known so far.

Avian Bornaviruses (*Psittacine bornavirus 1*): For example Spix macaw, also known as the little blue macaw (*Cyanopsitta spixii*), is a macaw native to Brazil susceptible to Borna virus and listed as critically endangered species (possibly extinct in the wild) according to IUCN and CITES.

Parameter 2 – Mortality in wild species

Mammalian bornaviruses (*Mammalian 1* and *2 bornavirus*): There are only few reports detailing case of death in wild animals, e.g. lynx, deer; infections have been described in animals originating from the wild and kept in zoos or private husbandries, e.g. vari monkey, alpaca, variegated squirrel (see also under Section 3.1.1.1) (Dürrwald and Ludwig, 1997; Kinnunen et al., 2007; Payne et al., 2012; Herden et al., 2013). Reports on naturally infected raccoons and macaques based on virus specific serum antibodies and viral RNA detection in the brain only also exist (Hagiwara et al., 2008; Hagiwara et al., 2009).

Studies in foxes indicate that they can exhibit virus specific serum antibodies (Bourg et al., 2016) in contrast to a former report on the presence of viral RNA in foxes (Dauphin et al., 2001).

Avian Bornaviruses (*Psittacine bornavirus 1* and *2, Passeriform bornavirus 1* and *2, waterbird 1 bornavirus*, unclassified bornaviruses): Most data describe infections and cases of death in captive birds (see under Section 3.1.1.1). For wild ranging animals, as shown for e.g. geese, animals that appear clinically inconspicuous can have typical histological lesions (Payne et al., 2012; Delnatte et al., 2013; Herden et al., 2013). Whether the latter could indicate that wild birds also die from the infection needs to be further investigated.

See also under Section 3.1.1.1.

Environment

Parameter 3 – Capacity of the pathogen to persist in the environment and cause mortality in wildlife

See under Section 3.1.1.5 Parameter 4.

3.1.3. Article 7(c) Its potential to generate a crisis situation and its potential use in bioterrorism

Parameter 1 − Listed in OIE/CFSPH classification of pathogens

Not listed.

Parameter 2 − Listed in the Encyclopaedia of Bioterrorism Defence of Australia Group

Not listed.

Parameter 3 − Included in any other list of potential bio-agro-terrorism agents

None identified.

3.1.4. Article 7(d) The feasibility, availability and effectiveness of the following disease prevention and control measures

3.1.4.1. Article 7(d)(i) Diagnostic tools and capacities

Availability

Diagnostic tools are detailed under Section 3.1.1.8. The existence of diagnostic and disease control tools, Diagnostic tools, 1 Existence of diagnostic tools.

Parameter 1 − Officially/internationally recognised diagnostic tool, OIE certified

There are no officially certified tools to date.

Effectiveness

Parameter 2 − Se and Sp of diagnostic test

See under Section 3.1.1.8.

Feasibility

Parameter 3 − Type of sample matrix to be tested (blood, tissue, etc.)

Mammalian bornaviruses (*Mammalian 1 bornavirus*): For the intra vitam diagnosis of infection with classical BoDV-1 in BD cases, serum and CSF is needed for the detection of virus specific antibodies. For the post-mortem diagnosis of BD, serum and CSF should be tested as well as fresh frozen samples of brain (nucleus caudatus, hippocampus, cerebral cortex), eye (retina), lacrimal and parotid gland, trigeminal ganglion, hypophysis and spinal cord for the detection of virus antigen, virus specific RNA and infectious virus represent suitable material. Similar tissues should be submitted fixed in 10% formalin.

Avian Bornaviruses (*Psittacine bornavirus 1* and *2*, *Passeriform bornavirus 1* and *2*, *waterbird 1 bornavirus*, unclassified bornaviruses): For the intra vitam diagnosis, serum, cloacal and crop swabs, feather calami as well as biopsies from the upper gastrointestinal tract can be used. For post-mortem diagnosis, CNS and gastrointestinal tract as well as samples from all other organs should be sampled and either be fresh frozen or fixed in 10% formalin.

3.1.4.2. Article 7(d)(ii) Vaccination

There is no commercially available vaccine for any mammalian or avian bornaviruses and only experimental data or older date from vaccination in eastern Germany exists. Due to the viral persistence with simultaneous presence of high levels of virus-specific antibodies, humoral immunity obviously does not play a major role, either for mammalian or avian bornaviruses (Narayan et al., 1983a; Herzog et al., 1985; Stitz et al., 1989; Heffels-Redmann et al., 2011; Heffels-Redmann et al., 2012; Piepenbring et al., 2012; Herden et al., 2013; Rubbenstroth et al., 2013; Rubbenstroth et al., 2014a; Piepenbring et al., 2016).

Mammalian bornaviruses (*Mammalian 1 bornavirus*): Attenuated virus but not killed vaccines showed protection experimentally. There was a lapinized live vaccine in eastern Germany, former GDR which was abandoned in 1992 because its efficacy was questionable (Herden et al., 2013). Moreover, there were concerns on potential viral shedding after vaccination and establishment of a persistent virus reservoir. Due to the underlying immunopathogenesis of the clinical disease in end/accidental host, routine vaccination strategies were even more questionable (Herden et al., 2013).

High virus titers and induction of a robust T-cell response for mounting an early elimination of the virus and preventing adverse effects of T-cell-mediated immunopathology seem to be important (Richt et al., 1994; Oldach et al., 1995; Lewis et al., 1999; Furrer et al., 2001; Stitz et al., 2002; Hausmann et al., 2005; Henkel et al., 2005). Vector-based vaccines have been used experimentally.

Avian Bornaviruses (*Psittacine bornavirus 1* and *2*, *Passeriform bornavirus 1* and *2*, *waterbird 1 bornavirus*, unclassified bornaviruses): Recently, vector-based vaccines have been generated which might open the avenue for vaccination strategies in the future (Olbert et al., 2016).

3.1.4.3. Article 7(d)(iii) Medical treatments

There are no commercial drugs available on the market neither for mammalian bornaviruses nor avian bornaviruses. Substances have been tested *in vitro* or experimentally only, often addressing the viral strategies to circumvent the antiviral immune response, e.g. interferon system (e.g. interferon-α, -γ). Viral spread could be also efficiently inhibited in cell lines and primary CNS cells by an inhibitor against a host enzyme used by the virus for the cleavage of its glycoprotein (Lennartz et al., 2016).

Mammalian bornaviruses (*Mammalian 1 bornavirus*): For classical BoDV-1 infections with BD, the use of amantadine sulfate (AS), a drug with antiviral activity against influenza A was recommended but could not be confirmed by others (Herden et al., 2013). Substances such as ribavirin, Ara-C or 2′-fluoro-2′-deoxycytidine have been tested *in vitro* or in animal models with effect on, e.g. viral transcription or replication, disease outcome (Herden et al., 2013).

Avian bornaviruses (*Psittacine bornavirus 1*): For avian bornaviruses, interferon-α and ribavirin could efficiently inhibit avian bornaviruses in cell culture, however, there is yet no confirmation *in vivo* (Reuter et al., 2010; Reuter et al., 2016; Musser et al., 2015).

In vivo, there is no curative therapy for PDD or ABV infection, and therapy is only symptomatic. Control of virus infection and prevention could include isolation of ABV-infected birds, sanitation and disinfection (Hoppes et al., 2010). Control of traffic and trading might further contribute to control viral spread.

3.1.4.4. Article 7(d)(iv) Biosecurity measures

No available biosecurity measures so far any mammalian or avian bornaviruses.

3.1.4.5. Article 7(d)(v) Restrictions on the movement of animals and products

No restriction movement measures so far for mammalian or avian bornaviruses.

3.1.4.6. Article 7(d)(vi) Killing of animals

No killing measures for mammalian or avian bornaviruses.

3.1.4.7. Article 7(d)(vii) Disposal of carcasses and other relevant animal by-products

No specific disposal options for infected animals available.

3.1.5. Article 7(e) The impact of disease prevention and control measures

3.1.5.1. Article 7(e)(i) The direct and indirect costs for the affected sectors and the economy as a whole

No cost calculations exist so far for mammalian or avian bornaviruses.

3.1.5.2. Article 7(e)(ii) The societal acceptance of disease prevention and control measures

Not applicable.

3.1.5.3. Article 7(e)(iii) The welfare of affected subpopulations of kept and wild animals

Parameter 1 − Welfare impact of control measures on domestic animals

No control measures anymore; obligation to report on cases of BD in horses was cancelled in Germany in 2011.

Parameter 2 − Wildlife depopulation as control measure

No control measures for mammalian or avian bornaviruses.

3.1.5.4. Article 7(e)(iv) The environment and biodiversity

Environment

Parameter 1 – Use and potential residuals of biocides or medical drugs in environmental compartments (soil, water, feed, manure)

This is not applicable.

Biodiversity

Parameter 2 – Mortality in wild species

See under Section 3.1.1.1.

3.2. Assessment according to Article 5 criteria

This section presents the results of the expert judgement on the criteria of Article 5 of the AHL about Borna disease (Table 1). The expert judgement was based on Individual and Collective Behavioural Aggregation (ICBA) approach described in detail in the opinion on the methodology (EFSA AHAW Panel, 2017). Experts have been provided with information of the disease fact-sheet mapped into Article 5 criteria (see supporting information, Annex A), based on that the experts indicate their Y/N or 'na' judgement on each criterion of Article 5, and the reasoning supporting their judgement.

The minimum number of judges in the judgement was 11. The expert judgement was conducted as described in the methodological opinion (EFSA AHAW Panel, 2017). For details on the interpretation of the questions, see Appendix B of the methodological opinion (EFSA AHAW Panel, 2017).

Table 1: Outcome of the expert judgement on the Article 5 criteria for Borna disease

Criteria to be met by the disease: According to AHL, a disease shall be included in the list referred to in point (b) of paragraph 1 of Article 5 if it has been assessed in accordance with Article 7 and meets all of the following criteria		Final outcome
A(i)	The disease is transmissible	Y
A(ii)	Animal species are either susceptible to the disease or vectors and reservoirs thereof exist in the Union	Y
A(iii)	The disease causes negative effects on animal health or poses a risk to public health due to its zoonotic character	NC
A(iv)	Diagnostic tools are available for the disease	Y
A(v)	Risk-mitigating measures and, where relevant, surveillance of the disease are effective and proportionate to the risks posed by the disease in the Union	N
At least one criterion to be met by the disease: In addition to the criteria set out above at points A(i)–A(v), the disease needs to fulfil at least one of the following criteria		
B(i)	The 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	N
B(ii)	The disease agent has developed resistance to treatments and poses a significant danger to public and/or animal health in the Union	na
B(iii)	The disease causes or could cause a significant negative economic impact affecting agriculture or aquaculture production in the Union	N
B(iv)	The disease has the potential to generate a crisis or the disease agent could be used for the purpose of bioterrorism	N
B(v)	The disease has or could have a significant negative impact on the environment, including biodiversity, of the Union	N

Colour code: green = consensus (Yes/No); yellow = no consensus (NC); red = not applicable (na), i.e. insufficient evidence or not relevant to judge.

3.2.1. Non-consensus questions

This section displays the assessment related to each criterion of Article 5 where no consensus was achieved in form of tables (Table 2). The proportion of Y, N or na answers are reported, followed by the list of different supporting views for each answer.

Table 2: Outcome of the expert judgement related to criterion 5 A(iii)

Question		Final outcome	Response		
			Y (%)	N (%)	na (%)
A(iii)	The disease causes negative effects on animal health or poses a risk to public health due to its zoonotic character	NC	36	64	0

NC: non-consensus; number of judges: 11.

Reasoning supporting the judgement

Supporting Yes:

- For VSBV-1, a zoonotic potential has been demonstrated.
- Borna disease can cause negative effects (mortality) on animals, particularly in mammals, e.g. in horses but also in cattle and sheep.
- Supporting No:
- Mostly a clinically inapparent infection and very few animals present with clinical signs (< 0.1% horses and < 0.01% sheep in endemic areas). Prognosis is poor for cases with clinical signs.
- The virus and antibodies can be detected, but often without clinical signs.
- Only novel recently identified bornavirus VSBV from asymptomatic captive variegated squirrels is confirmed as zoonotic, but the transmission route is not certain, suspected by very close contact with possibly intranasal transmission, bites or scratches.

3.2.2. Outcome of the assessment of Borna disease according to criteria of Article 5(3) of the AHL on its eligibility to be listed

As from the legal text of the AHL, a disease is considered eligible to be listed as laid down in Article 5 if it fulfils all criteria of the first set from A(i) to A(v) and at least one of the second set of criteria from B(i) to B(v). According to the assessment methodology (EFSA AHAW Panel, 2017), a criterion is considered fulfilled when the outcome is 'Yes'. According to the results shown in Table 1, BD does not comply with criterion A(v) and the assessment is inconclusive on compliance with criterion 5 A(iii). Therefore, BD cannot be considered eligible to be listed for Union intervention as laid down in Article 5 (3) of the AHL.

3.3. Assessment according to Article 9 criteria

This section presents the results of the expert judgement on the criteria of Annex IV referring to categories as in Article 9 of the AHL about Borna disease (Tables 3, 4, 5, 6 and 7). The expert judgement was based on ICBA approach described in detail in the opinion on the methodology. Experts have been provided with information of the disease fact-sheet mapped into Article 9 criteria (see supporting information, Annex A), based on that the experts indicate their Y/N or 'na' judgement on each criterion of Article 9, and the reasoning supporting their judgement.

The minimum number of judges in the judgement was 11. The expert judgement was conducted as described in the methodological opinion (EFSA AHAW Panel, 2017). For details on the interpretation of the questions see Appendix B of the methodological opinion (EFSA AHAW Panel, 2017).

Table 3: Outcome of the expert judgement related to the criteria of Section 1 of Annex IV (category A of Article 9) for Borna disease (CI = current impact; PI = potential impact)

Criteria to be met by the disease: The disease needs to fulfil all of the following criteria		Final outcome
1	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	NC
2.1	The disease is highly transmissible	N
2.2	There be possibilities of airborne or waterborne or vector-borne spread	NC
2.3	The disease affects multiple species of kept and wild animals OR single species of kept animals of economic importance	Y
2.4	The disease may result in high morbidity and significant mortality rates	N

	At least one criterion to be met by the disease: In addition to the criteria set out above at points 1–2.4, the disease needs to fulfil at least one of the following criteria	
3	The disease has a zoonotic potential with significant consequences on public health, including epidemic or pandemic potential OR possible significant threats to food safety	N
4(CI)	The disease 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	N
4 (PI)	The disease 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	N
5(a)(CI)	The disease has a significant impact on society, with in particular an impact on labour markets	N
5(a)(PI)	The disease has a significant impact on society, with in particular an impact on labour markets	N
5(b)(CI)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	N
5(b)(PI)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	N
5(c)(CI)	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	N
5(c)(PI)	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	N
5(d)(CI)	The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds	N
5(d)(PI)	The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds	N

Colour code: green = consensus (Yes/No); yellow = no consensus (NC).

Table 4: Outcome of the expert judgement related to the criteria of Section 2 of Annex IV (category B of Article 9) for Borna disease (CI = current impact; PI = potential impact)

	Criteria to be met by the disease: The disease needs to fulfil all of the following criteria	**Final outcome**
1	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	N
2.1	The disease is moderately to highly transmissible	NC
2.2	There be possibilities of airborne or waterborne or vector-borne spread	NC
2.3	The disease affects single or multiple species	Y
2.4	The disease may result in high morbidity with in general low mortality	N
	At least one criterion to be met by the disease: In addition to the criteria set out above at points 1–2.4, the disease needs to fulfil at least one of the following criteria	
3	The disease has a zoonotic potential with significant consequences on public health, including epidemic potential OR possible significant threats to food safety	N
4 (CI)	The disease 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	N
4 (PI)	The disease 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	N
5(a)(CI)	The disease has a significant impact on society, with in particular an impact on labour markets	N
5(a)(PI)	The disease has a significant impact on society, with in particular an impact on labour markets	N
5(b)(CI)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	N

5(b)(PI)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	N
5(c)(CI)	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	N
5(c)(PI)	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	N
5(d)(CI)	The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds	N
5(d)(PI)	The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds	N

Colour code: green = consensus (Yes/No); yellow = no consensus (NC).

Table 5: Outcome of the expert judgement related to the criteria of Section 3 of Annex IV (category C of Article 9) for Borna disease (CI=current impact; PI=potential impact)

Criteria to be met by the disease: The disease needs to fulfil all of the following criteria		Final outcome
1	The disease is present in the whole OR part of the Union territory with an endemic character	NC
2.1	The disease is moderately to highly transmissible	NC
2.2	The disease is transmitted mainly by direct or indirect transmission	Y
2.3	The disease affects single or multiple species	Y
2.4	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	N
At least one criterion to be met by the disease: In addition to the criteria set out above at points 1–2.4, the disease needs to fulfil at least one of the following criteria		
3	The disease has a zoonotic potential with significant consequences on public health, or possible significant threats to food safety	N
4(CI)	The disease has a significant impact on the economy of parts of the Union, mainly related to its direct impact on certain types of animal production systems	N
4(PI)	The disease has a significant impact on the economy of parts of the Union, mainly related to its direct impact on certain types of animal production systems	N
5(a)(CI)	The disease has a significant impact on society, with in particular an impact on labour markets	N
5(a)(PI)	The disease has a significant impact on society, with in particular an impact on labour markets	N
5(b)(CI)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	N
5(b)(PI)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	N
5(c)(CI)	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	N
5(c)(PI)	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	N
5(d)(CI)	The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds	N
5(d)(PI)	The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds	N

Colour code: green = consensus (Yes/No); yellow = no consensus (NC).

Table 6: Outcome of the expert judgement related to the criteria of Section 4 of Annex IV (category D of Article 9) for Borna disease

Criteria to be met by the disease: The disease needs to fulfil all of the following criteria		Final outcome
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	N
	The disease fulfils criteria of Sections 1, 2, 3 or 5 of Annex IV of AHL	NC

Colour code: green = consensus (Yes/No); yellow = no consensus (NC).

Table 7: Outcome of the expert judgement related to the criteria of Section 5 of Annex IV (category E of Article 9) for Borna disease

Diseases in category E need to fulfil criteria of Sections 1, 2 or 3 of Annex IV of AHL and/or the following:		Final outcome
E	Surveillance of the disease is necessary for reasons relating to animal health, animal welfare, human health, the economy, society or the environment (If a disease fulfils the criteria as in Article 5, thus being eligible to be listed, consequently category E would apply.)	N

Colour code: green = consensus (Yes/No).

3.3.1. Non-consensus questions

This section displays the assessment related to each criterion of Annex IV referring to the categories of Article 9 of the AHL where no consensus was achieved in form of tables (Tables 8, 9 and 10). The proportion of Y, N or 'na' answers are reported, followed by the list of different supporting views for each answer.

Table 8: Outcome of the expert judgement related to criterion 1 of Article 9

Question		Final outcome	Response		
			Y (%)	N (%)	na (%)
1(cat.A)	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	NC	9	91	0
1(cat.C)	The disease is present in the whole OR part of the Union territory with an endemic character	NC	91	9	0

NC: non-consensus; number of judges: 11.

Reasoning supporting the judgement

Supporting Yes for 1 (cat.A):

- There are only very limited endemic areas in four MSs, namely specific regions in Germany, Austria, Switzerland and Liechtenstein, where clinically apparent classical BDV-1 occurs and where endemic viral clusters with a strong geographical association have been reported being related to the occurrence of the viral reservoir.

Supporting Yes for 1 (cat.C):

- There are no officially free areas, but information about the distribution of Borna viruses is limited since no surveillance is in place in Europe.
- Presumably it is endemic in all MSs due to avian Borna viruses, although data are sparse.
- In MSs where surveys were initiated, seropositive cases have been detected.

Table 9: Outcome of the expert judgement related to criterion 2.1 of Article 9

Question		Final outcome	Response		
			Y (%)	N (%)	na (%)
2.1(cat.B,C)	The disease is moderately to highly transmissible	NC	55	0	45

NC: non-consensus; number of judges: 11.

Reasoning supporting the judgement

Supporting Yes:

- The rate of transmission is actually unknown, although the disease is endemic in certain areas, thus the infection is expected to spread over with a reproductive ratio of at least 1.

Supporting na:

- The incidence and speed of transmission is unknown and no data are available even within the known reservoir species. At times, only single animals present with manifest disease.
- Even in stables with an endemic problem, there are antibody-negative animals.
- No data are available, but apparently the transmission rate seems neither high nor moderate.

Table 10: Outcome of the expert judgement related to criterion 2.2 of Article 9

Question		Final outcome	Response		
			Y (%)	N (%)	na (%)
2.2	There be possibilities of airborne or waterborne or vector-borne spread	NC	0	73	27

NC: non-consensus; number of judges: 11.

Reasoning supporting the judgement

Supporting No:

- Airborne, waterborne or vector-borne spread has never been described for BD. Based on information presented in the fact sheet, there is not such kind of spread. Since the virus shed in secretions, excretions, urine and faeces, the most likely transmission route is via direct contact, inhalation or via the orofaecal route.

Supporting na:

- Suspected routes of transmission are described but not proven. No evidence is presented supporting or ruling out airborne, waterborne or vector-borne transmission and there is still much unknown about the nature and rate of transmission.

3.3.2. Outcome of the assessment of criteria in Annex IV for Borna disease for the purpose of categorisation as in Article 9 of the AHL

As from the legal text of the AHL, a disease is considered fitting in a certain category (A, B, C, D or E corresponding to point (a) to point (e) of Article 9(1) of the AHL) if it is eligible to be listed for Union intervention as laid down in Article 5(3) and fulfils all criteria of the first set from 1 to 2.4 and at least one of the second set of criteria from 3 to 5(d) as shown in Tables 3–7. According to the assessment methodology (EFSA AHAW Panel, 2017), a criterion is considered fulfilled when the outcome is 'Yes'. With respect to different type of impact where the assessment is divided into current and potential impact, a criterion will be considered fulfilled if at least one of the two outcomes is 'Y' and, in case of no 'Y', the assessment is inconclusive if at least one outcome is 'NC'.

A description of the outcome of the assessment of criteria in Annex IV for Borna disease for the purpose of categorisation as in Article 9 of the AHL is presented in Table 11.

Table 11: Outcome of the assessment of criteria in Annex IV for Borna disease for the purpose of categorisation as in Article 9 of the AHL (CI = current impact; PI = potential impact)

Category	Article 9 criteria										
	1° set of criteria					2° set of criteria					
	1	2.1	2.2	2.3	2.4	3	4	5a	5b	5c	5d
	Geographical distribution	Transmissibility	Routes of transmission	Multiple species	Morbidity and mortality	Zoonotic potential	Impact on economy	Impact on society	Impact on animal welfare	Impact on environment	Impact on biodiversity
A	NC	N	NC	Y	N	N	N	N	N	N	N
B	N	NC	NC	Y	N	N	N	N	N	N	N
C	NC	NC	Y	Y	N	N	N	N	N	N	N
D	N										
E	N										

According to the assessment here performed, BD complies with the following criteria of the Sections 1 to 5 of Annex IV of the AHL for the application of the disease prevention and control rules referred to in points (a) to (e) of Article 9(1):

1) To be assigned to category A, a disease needs to comply with all criteria of the first set (1, 2.1–2.4) and according to the assessment BD complies only with criterion 2.3, but not with 2.1 and 2.4, and the assessment is inconclusive on compliance with criterion 1 and 2.2. To be eligible for category A, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5a–d) and BD does not comply with any criteria.

2) To be assigned to category B, a disease needs to comply with all criteria of the first set (1, 2.1–2.4) and according to the assessment BD complies only with criterion 2.3, but not with 1 and 2.4, and the assessment is inconclusive on compliance with criterion 2.1 and 2.2. To be eligible for category B, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5a–d) and BD does not comply with any criteria.

3) To be assigned to category C, a disease needs to comply with all criteria of the first set (1, 2.1–2.4) and according to the assessment BD complies with criteria 2.2 and 2.3, but not with 2.4, and the assessment is inconclusive on the compliance with criteria 1 and 2.1. To be eligible for category C, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5a–d) and BD does not comply with any criteria.

4) To be assigned to category D, a disease needs to comply with criteria of Sections 1, 2, 3 or 5 of Annex IV of the AHL, and with the specific criterion D of Section 4, with which BD does not comply.

5) To be assigned to category E, a disease needs to comply with criteria of Sections 1, 2 or 3 of Annex IV of the AHL and/or the surveillance of the disease is necessary for reasons relating to animal health, animal welfare, human health, the economy, society or the environment. The latter is applicable if a disease fulfils the criteria as in Article 5 with which BD does not comply.

3.4. Assessment of Article 8

This section presents the results of the assessment on the criteria of Article 8(3) of the AHL about BD. The Article 8(3) criteria are about animal species to be listed, as it reads below:

'3. Animal species or groups of animal species shall be added to this list if they are affected or if they pose a risk for the spread of a specific listed disease because:

a) they are susceptible for a specific listed disease or scientific evidence indicates that such susceptibility is likely; or

b) they are vector species or reservoirs for that disease, or scientific evidence indicates that such role is likely'.

For this reason, the assessment on Article 8 criteria is based on the evidence as extrapolated from the relevant criteria of Article 7, i.e. the ones related to susceptible and reservoir species or routes of transmission, which cover also possible role of biological or mechanical vectors.[1] According to the mapping, as presented in Table 5, Section 3.2 of the scientific opinion on the *ad hoc* methodology (EFSA AHAW Panel, 2017), the main animal species to be listed for Borna disease according to the criteria of Article 8(3) of the AHL are as displayed in Table 12.

Table 12: Main animal species to be listed for Borna disease according to criteria of Article 8 (*source*: data reported in Section 3.1.1.1)

	Class	Order	Family	Genus/Species
Susceptible	Aves	Accipitriformes	Accipitridae	Bald eagle (*Haliaeetus leucocephalus*)
		Anseriformes	Anatidae	Northern pintail (*Anas acuta*), gadwall (*Anas strepera*), mallard (*Anas plytyrhynchos*), Canada goose(*Branta Canadensis*), Trumpeter swan (*Cygnus Cygnus buccinators*), mute swan (*Cygnus olor*)
		Charadriiformes	Charadriidae	Not specified
		Columbiformes	Columbidae	Pigeons (not specified)
		Galliformes	Phasianidae	*Gallus gallus*
		Gruiformes	Gruidae	Cranes (not specified)
			Emberizidae	Not specified
			Estrildidae	Munia (not specified), finches (not specified)
			Fringillidae	Canaries (not specified)
		Psittaciformes	Cacatuidae	Cockatoos (not specified)
			Psittacidae	African grey parrots (*Psittacus erithacus*), Patagonian conure (*Cyanoliseus patagonus*), Psitacinae (not specified)
	Mammalia	Artiodactyla	Bovidae	Domestic cattle (*Bos taurus*), domestic goat (*Capra aegagrus*), domestic sheep (*Ovis aries*)
			Camelidae	Alpaca (*Vicugna pacos*)
			Cervidae	Deer (not specified)
			Hippopotamidae	Hippopotamus (*Hippopotamus amphibius*)
		Carnivora	Canidae	Domestic dog (*Canis familiaris*), foxes (*Vulpes vulpes*)
			Felidae	Domestic cat (*Felis catus*), lynx (not specified)
			Mustelidae	Ferret (*Mustela putorius furo*), badger (*Meles meles*)
			Procyonidae	Racoon (*Procyon lotor*)
		Chiroptera	Not specified	
		Lagomorpha	Leporidae	Domestic rabbit (*Oryctolagus cuniculus*)
		Perissodactyla	Equidae	Domestic horse (*Equus caballus*)
			Rhinocerotidae	Great Indian rhinoceros (*Rhinoceros unicorni*)

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[1] A vector is a living organism that transmits an infectious agent from an infected animal to a human or another animal. Vectors are frequently arthropods. Biological vectors may carry pathogens that can multiply within their bodies and be delivered to new hosts, usually by biting. In mechanical vectors the pathogens do not multiply within the vector, which usually remains infected for shorter time than in biological vectors.

	Class	Order	Family	Genus/Species
		Pilosa	Bradypodidae	Sloths (not specified)
		Primates	Lemuridae	Vari monkey (*Lemur varius*), rhesus macaque (*Macaca mulatta*)
		Proboscidea	Elephantidae	Indian (Asian) elephant (*Elephas maximus indicus*)
		Rodentia	Sciuridae	Variegated squirrels (*Sciurus variegatoides*), Prevost's squirrels (*Callosciurus prevostii*)
			Cricetidae	Bank voles (*Myodes glareolus*), hamster (not specified)
			Caviidae	Guinea pig (*Cavia porcellus*)
			Muridae	Rats (not specified), mouse (not specified), gerbils (Not specified)
		Scandentia	Tupaiidae	Treeshrews (not specified)
	Reptiles	Squamata	Elapidae	Loveridge's garter snake (*Elapsoidea loveridgei*)
			Viperidae	Gaboon viper (*Bitis gabonica*)
Reservoir	Mammalia	Eulipotyphla	Soricidae	Bicoloured white toothed shrew (*Crocidura leucodon*) Suspected for: Variegated squirrels (*Sciurus variegatoides*) Prevost's squirrels (*Callosciurus prevostii*) Unknown for bird species
Vectors	None			

4.   Conclusions

TOR 1: *for each of those diseases an assessment, following the criteria laid down in Article 7 of the AHL, on its eligibility of being listed for Union intervention as laid down in Article 5(3) of the AHL;*

- According to the assessment here performed, BD does not comply with criterion 5 A(v) of the first set and therefore cannot be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL.

TOR 2a: *for each of the diseases which was found eligible to be listed for Union intervention, an assessment of its compliance with each of the criteria in Annex IV to the AHL for the purpose of categorisation of diseases in accordance with Article 9 of the AHL;*

- According to the assessment here performed, since BD cannot be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL, the assessment of its compliance with each of the criteria in Annex IV to the AHL for the purpose of categorisation of diseases in accordance with Article 9 of the AHL is not applicable.

TOR 2b: *for each of the diseases which was found eligible to be listed for Union intervention, a list of animal species that should be considered candidates for listing in accordance with Article 8 of the AHL.*

- According to the assessment here performed, since BD cannot be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL, there are no animal species that can be considered to be listed for BD according to Article 8(3) of the AHL.

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Abbreviations

ABBV	aquatic bird bornavirus
ABV	avian bornavirus
AHAW	EFSA Panel on Animal Health and Welfare
AHL	Animal Health Law
AIDS	acquired immune deficiency syndrome
AS	amantadine sulfate
BD	Borna disease
BDV	Borna disease virus
BoDV-1	Borna disease virus 1
CITES	Convention on International Trade in Endangered Species of Wild Fauna and Flora
CNS	central nervous system
CSF	cerebrospinal fluid
DALY	disability-adjusted life year
EBL	endogenous Bornavirus-like
ELISA	enzyme-linked immunosorbent assay
ICBA	Individual and Collective Behavioural Aggregation
IFA	indirect immunofluorescence assay
IHC	immunohistochemistry
ISH	*in situ* hybridisation
IUCN	International Union for Conservation of Nature
MS	Member State
OIE	World Organisation for Animal Health
PBMC	peripheral blood mononuclear cell
PDD	proventricular dilatation disease
RNA	ribonucleic acid

RT-PCR   reverse transcription polymerase chain reaction
ToR   Terms of Reference
VSBV-1   variegated squirrel 1 bornavirus
WB   western blot

33