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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): antimicrobial-resistant *Rhodococcus equi* in horses

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Abstract

Rhodococcus equi (*R. equi*) was identified among the most relevant antimicrobial-resistant (AMR) bacteria in the EU for horses in a previous scientific opinion. Thus, it 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 its eligibility to be listed, Annex IV for its categorisation according to disease prevention and control rules as in Article 9 and Article 8 for listing animal species related to the bacterium. The assessment has been performed following a methodology previously published. The outcome is the median of the probability ranges provided by the experts, which indicates whether each criterion is fulfilled (lower bound ≥ 66%) or not (upper bound ≤ 33%), or whether there is uncertainty about fulfilment. Reasoning points are reported for criteria with uncertain outcome. According to the assessment here performed, it is uncertain whether AMR *R. equi* can be considered eligible to be listed for Union intervention according to Article 5 of the AHL (10–66% probability). According to the criteria in Annex IV, for the purpose of categorisation related to the level of prevention and control as in Article 9 of the AHL, the AHAW Panel concluded that the bacterium does not meet the criteria in Sections 1 and 2 (Categories A and B; 5–10% and 10–33% probability of meeting the criteria, respectively), and the AHAW Panel is uncertain whether it meets the criteria in Sections 3, 4 and 5 (Categories C, D and E; 10–66% probability of meeting the criteria in all three categories). The animal species to be listed for AMR *R. equi* according to Article 8 criteria are mainly horses and other species belonging to the Perissodactyla and Artiodactyla orders.

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1. Introduction

The European Food Safety Authority (EFSA) received a mandate from the European Commission to investigate the global state of play as regards antimicrobial-resistant (AMR) animal pathogens that cause transmissible animal diseases (Term of Reference (ToR) 1), to identify the most relevant AMR bacteria in the European Union (EU) (first part of ToR 2), to summarise the existing or potential animal health impact of those identified bacteria in the EU (second part of ToR 2), and to perform the assessment of those bacteria to be listed and categorised according to the criteria in Article 5, Annex IV according to Article 9 and Article 8 within the Regulation (EU) No 2016/429[1] on transmissible animal diseases ('Animal Health Law') (ToR 3).

The global state of play for AMR animal pathogens that cause transmissible animal diseases (ToR 1) and the results of the assessment of the most relevant AMR bacteria in the EU (first part of ToR 2) for horses were published in a separate EFSA scientific opinion (EFSA AHAW Panel, 2021a).

According to the results of the assessment already conducted, *Rhodococcus equi* (*R. equi*) was identified among the most relevant AMR bacteria in the EU for horses due to the ubiquitous occurrence of this horse pathogen in Europe, the potential severity of infections and the alarming levels of resistance to the only therapeutic option available for treatment of the disease caused by this pathogen (as reported in several studies in North America). This resistance includes an antimicrobial in the A category of the Antimicrobial Advice Ad Hoc Expert Group classification, rifampicin, combined with a macrolide (EFSA AHAW Panel, 2021a). Previous studies have suggested an increase in the frequency of this resistance in the last 20 years at least in the USA (probably due to the extended treatment of subclinical infections) (Giguère et al., 2017), including the emergence of horizontally transferrable resistance to macrolides and the increasing isolation of strains resistant to both macrolides and rifampicin. The low number of studies retrieved for this pathogen in the extensive literature review performed previously is probably attributable to the difficulty of collecting clinical specimens due to the acute progression of the disease and the invasiveness of the procedure required for the collection of specimens from the lower respiratory tract and the abdominal cavity of infected foals. This has resulted in very limited information on the frequency of antimicrobial resistance in this important equine pathogen.

This scientific opinion presents the results of the assessment on AMR *R. equi* in horses on its eligibility to be listed and categorised within the AHL framework. Special focus is placed on the animal health impact of AMR *R. equi* in horses in the EU, which is also summarised here as part of the assessment conducted according to the profile of the infection and its impact on animal welfare (Article 7).

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

The background and ToRs as provided by the European Commission for the present document are reported in Sections 1.1 and 1.2 of the scientific opinion on the ad hoc method to be followed for the assessment of animal diseases caused by bacteria resistant to antimicrobials within the AHL framework (EFSA AHAW Panel, 2021b).

1.2. Interpretation of the Terms of Reference

The interpretation of the ToRs is as in Sections 1.2.3 and 1.3.3 of the scientific opinion on the ad hoc method to be followed for the assessment of animal diseases caused by bacteria resistant to antimicrobials within the AHL framework (EFSA AHAW Panel, 2021b).

The present document reports the results of the assessment on AMR *R. equi* in horses according to the criteria of the AHL articles as follows:

- Article 7: AMR *R. equi* infection profile and impacts;
- Article 5: eligibility of AMR *R. equi* infection to be listed;
- Article 9: categorisation of AMR *R. equi* infection according to disease prevention and control rules as in Annex IV;
- Article 8: list of animal species (also apart from horses) related to AMR *R. equi* infection.

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[1] Regulation (EU) 2016/429 of the European Parliament and of the Council of 9 March 2016 on transmissible animal diseases and amending and repealing certain acts in the area of animal health ('Animal Health Law'). OJ L 84, 31.3.2016, p. 1–208.

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 listing and categorisation of animal diseases within the AHL framework (EFSA AHAW Panel, 2017).

In order to take into account the specifics related to animal diseases caused by bacteria resistant to antimicrobials, the term 'disease' as in the AHL was interpreted in a broader sense, referring also to colonisation by commensal and potentially opportunistic bacteria, and the general presence of the identified AMR bacteria in the EU, depending on each criterion.

The following assessment was performed by the EFSA Panel on Animal Health and Welfare (AHAW) based on the information collected and compiled in form of a fact sheet as in Section 3.1 of the present document. The outcome is the median of the probability ranges provided by the experts, which are accompanied by verbal interpretations as spelled out in Table 1.

Table 1: Approximate probability scale recommended for harmonised use in EFSA (EFSA Scientific Committee, 2018)

Probability term	Subjective probability range
Almost certain	99–100%
Extremely likely	95–99%
Very likely	90–95%
Likely	66–90%
About as likely as not	33–66%
Unlikely	10–33%
Very unlikely	5–10%
Extremely unlikely	1–5%
Almost impossible	0–1%

3. Assessment

3.1. Assessment of AMR *Rhodococcus equi* according to Article 7 criteria of the AHL

3.1.1. Article 7(a) Disease profile

R. equi is a Gram-positive, aerobic, non-motile, encapsulated, facultative intracellular bacillus. It is ubiquitous in soil and frequently isolated from the faeces of wild and domestic animals.

Macrolides (erythromycin, azithromycin and clarithromycin) and rifampicin are the drugs of choice for treatment of *R. equi* infections in horses. When possible, information in this fact-sheet has been specified for macrolide and rifampicin-resistant isolates. Resistance to macrolides is mediated by transferable plasmids, whereas rifampicin resistance is due to mutations in the gene (*rpoB*) encoding the drug target (β-subunit of bacterial RNA polymerase). Macrolide resistance is associated with *erm(46)*, a rRNA methylase-encoding gene that has been identified only in *R. equi* to date (Giguère et al., 2017).

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

This bacterial species is a cause of suppurative pneumonia and lung abscesses in young (1- to 4-month-old) horse foals. Adult horses (*Equus caballus*) are usually asymptomatic unless immunocompromised, but they are not permanent carriers. Disease in foals is caused by virulent strains carrying plasmid-mediated virulence-associated protein A (*vapA*) (Ocampo-Sosa et al., 2007). There is no evidence that *R. equi* can cause similar disease in other members of the family Equidae such as donkeys (*Equus africanus asinus*) and zebras (*Equus zebra*). *VapA*-positive strains have been isolated from pyogranulomatous infections involving the lung or the intestinal tract of llama (*Lama glama*) (Löhr et al., 2019) and dromedary (*Camelus dromedarius*) (Kinne et al., 2011), suggesting that these camelids are susceptible to the disease. Sporadic cases of cervical lymphadenopathy are observed in slaughtered pigs (*Sus scrofa domesticus*) and cattle (*Bos taurus*). Porcine and bovine strains are associated with distinct virulence factors (*VapB* and *VapN*, respectively) and are generally referred to as intermediate virulent (Witkowski et al., 2016; Ribeiro et al., 2018). *VapN* has also been

reported in rare forms of systemic pyogranulomatous infections in goats (*Capra aegagrus hircus*) (Stranahan et al., 2018; Żychska et al., 2021). Pulmonary and skin infections have been reported in cats (*Felis catus*) (Aslam et al., 2020) and dogs (*Canis lupus familiaris*) (Bryan et al., 2017), especially immunocompromised individuals or those with endocrine dysfunction. The opportunistic nature of infections in dogs and cats is evidenced by the fact that strains isolated from these animal species can be avirulent or carry any of the three virulence factors reported in horses (*vapA*), pigs (*VapB*) and ruminants (*VapN*) (Takai et al., 2003; Bryan et al., 2017).

Susceptible animal species

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

Intermediate virulent (*VapB*-positive) strains have been isolated from submaxillary lymph nodes of free-living wild boar (*Sus scrofa*) (Rzewuska et al., 2014), and avirulent strains have been detected in lymph nodes of other animal species including peccaries (*Tayassu pecari* and *Tayassu tajacu*) (de Morais et al., 2018), red deer (*Cervus elaphus*) and roe deer (*Capreolus capreolus*) (Rzewuska et al., 2014). Rare cases of disease have been reported in a wide range of host species, including Baikal seals (*Pusa sibirica*), koala (*Phascolarctos cinereus*), cotton-top tamarin (*Saguinus oedipus*), American crocodile (*Crocodylus acutus*) and American alligator (*Alligator mississippiensis*) (Prescott, 1991). Wild horses and goats are likely susceptible given the occurrence of *R. equi* disease in domesticated members of these animal species.

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

Mainly horses, namely young foals below 4 months old, are susceptible. Cattle, pigs, goats, camelids (e.g. dromedary and llama), dogs and cats are also susceptible although infections are infrequent in these animal species. Rare cases of disease have been reported in alpacas (*Lama pacos*) (Cuteri et al., 2001) and dromedaries are likely susceptible.

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

No information is available on experimentally susceptible wildlife species.

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

A murine lung infection model is available (González-Iglesias et al., 2014). Mouse models require the use of immunosuppressive drugs to reproduce lung lesions similar to those observed in foals. Other experimentally susceptible animal species include pig (piglets) and guinea pig, but these animals develop a clinically distinct form of suppurative pneumonia without the typical abscesses observed in foals (von Bargen and Haas, 2009).

Reservoir animal species

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

No wild reservoir species are known. *R. equi* is ubiquitously distributed in soil and there is no evidence that the disease can be transmitted from animal to animal. Thus, although *R. equi* can be isolated from several animal species, including the gastrointestinal contents of earthworms (Annelida; Megascolecidae) (Takai et al., 2021), none of them is regarded as a disease reservoir.

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

Soil is the natural reservoir of *R. equi*. Although infected horse foals exhale high concentrations of virulent *R. equi* in their breath (Muscatello et al., 2009), foal-to-foal transmission has yet to be demonstrated. However, since the prevalence of *R. equi* pneumonia was associated with the airborne burden of virulent *R. equi* (Muscatello et al., 2006), shedding of virulent strains by infected foals likely contributes to air contamination, therefore increasing the risk of infection.

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

Morbidity

Parameter 1 – Prevalence/incidence

It is difficult to accurately estimate the frequency of this disease at the population level, because the cumulative incidence of disease is extremely variable among breeding farms and between years.

R. equi pneumonia occurs endemically on some farms, typically breeding farms and only sporadically or not at all on other farms. A cumulative incidence above 30% among foals (measured from birth until 150 days of age) in endemic farms has been reported (Chaffin et al., 2011). It has been estimated that cumulative incidences are usually 10–20% from birth through weaning, although higher cumulative incidences have been reported (Cohen, 2014). This high variability across studies is influenced by the case definition and the methodology used for disease screening. For example, it has been shown that clinical signs of pneumonia occur in approximately 21% of foals showing lung consolidations by thoracic ultrasonography (Chaffin et al., 2013).

Seroprevalence of antibodies to *R. equi* has been hypothesised to be associated with environmental exposure. In Central Italy in 1999, 602 healthy horse foals (1- to 6-month old) from 20 independent farms were sampled to determine the incidence of *R. equi* infections among this age group. Serum samples were tested by enzyme-linked immunosorbent assay (ELISA) and approximately 13% (60% of farms) of those showed a positive test result (Cuteri et al., 2003). In Southeast Turkey from 2009 to 2010, the sera of 679 healthy foals and adult horses, as well as 78 donkeys, were screened for antibodies to *R. equi* – 11.7% of horses and 11.5% of donkeys resulted positive, while horses between 1 and 5 years of age were characterised by the highest seropositivity (Tel et al., 2011). In three other provinces of Turkey from 2003 to 2004, the sera of 696 healthy foals and adult horses from 19 farms were run through ELISA, among which 14.8% showed a positive test result. In this case, foals younger than 1 year and horses from 5 to 10 years of age had the highest antibody titres (Attili et al., 2006). A prospective cohort study, conducted in Japan, enrolled 144 foals (30- and 45-day old) and collected serum samples over a time period of 2 years. Horse farms were selected according to the clinical manifestation of *R. equi*-like *disease among foals. Farms with endemic, sporadic and no occurrence of the disease were included. Study results showed that seropositivity by ELISA was higher for foals from farms with endemic or sporadic occurrence of disease symptoms, compared to those without (Higuchi et al., 1998). In Israel, 144 (2011) and 293 (2014) healthy adult horses from different farming systems and geographical areas were sampled and tested for the presence of antibodies to R. equi* by ELISA. The seroprevalence detected in this study was rather low with 7.6% in 2011 and 5.1% in 2014. Risk factors were not identified (Tirosh-Levy et al., 2017). In Japan, 2,879 sera of adult horses from 224 horse breeding farms were screened similarly and 11% of those samples turned out to be positive (Sanada et al., 1992). The role of antibody-positive adult horses as a source of exposure for foals remains unknown, but they possibly serve as sentinels reflecting environmental exposure.

There are only few available studies on prevalence of AMR *R. equi*. Based on a recent literature review on antimicrobial resistance in horse pathogens, it appears that resistance to macrolides and rifampicin has mainly emerged in the USA with studies reporting up to 25.7% of the isolates resistant to both antimicrobials, whereas the single European study of the review reported 1.7% of isolates in France resistant to these drugs (EFSA AHAW Panel, 2021a). Up to date, isolates of *R. equi* resistant to macrolides and rifampicin have been identified in the USA in at least five states. Nevertheless, the true prevalence of AMR *R. equi* in the USA and elsewhere is unknown. Reports of macrolide resistance in veterinary isolates of *R. equi* outside the USA have been extremely rare. There is one report of isolation of a macrolide- and rifampicin-resistant strain from a foal in China (Giguère et al., 2017).

Recent studies in the USA suggest that antimicrobial resistance was mainly due to mass antimicrobial treatment of subclinically affected foals over time, e.g. treating subclinical pneumonia detected by thoracic ultrasonographic screening. Huber et al. (2018) reported resistance of 1% out of 2,169 isolates for erythromycin and 2% for rifampicin in the decade 1995–2006 in the USA, and this increased to 14% and 16%, respectively, in the following 10 years. The same authors (Huber et al., 2019) detected 76% horse breeding farms in Kentucky yielding *R. equi* in soil resistant to macrolides and rifampicin.

In Texas and Florida, the overall prevalence of macrolide- and rifampicin-resistant isolates between 1997 and 2008 was 4%, with most resistant isolates detected after 2001. The odds of death were approximately seven times higher in foals infected with resistant isolates (Giguère et al., 2017).

In another US study conducted between 2011 and 2019, from 256 necropsied foals with rhodococcosis, *R. equi* isolates resistant to rifampicin and different macrolide compounds were detected in 22.7 and 14.8–16.0%, respectively (Erol et al., 2020). Resistance to antimicrobials in the *R. equi* isolates from necropsied foals was significantly higher in treated foals with dual therapy than in untreated foals.

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

Case-morbidity rate is unknown, since its calculation would require confirmation of *R. equi* infection using the gold standard diagnostic procedure based on identification of *R. equi* in tracheobronchial aspirates. This diagnostic approach is rarely used for disease screening in real life due to health risks associated with invasive sampling and higher costs for sampling and laboratory analysis. As mentioned before, morbidity rates are usually calculated based on detection of pulmonary lesions by thoracic ultrasonography, which does not prove *R. equi* infection and detects subclinical lesions that do not necessarily develop into clinical pneumonia.

Mortality

Parameter 3 – Case-fatality rate

The survival rate of foals with pneumonia caused by *R. equi* is highly influenced by the severity of the disease, and therefore by the time in which the disease is detected and treated. Older studies reported case-fatality rates from 40% to 80% (Elissalde et al., 1980). However, mortality was significantly reduced by the introduction of macrolide/rifampicin combination therapy and control programmes based on early detection of pneumonia by thoracic ultrasonography and antimicrobial treatment of diseased foals. A recent study conducted in a German breeding farm with a history of endemic *R. equi* infection showed that the percentage of horses that died from *R. equi* infection was approximately 0.5% amongst 2,756 foals with pneumonia observed in 2008–2016 (Arnold-Lehna et al., 2019). According to various studies, the success rate of antimicrobial therapy ranges between 80 and 97% in foals with clinical signs of mild to moderate pneumonia that receive early treatment (Venner et al., 2013; Hildebrand et al., 2015; Rutenberg et al., 2017; Arnold-Lehna et al., 2019). The same studies indicate that the proportion of foals that recover without antimicrobial therapy is extremely variable (27–66%), depending on the case definition. The antimicrobial resistance phenotype of the infecting strain is another important factor influencing mortality. A study on treatment outcome showed that survival was significantly lower in foals infected with strains resistant to macrolides or rifampicin (25%) than in foals infected with susceptible strains and receiving the same antimicrobial treatment (70%) (Giguère et al., 2010).

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

Parameter 1 – Report of zoonotic human cases (anywhere)

R. equi is an unusual cause of infection in humans. Human infections mainly occur in immunocompromised patients, whereas in immunocompetent patients, it is extremely rare (Kedlaya et al., 2001). The first human case of *R. equi* infection was described in 1967 in an immunocompromised patient who was working in a stockyard cleaning animal pen (Golub et al., 1967). In the 15 years after this initial description, only 12 more cases of human infection were documented in patients who were similarly immunocompromised (Van Etta et al., 1983). Since then (1983), more than 200 sporadic cases of human infections have been reported worldwide, and this increasing prevalence seems to coincide with the human immunodeficiency virus (HIV) epidemic and advances in transplant medicine and cancer chemotherapy (Weinstock and Brown, 2002; Lin et al., 2019). Even though sources and routes of *R. equi* infection in humans remain unclear, the infection seems to be associated with exposure to livestock or farming environments, particular in immunocompromised patients (Golub et al., 1967; Prescott, 1991; Arlotti et al., 1996; Ocampo-Sosa et al., 2007; Yamshchikov et al., 2010).

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

There is evidence indicating that the occurrence of multidrug resistance in *R. equi* has increased over time, including strains resistant to the two antimicrobial classes that are used for combination therapy of *R. equi* infections, macrolides and rifampicin. According to a retrospective study including 2,169 clinical isolates from diagnostic laboratories in the USA, the proportion of resistant isolates was approximately 1% for erythromycin and 2% for rifampicin in 1995–2006, and increased to approximately 14 and 16%, respectively, in 2007–2017 (Huber et al., 2018). This increase in resistance has been attributed to the practice of treating subclinical pneumonia detected by thoracic ultrasonographic screening. The same authors (Huber et al., 2019) detected 76% horse breeding farms in Kentucky yielding *R. equi* in soil resistant to macrolides and rifampicin. In Texas and Florida,

the overall prevalence of macrolide- and rifampicin-resistant isolates between 1997 and 2008 was 4%, with most resistant isolates detected after 2001. The occurrence of multidrug-resistant strains has also been reported in China (Giguère et al., 2017) and in Europe, with increasing minimum inhibitory concentration (MIC) values for rifampicin and erythromycin in isolates from foals retrieved in Ireland in the 1996–2006 period (Buckley et al., 2007), and a low (< 10%) prevalence of isolates resistant to either or both antimicrobials in *R. equi* isolates from horses in France (Duchesne et al., 2019) and Poland (Kalinowski et al., 2020), and no indication of increase of resistance over time. Prevalence seems to be higher compared to the USA (Álvarez-Narváez et al., 2021a), where isolates of *R. equi* resistant to macrolides and rifampicin have been identified in at least five states. In another US study conducted between 2011 and 2019, from 256 necropsied foals with rhodococcosis, *R. equi* isolates resistant to rifampicin and different macrolide compounds were detected in 22.65 and 14.8–16.01%, respectively (Erol et al., 2020). Resistance to antimicrobials in the *R. equi* isolates from necropsied foals was significantly higher in treated foals with dual therapy than in untreated foals. While rifampicin resistance is due to random point mutations in the target *rpoB* gene, macrolide resistance is mediated by methyltransferase genes (i.e. *erm(46)* and *erm(51)*) that are located on mobile genetic elements and thus can be transferred between different *R. equi* strains horizontally (Álvarez-Narváez et al., 2021a). However, *erm(46)* has been assumed to be limited to 2287, a certain *R. equi* clone, which also carries a mutation related to high-level rifampicin resistance. This clone has been isolated in the USA since 2002, but its spatial occurrence is still relatively limited (Álvarez-Narváez et al., 2019). Recently, a novel multidrug-resistant *R. equi* clone, G2016, has been described after sequencing 30 isolates from five US states, collected between 2012 and 2017 (Álvarez-Narváez et al., 2021b). This clone carries a mutation in the *rpoB* gene and proves that 2,287 has recently participated in horizontal gene transfer. The authors suggest that the increased occurrence of multidrug-resistant *R. equi* in the USA in the last two decades is attributable to the spread of 2,287 in the country (Álvarez-Narváez et al., 2021b). More information on AMR *R. equi* can be retrieved from Table 2.

Table 2: Weighted arithmetic mean, minimum and maximum proportion of resistance (% R or % R + I) and weighted SD in *R. equi* for the target antimicrobials on each continent included in the studies (EFSA AHAW Panel, 2021a)

Antibiotic	Continent	No. of papers	No. of isolates	Weighted arithmetic average proportion of resistance (%)	Minimum resistance % observed	Maximum resistance % observed	Weighted standard deviation
Erythromycin	Europe	1	462	1.7	1.7	1.7	NA
Erythromycin	North America	4	1,716	15.6	0	25.7	10.6
Rifampicin	Europe	1	462	1.7	1.7	1.7	NA
Rifampicin	North America	3	1,686	15.7	13.6	25.7	6.3

NA: SD cannot be calculated as only one study is included.

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

Animal population

Parameter 1 – Duration of infectious period in animals

The infectious period is unknown.

Parameter 2 – Presence and duration of latent infection period

The latent infection period is unknown. Incubation periods range from 6 to 18 days in experimentally infected foals, whereas a theoretical incubation period of 49 days has been estimated in naturally infected foals (Muscatello, 2012).

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

There is evidence that *R. equi* is excreted in faeces by most healthy foals and adult horses. Concentrations peak between 3 and 12 weeks of age with virulent strains representing 10–40% of the faecal *R. equi* population (Muscatello, 2012). Adult horses are usually asymptomatic unless immunocompromised, but they are not permanent carriers.

Environment

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

R. equi is a normal inhabitant of soil. Survival in this habitat up to 24 months has been demonstrated under environmental conditions (Willingham-Lane et al., 2019). Rifampicin- and macrolide-resistant strains exhibit similar fitness than susceptible strains in soil at cold temperatures ($-20°C$ and $4°C$) but are outcompeted by susceptible strains at higher temperatures ($25°C$ and $37°C$) (Willingham-Lane et al., 2019). No studies are available about the length of survival of this bacterial species in water and air.

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)

The surface soil of 50–95% of horse farms has high concentrations of *R. equi*, where inhalation of infected aerosols and dust particles seems to be the predominant route of disease transmission; ingestion of infected sputum or contaminated water and feed is a less frequent route of infection, leading to gastrointestinal forms of disease (e.g. ulcerative colitis and mesenteric lymphadenitis) (Yamshchikov et al., 2010). Although large amounts of virulent strains are present in the breath of infected foals, transmission of *R. equi* pneumonia from foal to foal has been hypothesised but never documented (Muscatello, 2012).

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

Infection with *R. equi* from animals to humans is likely to occur through similar routes already described in animals, as human infections seem to be associated with exposure to livestock or farming environments in immunocompromised patients (Golub et al., 1967; Prescott, 1991; Arlotti et al., 1996; Ocampo-Sosa et al., 2007; Yamshchikov et al., 2010; Witkowski et al., 2016), whereas in immunocompetent individuals, a review of *R. equi* disease showed no suggestive epidemiological exposures in 10 of the 19 patients in the case series (Arlotti et al., 1996; Kedlaya et al., 2001). *Rhodococcus* spp. have been isolated from resident bacterial flora of healthy adults, but no further evidence exists that endogenous colonisation with *R. equi* can be a source of clinical disease in humans (Yamshchikov et al., 2010). Although nosocomial or person-to-person transmission of *R. equi* is rare, Arlotti et al. (1996) described potential transmission of pulmonary disease to two patients infected with HIV sharing a hospital room with another patient infected with HIV and being treated for *R. equi* pneumonia. Additionally, two cases of nosocomial ventriculoperitoneal shunt infection with *R. equi* have been reported (Scotton et al., 2000; Strunk et al., 2007), as well as cases of *R. equi* peritonitis associated with ambulatory peritoneal dialysis in the absence of other epidemiological risk factors (Chow et al., 2003). From clinical cases of infections in humans, the strains of pig or bovine type (i.e. carrying these animal-adapted plasmids) have been isolated more often than avirulent or equine strains (Ocampo-Sosa et al., 2007), and even though sources and routes of human infection remain unclear, consumption of raw and undercooked pig or bovine meat might be also a probable way of transmission to humans (Ocampo-Sosa et al., 2007; Witkowski et al., 2015). Furthermore, a pattern of geographical distribution of strains is similar in humans and animals; e.g. VapB type 5 is predominant among isolates from humans and animals in Europe, type 8 in South America and types 1 and 2 in Asia (Witkowski et al., 2015).

Speed of transmission

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

This is not applicable, because animal-to-animal and animal-to-human transmission has not been demonstrated yet.

Parameter 4 – Transmission rate (β) (from R0 and infectious period) between animals and, when relevant, between animals and humans

This is not applicable, because animal-to-animal and animal-to-human transmission has not been demonstrated yet.

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

The distribution of *R. equi* is endemic, since this is a ubiquitous bacterial species in soil worldwide. However, the disease is endemic in some farms and absent in others.

Risk of introduction

This section is irrelevant for this pathogen, since it is present in all Member States.

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

Diagnostic tools

Parameter 1 – Existence of diagnostic tools

The gold standard for laboratory diagnosis is the isolation of *R. equi* from tracheobronchial aspirates, followed by species identification by polymerase chain reaction (PCR) or matrix-assisted laser desorption ionisation–time-of-flight mass spectrometry (MALDI-TOF MS). However, due to health risks to foals and increased costs associated with the invasive bronchoscopic procedure for collection of tracheobronchial aspirates, diagnosis is usually based on clinical signs suggestive of pneumonia, depression and fever, or by active screening by ultrasound or radiography. PCR is useful for rapid identification of virulent strains carrying the virulence gene *vapA*. An older study showed that direct PCR on clinical specimens can be even more sensitive than culture for detection of *R. equi* (Sellon et al., 2001). Since then, various PCR methods have been developed, including a quantitative PCR method targeting *chloE* and *vapA* for quantification and genotyping (Rodríguez-Lázaro et al., 2006). However, PCR-based methods for direct detection of *R. equi* in clinical specimens are seldom available at veterinary diagnostic laboratories and not readily available to most veterinarians. Serological tests (e.g. ELISAs) have been developed and may be used to detect exposure to *R. equi* or maternal antibodies, but according to a consensus statement by the American College of Veterinary Internal Medicine (ACVIM), their use for diagnosis of *R. equi* pneumonia is not recommended due to poor performance in terms of sensitivity and/or specificity (Giguère et al., 2011).

Parameter 2 – Existence of control tools

No effective vaccine with adequate protection of foals is commercially available. Among different studies testing vaccine candidates experimentally, one recent study showed a promising effect of a conjugate vaccine targeting the highly conserved microbial surface polysaccharide, poly-N-acetyl glucosamine (PNAG). In that study, mares were vaccinated 6 and 3 weeks prior to parturition, and their foals were experimentally infected intrabronchially with *R. equi* at 4 weeks of age. Eleven of 12 foals from vaccinated mares did not develop *R. equi* pneumonia, whereas six of seven foals from non-vaccinated mares developed the disease (Cywes-Bentley et al., 2018).

Currently, the most effective control tool available is early detection of the lung lesions by thoracic ultrasonography followed by antimicrobial treatment of affected foals. Based on the evidence, treatment of foals with small lesions detected by ultrasonography is unnecessary, costly and may contribute to selection of antimicrobial resistance (Giguère et al., 2010; Venner et al., 2013; Hildebrand et al., 2015; Rutenberg et al., 2017); the current policy is to treat only foals with larger lesions (Arnold-Lehna et al., 2019). It appears from some studies that use of the combination treatment (macrolide and rifampicin) may improve survival in infected foals from approximately 20–80% (Hillidge, 1987; Reuss et al., 2009).

Management strategies to decrease the incidence of *R. equi* pneumonia on endemic farms focus on reducing air contamination by maintaining well-ventilated, dust-free areas, and by avoiding dirt paddocks and overcrowding. Administration of hyperimmune plasma might reduce the incidence and severity of *R. equi* infections, but it is laborious, expensive and not completely effective in preventing the disease (Muscatello, 2012).

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

Pulmonary disease caused by *R. equi* occurs in all Member States and broadly in any country of the world due to the ubiquitous occurrence of this bacterial species in soil.

Resistance of *R. equi* to macrolides and rifampicin has been identified in the USA in at least five states. Nevertheless, the true prevalence of AMR *R. equi* in the USA and elsewhere is unknown. Reports of macrolide resistance in veterinary isolates of *R. equi* outside the USA have been extremely rare. However, there is no surveillance in place for this pathogen in the EU.

The loss of production due to the disease

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

The economic consequences due to foal pneumonia caused by *R. equi* include death, prolonged treatment, surveillance programmes for early detection and relatively expensive prevention strategies, which consist of routine screening by thoracic ultrasonography and antimicrobial therapy. The disease causes economic losses to the equine breeding industry, but no specific estimates are available on the magnitude of this impact at farm, national or regional level.

Nevertheless, horses can be considered of economic importance in the EU, contributing with an economic value of €52.1 billion each year (sport horse, horseracing and breeding industry) (European Taskforce for Brexit and EU Animal Health Law, online).

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

It has been suggested that the contact with farm animals or their environment may play a role in some cases of human infection, and food-borne transmission might be a likely route of transmission, especially through the consumption of raw, undercooked or contaminated meat. This theory is supported by the epidemiological relationship between human and animal *R. equi* infections (Witkowski et al., 2016).

Parameter 2 – Incidence of zoonotic cases

The first human case of *R. equi* infection was described in 1967 in an immunocompromised patient who was working in a stockyard cleaning animal pen (Golub et al., 1967). In the 15 years after this initial description, only 12 more cases of human infection were documented in patients who were similarly immunocompromised (Van Etta et al., 1983). Since then (1983), more than 200 sporadic cases of human infections have been reported worldwide, and this increasing prevalence seems to coincide with the HIV epidemic and advances in transplant medicine and cancer chemotherapy (Weinstock and Brown, 2002; Lin et al., 2019).

Transmissibility between humans

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

With the exception of a single case of human-to-human transmission of pulmonary *R. equi* infection in two HIV patients living together (Arlotti et al., 1996), two cases of nosocomial ventriculoperitoneal shunt infection (Scotton et al., 2000; Strunk et al., 2007), as well as cases of *R. equi* peritonitis associated with ambulatory peritoneal dialysis in the absence of other epidemiological risk factors (Chow et al., 2003), there is no additional evidence indicating that the disease can be transmitted between humans.

Parameter 4 – Sporadic, epidemic or pandemic potential

This is a sporadic disease in humans with no endemic, epidemic or pandemic potential.

The severity of human forms of the disease

Parameter 5 – Disability-adjusted life year (DALY)

Immunocompromised people (e.g. HIV and cancer patients) can be infected with *R. equi* and develop severe forms of pyogranulomatous pneumonia. According to a recent review (Lin et al., 2019), approximately 80% of immunocompromised patients suffer pulmonary infections, usually in association with HIV (61%). *R. equi* infections are extremely rare and usually localised (e.g. wound infections) in healthy individuals. Case-fatality in individuals with acquired immunodeficiency syndrome (AIDS) is 50–61% and is significantly associated with the lack of adherence to antiretroviral therapy (Lin et al., 2019).

There are no data to assess DALY attributable to *R. equi* infections in humans.

The availability of effective prevention or medical treatment in humans

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

Severe human infections are treated with combinations of parenteral antibiotics, including vancomycin, macrolides, fluoroquinolones, rifampicin and imipenem–cilastatin. Rare cases of treatment failures have been reported in the scientific literature. The immunological status of the patient is the principal determinant of the success of therapy (Lin et al., 2019).

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

No commercial vaccines are available.

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

Due to the introduction of effective prevention and control programmes based on screening and antimicrobial therapy, severe infections are less frequently observed than in the past. Based on the current antibiotic policies (i.e. only treat foals displaying large pulmonary abscesses), approximately 51% of the foals that display ultrasonographic signs of *R. equi* pneumonia receive therapy with a rate of treatment failure (defined as an increase of severity of pulmonary findings during treatment) of approximately 6% and a case-fatality rate below 1% (Arnold-Lehna et al., 2019). Treatment generally lasts a few weeks until resolution of clinical signs. The most severe cases display the typical clinical signs of lower respiratory tract infections, including coughing, dyspnoea, fever and depression. Loss of appetite and weight may be observed, especially in chronic cases. Foals may also manifest extrapulmonary disorders, often concurrently with pneumonia (e.g. diarrhoea, polysynovitis, intra-abdominal abscessation or lymphadenitis, and uveitis). Duration of impairment is extremely variable as it depends on immune response and timeliness of therapy. The duration of treatment varies between 3 and 12 weeks depending on severity of the pulmonary lesions and response to treatment, and is usually shorter in foals treated based on detection of subclinical lesions by ultrasonographic screening (Giguère et al., 2011). Treatment is terminated after resolution of clinical signs, normalisation of plasma fibrinogen concentrations and radiographic or ultrasonographic resolution of lung lesions.

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

No information is available on disease caused by *R. equi* in wild horses and other endangered animal species.

Parameter 2 – Mortality in wild species

R. equi has been isolated from several wild species, including fatal cases.

Environment

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

R. equi is a normal inhabitant of soil, which is the natural reservoir of this bacterial pathogen. Survival in this habitat up to 24 months has been demonstrated under environmental conditions (Willingham-Lane et al., 2019). Rifampicin- and macrolide-resistant strains exhibit similar fitness than susceptible strains in soil at cold temperatures ($-20°C$ and $4°C$) but are outcompeted by susceptible

strains at higher temperatures (25°C and 37°C) (Willingham-Lane et al., 2019). No studies are available about the length of survival of this bacterial species in water and air.

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

Not listed.

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

Parameter 1 − Officially/internationally recognised diagnostic tools, OIE-certified

According to the ACVIM consensus statement (Giguère et al., 2011), a definitive diagnosis of rhodococcal pneumonia can be reached by bacteriological culture of a virulent *R. equi* strain combined with one or more of the following: (i) clinical signs of lower respiratory disease, (ii) cytological evidence of septic airway inflammation, (iii) radiographic or ultrasonographic evidence of bronchopneumonia. Direct PCR culture-based detection of the *vapA* virulence gene in specimens is also possible, but should not replace bacteriological culture, since then antimicrobial susceptibility testing and potential detection of other pathogens would not be possible.

Effectiveness

Parameter 2 − Sensitivity and specificity of diagnostic tests

There is a general lack of information concerning these quality parameters of available diagnostic tests. It has been stated that there is no single diagnostic test that is readily available and of high specificity and sensitivity for the diagnosis of *R. equi* pneumonia (Muscatello, 2012).

Feasibility

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

Tracheobronchial aspirate should be used for diagnostic microbiology of *R. equi* respiratory infections. Other specimens, depending on the infection site, may be needed for detection of *R. equi* in extrapulmonary manifestations.

3.1.4.2. Article 7(d)(ii) Vaccination

Availability

Parameter 1 − Types of vaccines available on the market (live, inactivated, DIVA, etc.)

No effective vaccine with adequate protection of foals is commercially available.

Parameter 2 − Availability/production capacity (per year)

No effective vaccine with adequate protection of foals is commercially available.

Effectiveness

Parameter 3 − Field protection as reduced morbidity (as reduced susceptibility to infection and/or to disease)

Among different studies testing vaccine candidates experimentally, one recent study showed a promising effect of a conjugate vaccine targeting the highly conserved microbial surface

polysaccharide, PNAG. In that study, mares were vaccinated 6 and 3 weeks prior to parturition, and their foals were experimentally infected intrabronchially with *R. equi* at 4 weeks of age. Eleven of 12 foals from vaccinated mares did not develop *R. equi* pneumonia, whereas six of seven foals from non-vaccinated mares developed the disease (Cywes-Bentley et al., 2018).

Parameter 4 – Duration of protection

This information is not available.

Feasibility

Parameter 5 – Way of administration

This information is not available.

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

Availability

Parameter 1 – Types of drugs available on the market

Different macrolides (e.g. erythromycin, clarithromycin, azithromycin) have shown effect alone and in combination with rifampicin against *R. equi* pneumonia in foals. None of these drugs are licensed for use in horses; hence, the cascade rule must be followed to use them. Other antimicrobial drugs seem less useful, although doxycycline combined with a macrolide has been proposed as an alternative to avoid the risk of rifampicin side effects (Wetzig et al., 2020). Apart from antimicrobial treatment, various supportive treatment involving nonsteroidal anti-inflammatory drugs, oxygen, fluid therapy, etc., are recommended.

Hyperimmune plasma (HIP) with antibodies specific for *vapA* is not treatment as such but rather a passive immunisation measure to prevent *R. equi* pneumonia in foals. HIP does not fully protect against the disease. Therefore, HIP administration cannot stand alone in farms where *R. equi* infections are endemic (Giguère et al., 2011; Rakowska et al., 2020).

Parameter 2 – Availability/production capacity (per year)

Various macrolides (erythromycin, azithromycin and clarithromycin) and rifampicin are widely available, although none of these drugs is licensed for use in horses. Thus, off-label prescription and use of antibiotics for treatment of *R. equi* infections are widespread.

Effectiveness

Parameter 3 – Therapeutic effects in the field (effectiveness)

The efficacy of antimicrobial therapy depends on timeliness of treatment. Old studies suggest that a survival rate of up to around 80% can be expected following appropriate antimicrobial therapy, whereas inappropriate therapy or lack of antimicrobial use only leads to around 20% survival rate (Hillidge, 1987). Survival, however, also depends on the severity of disease, in particular the presence of extrapulmonary manifestations worsens the prognosis (Reuss et al., 2009).

Older studies reported case-fatality rates from 40% to 80% (Elissalde et al., 1980). However, mortality was significantly reduced by the introduction of macrolide/rifampicin combination therapy and control programmes based on early detection of pneumonia by thoracic ultrasonography and antimicrobial treatment of diseased foals.

According to various studies, the success rate of antimicrobial therapy ranges between 80% and 97% in foals with clinical signs of mild to moderate pneumonia that receive early treatment (Venner et al., 2013; Hildebrand et al., 2015; Rutenberg et al., 2017; Arnold-Lehna et al., 2019). The same studies indicate that the proportion of foals that recover without antimicrobial therapy is extremely variable (27–66%) depending on the case definition.

Feasibility

Parameter 4 – Way of administration

The antibiotics mentioned above are administered to foals orally.

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

Availability

Parameter 1 − Available biosecurity measures

Various ways to reduce exposure to *R. equi* have been proposed, e.g. foaling on pasture, and reducing density of foals and mares. Management strategies to decrease the incidence of *R. equi* pneumonia on endemic farms focus on reducing air contamination by maintaining well-ventilated, dust-free areas, and by avoiding dirt paddocks and overcrowding.

Effectiveness

Parameter 2 − Effectiveness of biosecurity measures in preventing the pathogen introduction

There is insufficient evidence to conclude effectiveness of proposed biosecurity measures (Giguère et al., 2011).

Feasibility

Parameter 3 − Feasibility of biosecurity measures

Feasibility depends on the situation in individual farms. Reducing density of horses and thereby reducing air concentrations of *R. equi* may be feasible in some, but not other farms. The questionable effect of such measures should also be taken into account.

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

Availability

Parameter 1 − Available movement restriction measures

To the author's knowledge, this has not been investigated.

Effectiveness

Parameter 2 − Effectiveness of restriction of animal movement in preventing the between-farm spread

The effects of movement restriction measures would also be questionable considering *R. equi* is acquired from the environment and is not transmitted animal-to-animal. Nevertheless, two multiresistant *R. equi* clones seem to have spread in the USA following prophylactic overuse of macrolide and rifampicin in foals (Álvarez-Narváez et al., 2021a). The authors of that paper speculate that such resistant strains may potentially be disseminated across borders during transportation of horses; hence, it is possible that future restrictions of movement may be useful to prevent this scenario.

Feasibility

Parameter 3 − Feasibility of restriction of animal movement

This is unknown.

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

Availability

Parameter 1 − Available methods for killing animals

Horses can be euthanised in various ways, but to the authors' knowledge, killing to control *R. equi* infections has not been described in the literature.

Effectiveness

Parameter 2 − Effectiveness of killing animals (at farm level or within the farm) for reducing/stopping spread of the disease

Killing of infected animals is not an effective or feasible way to control *R. equi* infections due to the endemic and non-transmissible nature of the disease, and availability of other control and treatment options.

Feasibility

Parameter 3 − Feasibility of killing animals

Killing of infected animals is not an effective or feasible way to control *R. equi* infections.

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

Bodies of animals that died from *R. equi* infections are disposed using the same methods (e.g. burial, incineration, etc.) as for animals that died from other diseases. Bodies of dead animals infected with *R. equi* do not pose any special risks to public or animal health.

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

Parameter 1 − Cost of control (e.g. treatment/vaccine, biosecurity)

The costs associated with diagnostic screening, treatment, morbidity and mortality may be very high on farms where the disease is endemic (Giguère et al., 2011), but no figures are available to quantify such costs. The costs of treatment are likely to increase when infections are caused by macrolide- and rifampicin-resistant strains, since these two antimicrobials are routinely used in combination therapy of *R. equi* infections. Treatment failure may result in prolonged disease or death of the infected animal and increase veterinary expenditures due to additional visits, diagnostic tests and therapies. Treatment of infections caused by strains resistant to macrolides and rifampicin is problematic due to the limited availability of effective antimicrobial alternatives. Currently, there are no recommendations on drug choice for treatment of foals infected with resistant strains.

Parameter 2 − Cost of eradication (culling, compensation)

No eradication programmes are used for controlling *R. equi* infections.

Parameter 3 − Cost of surveillance and monitoring

No national or regional surveillance programmes are in place for this pathogen.

Parameter 4 − Trade loss (bans, embargoes, sanctions) by animal product

It has been hypothesised that multidrug-resistant *R. equi* and plasmid-mediated macrolide resistance are currently disseminating in the USA and internationally through horse movement (Álvarez-Narváez et al., 2021a). However, there are currently no specific trade restrictions associated with prevent the spread of those strains.

Parameter 5 − Importance of the disease for the affected sector (% loss or € lost compared to business amount of the sector)

No data are available to estimate the economic impact of *R. equi* infections within the horse industry.

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

Disease prevention and control measures are likely to be acceptable to society, except that some horse farmers and owners may not be able to sustain the veterinary expenditures associated with active surveillance to control *R. equi* disease in endemic farms.

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

As stated above (Parameter 1 in Section 3.1.4.3), early antimicrobial treatment may reduce mortality dramatically. However, the use of macrolides implies the risk of side effects, mainly diarrhoea in treated foals or rarely in mares of foals that are being treated due to the ingestion of small amounts of antibiotic residues. It has been estimated that the incidence of diarrhoea in foals treated with erythromycin-rifampicin ranges between 17% and 36% (Giguère et al., 2011). Currently, there seems to be only limited antimicrobial resistance in European equine *R. equi* isolates, but potentially this

picture may change over the years, thereby making treatment more complex and with a potential impact on animal welfare.

Parameter 2 – Wildlife depopulation as control measure

Wildlife depopulation is not a measure for control of *R. equi* infections.

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)

There are no data to quantify the environmental impact caused by the measures for control and prevention of *R. equi* infections in horses and other animals. It is, however, known that active drug residues derived from antimicrobial therapy can be introduced into the environment via urine and faeces from treated animals, contributing to selection and spread of antimicrobial resistance in different ecosystems (Polianciuc et al., 2020). The amount, persistence and bioavailability of residues released into the environment depend on drug pharmacokinetics and chemical structure. Antimicrobials used for treatment of *R. equi* infections in horses account for a negligible fraction of the overall antimicrobial consumption in humans and livestock. With regard to the types of antimicrobials used, it has been shown that macrolides are rapidly neutralised via mineralisation and do not persist year-to-year in agricultural soil (Topp et al., 2016). No information is available on fate and persistence of rifampicin in soil.

Biodiversity

Parameter 1 – Mortality in wild species

There is no evidence of mortality in wildlife species due to control measures for control and prevention of *R. equi* infections in horses.

3.2. Assessment of AMR *Rhodococcus equi* according to Article 5 criteria of the AHL on its eligibility to be listed

3.2.1. Detailed outcome on Article 5 criteria

In Table 3 and Figure 1, the results of the expert judgement on the Article 5 criteria of the AHL for AMR *R. equi* in horses are presented.

The distribution of the individual answers (probability ranges) provided by each expert for each criterion is reported in Sections A.1 and A.2 of Annex A.
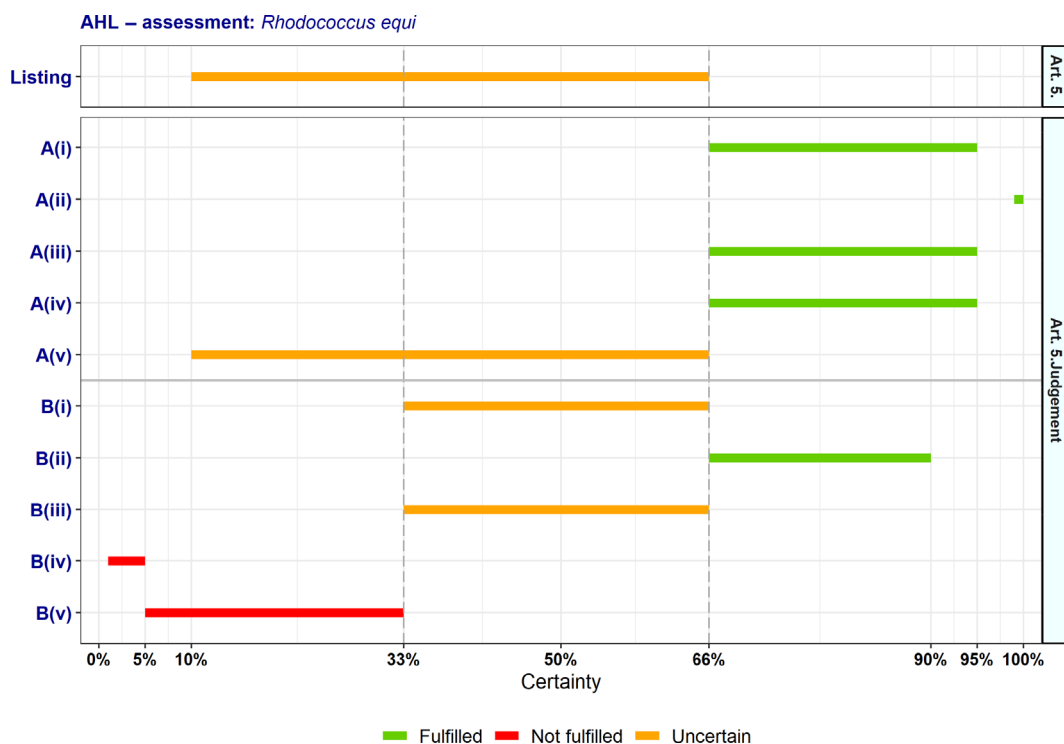
Table 3: Outcome of the expert judgement on Article 5 criteria

Criteria to be met by the disease:		Outcome			
According to the 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		Median range (%)	Criterion fulfilment	Number of na	Number of experts
A(i)	The disease is transmissible	66–95	Fulfilled	0	16
A(ii)	Animal species are either susceptible to the disease or vectors and reservoirs thereof exist in the Union	99–100	Fulfilled	0	16
A(iii)	The disease causes negative effects on animal health or poses a risk to public health due to its zoonotic character	66–95	Fulfilled	0	16
A(iv)	Diagnostic tools are available for the disease	66–95	Fulfilled	0	15
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	10–66	Uncertain	0	15

Criteria to be met by the disease: According to the 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		Outcome			
		Median range (%)	Criterion fulfilment	Number of na	Number of experts
At least one criterion to be met by the disease: In addition to the criteria set out above at point 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	33–66	Uncertain	0	15
B(ii)	The disease agent has developed resistance to treatments which poses a significant danger to public and/or animal health in the Union	66–90	Fulfilled	0	15
B(iii)	The disease causes or could cause a significant negative economic impact affecting agriculture or aquaculture production in the Union	33–66	Uncertain	0	15
B(iv)	The disease has the potential to generate a crisis or the disease agent could be used for the purpose of bioterrorism	1–5	Not fulfilled	0	16
B(v)	The disease has or could have a significant negative impact on the environment, including biodiversity, of the Union	5–33	Not fulfilled	0	15

na: not applicable.

In Figure 1, the outcome of the expert judgement is graphically shown together with the estimated overall probability of the AMR bacterium meeting the criteria of Article 5 on its eligibility to be listed.

Listing: the probability of the disease to be listed according to Article 5 criteria of the AHL (overall outcome).

Figure 1: Outcome of the expert judgement on Article 5 criteria and overall probability of AMR *R. equi* on its eligibility to be listed

3.2.1.1. Reasoning for uncertain outcome on Article 5 criteria

Criterion 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)

- The bacterium is a natural inhabitant of the soil.
- Diagnostics are available but can be difficult to implement in the field.
- No commercial vaccines are available.
- There is no harmonised surveillance in place.
- Drug treatment as risk-mitigating measure is available and effective against the bacterium and multidrug-resistant clones are rare in the EU. Thus, control can be considered proportionate.
- Other risk-mitigating measures related to on-farm biosecurity and management can be used, such as reducing air contamination by maintaining well-ventilated, dust-free areas, keeping clean paddocks and avoiding overcrowding.
- Although the available risk-mitigating measures are not totally effective, these could be considered proportionate to the risks posed by AMR *R. equi* in the EU, since multidrug-resistant clones are common in the USA and China but not in the EU.
- The interactions between a ubiquitous opportunistic pathogen, lack of data on risk factors for development of disease and lack of data on drivers of antimicrobial resistance results in large uncertainty.

Criterion 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):

- The bacterium causes negative effects on horses, especially on foals. These effects would increase if effective treatment was no longer available.
- It is difficult to assess whether multidrug-resistant clones cause negative effects in more than one EU country.
- Real prevalence/incidence estimates are not available. High morbidity and case-fatality in foals have been reported in endemic farms.
- The zoonotic potential is unknown, as infections occur essentially in immunocompromised patients.

Criterion B(iii) (the disease causes or could cause a significant negative economic impact affecting agriculture or aquaculture production in the Union)

- The impact of *R. equi* is very sectorial (horse breeding farms) and does not affect the whole agriculture of the Union. It usually causes sporadic, local and limited impact.
- Disease caused by the bacterium is not always severe and can be treated.
- Horses are economically important, especially in some EU countries (e.g. France).
- Multidrug-resistant clones could cause higher impact in future.
- The bacterium has been around for many years, but there are only a few reports on AMR *R. equi* in scientific literature.
- There are no quantifications of the costs associated with this bacterium.

3.2.2. Overall outcome on Article 5 criteria

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, a criterion is considered fulfilled when the lower bound of the median range lays above 66%.

According to the results shown in Table 3, AMR *R. equi* complies with four criteria of the first set (A (i)–A(iv)), but there is uncertainty (10–66% probability) on the assessment on compliance with criterion A(v). Therefore, it is uncertain whether AMR *R. equi* can be considered eligible to be listed for Union intervention as laid down in Article 5 of the AHL. The estimated overall probability range for the AMR bacterium being eligible to be listed is 10–66% (Figure 1).

3.3. Assessment of AMR *Rhodococcus equi* according to criteria in Annex IV for the purpose of categorisation as in Article 9 of the AHL

In Tables 4–8 and related graphs (Figures 2–4), the results of the expert judgement on AMR *R. equi* in horses according to the criteria in Annex IV of the AHL, for the purpose of categorisation as in Article 9, are presented.
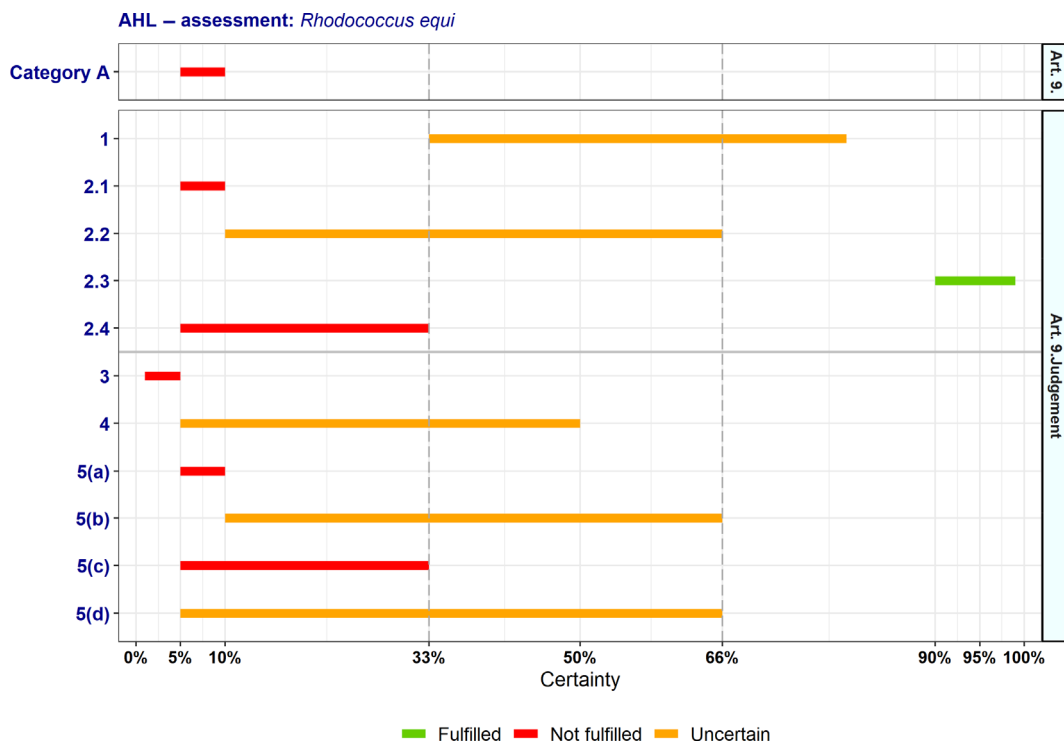
The distribution of the individual answers (probability ranges) provided by each expert for each criterion is reported in Sections B.1 and B.2 of Annex B.

3.3.1. Detailed outcome on Category A criteria

Table 4: Outcome of the expert judgement related to the criteria of Section 1 of Annex IV (Category A of Article 9)

Criteria to be met by the disease: The disease needs to fulfil all of the following criteria		Outcome			
		Median range (%)	Criterion fulfilment	Number of na	Number of experts
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	33–80	Uncertain	0	13
2.1	The disease is highly transmissible	5–10	Not fulfilled	0	14
2.2	There are possibilities of airborne or waterborne or vector-borne spread	10–66	Uncertain	0	14
2.3	The disease affects multiple species of kept and wild animals or single species of kept animals of economic importance	90–99	Fulfilled	0	14
2.4	The disease may result in high morbidity and significant mortality rates	5–33	Not fulfilled	0	14
At least one criterion to be met by the disease: In addition to the criteria set out above at point 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 for public health, including epidemic or pandemic potential or possible significant threats to food safety	1–5	Not fulfilled	0	16
4	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	5–50	Uncertain	0	15
5(a)	The disease has a significant impact on society, with in particular an impact on labour markets	5–10	Not fulfilled	0	14
5(b)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	10–66	Uncertain	0	14
5(c)	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	5–33	Not fulfilled	0	14
5(d)	The disease has a significant impact in 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	5–66	Uncertain	0	14

na: not applicable.

AHL − assessment: *Rhodococcus equi*

Legend: Fulfilled (green) — Not fulfilled (red) — Uncertain (orange)

Category A: The probability of the disease to be categorised according to Section 1 of Annex IV of the AHL (overall outcome).

Figure 2: Outcome of the expert judgement on criteria of Section 1 of Annex IV and overall probability of the AMR bacterium to be fitting in Category A of Article 9

3.3.1.1. Reasoning for uncertain outcome on Category A criteria

Criterion 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):

- Resistance to macrolides and rifampicin has only occasionally been described in Europe. It is more common outside of the Union, in the USA and China.
- The bacterium itself is ubiquitous and endemic in all Member States.
- No surveillance is in place; hence, there is a lack of information and large uncertainty.

Criterion 2.2 (there are possibilities of airborne or waterborne or vector-borne spread)

- There are different interpretations of waterborne spread.
- Only short-distance spread through respiratory droplets and dust seems possible. This is not considered airborne spread.
- There may be possibilities, but information is very limited.
- Foal-to-foal transmission has not been demonstrated.
- There is no vector-borne spread.

Criterion 4 (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):

- The impact of *R. equi* is very sectorial (horse breeding farms) and does not affect the whole agriculture of the Union. It usually causes sporadic, local and limited impact.
- Disease caused by the bacterium is usually not severe and can be treated.
- Horses are economically important, especially in some EU countries (e.g. France).
- Potential impact: If antimicrobial treatment was not available, case-fatality would be higher and the impact would increase.
- Multidrug-resistant clones could cause higher impact when introduced from overseas in future.
- There are only few data available to assess the economic impact.

Criterion 5(b) (the disease has a significant impact on animal welfare, by causing suffering of large numbers of animals)

- It is difficult to interpret 'large' numbers of animals.
- Digestive and respiratory manifestations cause suffering to individual animals; however, 'large' numbers are not affected.
- The disease is not epidemic and limited to foals.
- Treatment is available, but not effective against multidrug-resistant strains.
- The impact may increase if multidrug-resistant clones spread in the Union.
- Increasing resistance will not affect welfare but only treatment.

Criterion 5(d) (the disease has a significant impact in 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):
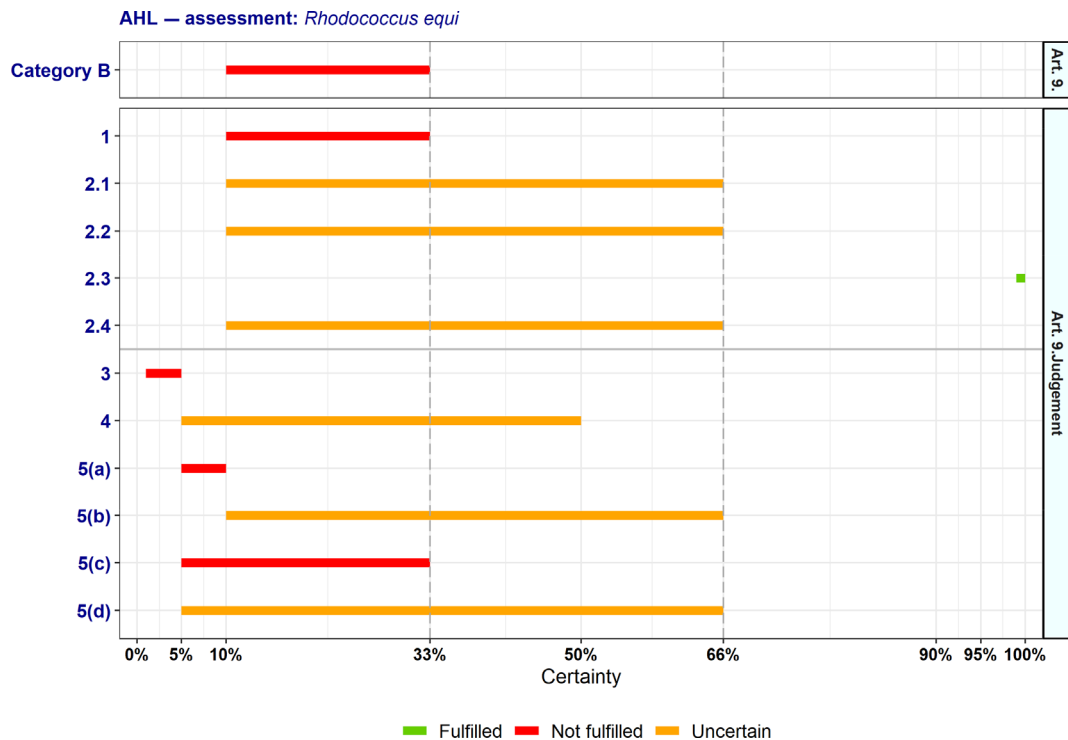
- The bacterium has been detected in several wildlife species; hence, there is a possibility of fatal infections if not treated.
- Endangered species that can be affected are present in the Union. There may potentially be a long-term damage to rare breeds.
- There is high uncertainty, due to the lack of evidence.

3.3.2. Detailed outcome on Category B criteria

Table 5: Outcome of the expert judgement related to the criteria of Section 2 of Annex IV (Category B of Article 9)

Criteria to be met by the disease: The disease needs to fulfil all of the following criteria		Outcome			
		Median range (%)	**Criterion fulfilment**	**Number of na**	**Number of experts**
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	10–33	Not fulfilled	0	14
2.1	The disease is moderately to highly transmissible	10–66	Uncertain	0	14
2.2	There are possibilities of airborne or waterborne or vector-borne spread	10–66	Uncertain	0	14
2.3	The disease affects single or multiple species	–	Fulfilled	0	16
2.4	The disease may result in high morbidity with in general low mortality	10–66	Uncertain	0	14
At least one criterion to be met by the disease: In addition to the criteria set out above at point 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 for public health, including epidemic potential or possible significant threats to food safety	1–5	Not fulfilled	0	16
4	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	5–50	Uncertain	0	15
5(a)	The disease has a significant impact on society, with in particular an impact on labour markets	5–10	Not fulfilled	0	14
5(b)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	10–66	Uncertain	0	14
5(c)	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	5–33	Not fulfilled	0	14
5(d)	The disease has a significant impact in 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	5–66	Uncertain	0	14

na: not applicable.

Category B: The probability of the disease to be categorised according to Section 2 of Annex IV of the AHL (overall outcome).

Figure 3: Outcome of the expert judgement on criteria of Section 2 of Annex IV and overall probability of the AMR bacterium to be fitting in Category B of Article 9

3.3.2.1. Reasoning for uncertain outcome on Category B criteria

Criterion 2.1 (the disease is moderately to highly transmissible)

- Indirect transmission and infection from the environment seem to occur (e.g. dust).
- Foal-to-foal transmission has not been demonstrated. Direct transmission is unlikely. Therefore, it is not highly transmissible.
- Seroprevalence data suggest that there is at least moderate transmission.
- Data are scarce.

Criterion 2.2 (there are possibilities of airborne or waterborne or vector-borne spread): See above in Section 3.3.1.1.

Criterion 2.4 (the disease may result in high morbidity with in general low mortality)

- Interpretation of 'may'?
- Morbidity seems low despite high seroprevalence.
- Mortality has been reduced due to antimicrobial treatment, but case-fatality can be high in endemic farms. Multidrug-resistant clones can increase mortality, but morbidity would still be low or moderate.
- Data on morbidity are scarce. It is variable.

Criterion 4 (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): See above in Section 3.3.1.1.

Criterion 5(b) (the disease has a significant impact on animal welfare, by causing suffering of large numbers of animals): See above in Section 3.3.1.1.
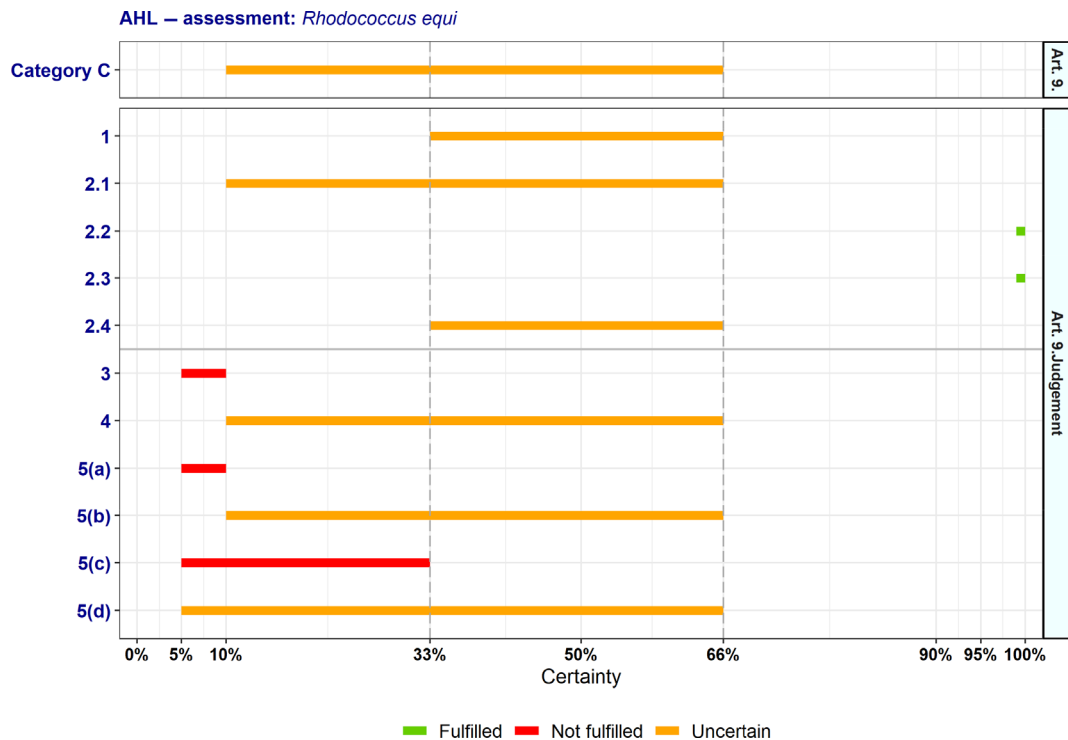
Criterion 5(d) (the disease has a significant impact in the long term on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds): See above in Section 3.3.1.1.

3.3.3. Detailed outcome on Category C criteria

Table 6: Outcome of the expert judgement related to the criteria of Section 3 of Annex IV (Category C of Article 9)

Criteria to be met by the disease: The disease needs to fulfil all of the following criteria		Outcome			
		Median range (%)	Criterion fulfilment	Number of na	Number of experts
1	The disease is present in the whole or part of the Union territory with an endemic character	33–66	Uncertain	0	13
2.1	The disease is moderately to highly transmissible	10–66	Uncertain	0	14
2.2	The disease is transmitted mainly by direct or indirect transmission	–	Fulfilled	0	16
2.3	The disease affects single or multiple species	–	Fulfilled	0	16
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	33–66	Uncertain	0	15

At least one criterion to be met by the disease:
In addition to the criteria set out above at point 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 for public health or possible significant threats to food safety	5–10	Not fulfilled	0	15
4	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	10–66	Uncertain	0	14
5(a)	The disease has a significant impact on society, with in particular an impact on labour markets	5–10	Not fulfilled	0	14
5(b)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	10–66	Uncertain	0	14
5(c)	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	5–33	Not fulfilled	0	14
5(d)	The disease has a significant impact in 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	5–66	Uncertain	0	14

na: not applicable.

AHL — assessment: *Rhodococcus equi*

Category C: The probability of the disease to be categorised according to Section 3 of Annex IV of the AHL (overall outcome).

Figure 4: Outcome of the expert judgement on criteria of Section 3 of Annex IV and overall probability of the AMR bacterium to be fitting in Category C of Article 9

3.3.3.1. Reasoning for uncertain outcome on Category C criteria

Criterion 1 (the disease is present in the whole or part of the Union territory with an endemic character)

- Multidrug-resistant clones have been described in at least one EU country, but it is difficult to assess whether its character is endemic.
- No surveillance is in place; hence, there is a lack of information and large uncertainty.

Criterion 2.1 (the disease is moderately to highly transmissible): See above in Section 3.3.2.1.

Criterion 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)

- There is a contradiction between 'negligible or no mortality' and production loss, if loss (mortality) of foals is considered.
- Mortality has been reduced due to antimicrobial treatment, but case-fatality can be high in endemic farms. Multidrug-resistant clones can increase mortality, but morbidity would still be low or moderate.
- Foals with pneumonia grow less and often they may have lung problems which impair their performance.
- Morbidity is variable.

Criterion 4 (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)

- Introduction of multidrug-resistant clones from overseas may increase mortality and impact on foals (breeding farms). Some animals may be of high value.
- Potential impact: If antimicrobial treatment was not available, case-fatality would be higher and the impact would increase.
- There are only few data available to assess the economic impact.

Criterion 5(b) (the disease has a significant impact on animal welfare, by causing suffering of large numbers of animals): See above in Section 3.3.1.1.

Criterion 5(d) (the disease has a significant impact in 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): See above in Section 3.3.1.1.

3.3.4. Detailed outcome on Category D criteria

Table 7: Outcome of the expert judgement related to the criteria of Section 4 of Annex IV (Category D of Article 9)

Diseases in Category D **need to fulfil criteria of Section 1, 2, 3 or 5 of Annex IV** of the AHL **and the following**:		**Outcome**			
		Median range (%)	**Criterion fulfilment**	**Number of na**	**Number of experts**
D	The risk posed by the disease can be effectively and proportionately mitigated by measures concerning movements of animals and products in order to prevent or limit its occurrence and spread	10–66	Uncertain	0	14

na: not applicable.

3.3.4.1. Reasoning for uncertain outcome on Category D criteria

Criterion D (the risk posed by the disease can be effectively and proportionately mitigated by measures concerning movements of animals and products in order to prevent or limit its occurrence and spread):

- There is no direct transmission from horse to horse; hence, movement restrictions are unlikely to be helpful.
- The pathogen is mostly present in horse farms, hence moved around by horses. This can be controlled.
- Even if the bacterium is ubiquitous, restricting movement of carriers may decrease inoculum (soil contamination with faeces) in farms and limit occurrence, but no evidence is available.
- Some control/monitoring could prevent further spread of multidrug-resistant clones, as they may potentially be disseminated across borders during transportation of horses.
- Prevention of movement from affected farms may be effective.
- It is not feasible to test all the horses before movement.
- There is large uncertainty.

3.3.5. Detailed outcome on Category E criteria

Table 8: Outcome of the expert judgement related to the criteria of Section 5 of Annex IV (Category E of Article 9)

Diseases in Category E **need to fulfil criteria of Section 1, 2 or 3 of Annex IV** of the AHL **and/or the following**:		**Outcome**	
		Median range (%)	**Fulfilment**
E	Surveillance of the disease is necessary for reasons related 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.)	10–66	Uncertain

3.3.6. Overall outcome on criteria in Annex IV for the purpose of categorisation as in Article 9

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 points (a) to (e) of Article 9(1) of the AHL), if it 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 4–8.

According to the assessment methodology, a criterion is considered fulfilled when the lower bound of the median range lays above 66%.

The overall outcome of the assessment on criteria in Annex IV of the AHL, for the purpose of categorisation of AMR *R. equi* as in Article 9, is presented in Table 9 and Figure 5.

Table 9: Outcome of the assessment on criteria in Annex IV of the AHL for the purpose of categorisation as in Article 9

Category	Article 9 criteria										
	1° set of criteria					2° set of criteria					
	1	**2.1**	**2.2**	**2.3**	**2.4**	**3**	**4**	**5(a)**	**5(b)**	**5(c)**	**5(d)**
	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	33–80	5–10	10–66	90–99	5–33	1–5	5–50	5–10	10–66	5–33	5–66
B	10–33	10–66	10–66	–	10–66	1–5	5–50	5–10	10–66	5–33	5–66
C	33–66	10–66	–	–	33–66	5–10	10–66	5–10	10–66	5–33	5–66
D	10–66										
E	10–66										

Probability ranges (% certainty) (green: fulfilled; red: not fulfilled; orange: uncertain).
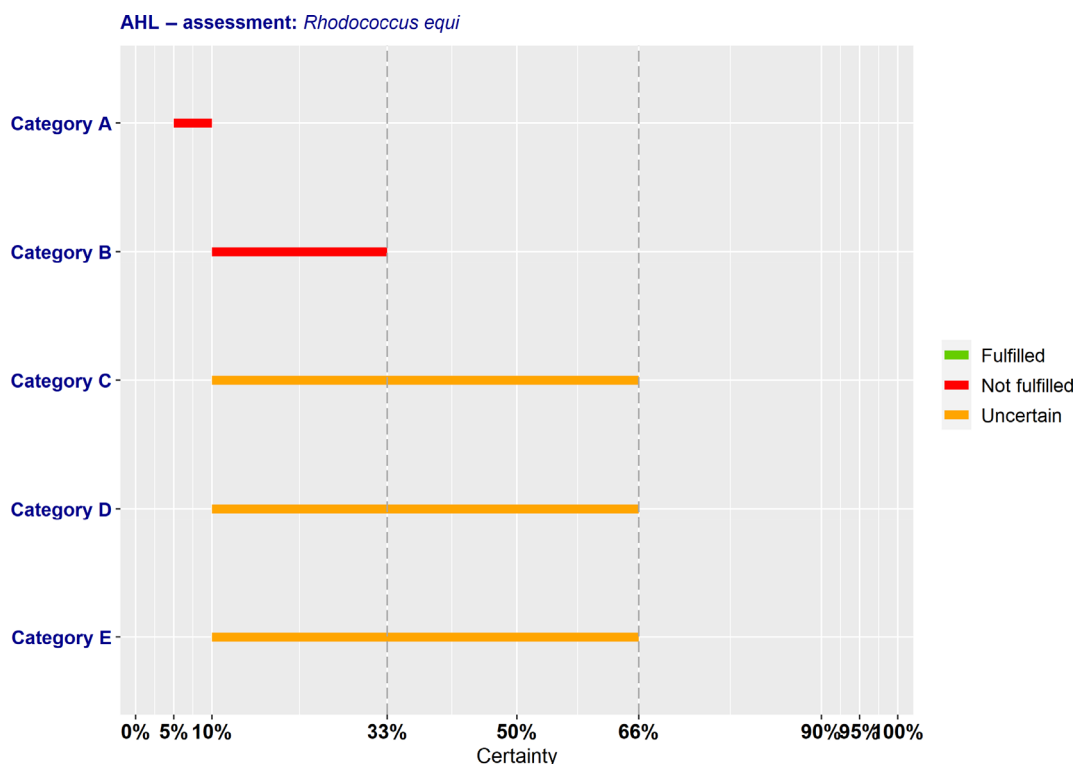
Figure 5: Outcome of the expert judgement on criteria in Annex IV and overall probabilities for categorisation of the AMR bacterium in accordance with Article 9

According to the assessment here performed, AMR *R. equi* complies with the following criteria of Sections 1–5 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, AMR *R. equi* complies only with criterion 2.3 (90–99% probability). The assessment was inconclusive on compliance with criteria 1 (33–80% probability) and 2.2 (10–66% probability). To be eligible for Category A, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5(a)–(d)) and AMR *R. equi* does not comply with any of them. The assessment was inconclusive on compliance with criteria 4 (5–50% probability), 5(b) (10–66% probability) and 5(d) (5–66% probability). Overall, it was assessed with 5–10% probability that AMR *R. equi* may be assigned to Category A according to criteria in Section 1 of Annex IV for the purpose of categorisation as in Article 9 of the AHL.

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, AMR *R. equi* complies only with criterion 2.3. The assessment was inconclusive on compliance with criteria 2.1 (10–66% probability) and 2.2 (10–66% probability). To be eligible for Category B, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5(a)–(d)) and AMR *R. equi* does not comply with any of them. The assessment was inconclusive on compliance with criteria 4 (5–50% probability), 5(b) (10–66% probability) and 5(d) (5–66% probability). Overall, it was assessed with 10–33% probability that AMR *R. equi* may be assigned to Category B according to criteria in Section 2 of Annex IV for the purpose of categorisation as in Article 9 of the AHL.

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, AMR *R. equi* complies with criteria 2.2 and 2.3. The assessment was inconclusive on compliance with criteria 1 (33–66% probability), 2.1 (10–66% probability) and 2.4 (33–66% probability). To be eligible for Category C, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5(a)–(d)) and AMR *R. equi* does not comply with any of them. The assessment was inconclusive on compliance with criteria 4 (10–66% probability), 5(b) (10–66% probability) and 5(d) (5–66% probability). Overall, it was assessed with 10–66% probability that AMR *R. equi* may be assigned to Category C according to criteria in Section 3 of Annex IV for the purpose of categorisation as in Article 9 of the AHL.

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, for which the assessment was inconclusive (10–66% probability).

5) To be assigned to Category E, a disease needs to comply with criteria of Section 1, 2 or 3 of Annex IV of the AHL, and/or the surveillance of the disease is necessary for reasons related 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, for which the assessment was inconclusive (10–66% probability of fulfilling the criteria).

3.4. Assessment of AMR *Rhodococcus equi* according to Article 8 criteria of the AHL

In this section, the results of the assessment on the criteria of Article 8(3) of the AHL for AMR *R. equi* are presented. 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 the list if they are affected or if they pose a risk for the spread of a specific listed disease because:

a) they are susceptible to 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 the possible role of biological or mechanical vectors.[2]

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 animal species to be listed for AMR *R. equi* according to the criteria of Article 8(3) of the AHL are as displayed in Table 10 (elaborated from information reported in Section 3.1.1.1 of the present document).

The table contains all animal species in which AMR *R. equi* has been described, but also those animal species from which only the bacterium itself has been isolated. The latter makes susceptibility to AMR clones likely.

Table 10: Animal species to be listed for AMR *R. equi* according to the criteria of Article 8

	Class/order	Family	Genus/species
Susceptible	Perissodactyla	Equidae	Horse (*Equus caballus ferus*)
		Bovidae	Cattle (*Bos taurus*)
			Goat (*Capra aegagrus hircus*)
	Artiodactyla	Camelidae	Llama (*Lama glama*)
			Alpaca (*Lama pacos*)
			Dromedary (*Camelus dromedarius*)
		Suidae	Domestic pig (*Sus scrofa domesticus*)
			Wild boar (*Sus scrofa*)
		Tayassuidae	Peccary (*Tayassu pecari, Tayassu tajacu*)
		Cervidae	Red deer (*Cervus elaphus*)
			Roe deer (*Capreolus capreolus*)
	Carnivora	Felidae	Domestic cat (*Felis catus*)
		Canidae	Domestic dog (*Canis lupus familiaris*)
		Phocidae	Baikal seal (*Pusa sibirica*)
	Diprotodontia	Phascolarctidae	Koala (*Phascolarctos cinereus*)
	Primates	Callitrichidae	Cotton-top tamarin (*Saguinus oedipus*)
	Crocodilia	Crocodylidae	American crocodile (*Crocodylus acutus*)
		Alligatoridae	American alligator (*Alligator mississippiensis*)
	Rodentia	Muridae	House mouse (*Mus musculus*)
		Caviidae	Guinea pig (*Cavia porcellus*)
Reservoir	Perissodactyla	Equidae	Horse (*Equus caballus ferus*)
Vector	None		

4. Conclusions

The AHAW Panel emphasises that the assessment of impacts, as well as prevention and control measures, related to AMR bacteria using the criteria as laid down in Articles 5 and 9 of the AHL is particularly challenging for opportunistic pathogens that can also be found as commensal bacteria in healthy animals.

TOR 1: *For each of those identified AMR bacteria considered most relevant in the EU, following the criteria laid down in Article 7 of the AHL, an assessment on its eligibility to be listed for Union intervention as laid down in Article 5(3) of the AHL;*

- It is uncertain (10–66% probability, from 'unlikely' to 'as likely as not') whether AMR *R. equi* can be considered eligible to be listed for Union intervention as laid down in Article 5 of the AHL.

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[2] 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.

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

- The AHAW Panel considered with 5–10% probability ('very unlikely') that AMR *R. equi* meets the criteria as in Section 1 of Annex IV of the AHL, for the application of the disease prevention and control rules referred to in point (a) of Article 9(1) of the AHL.
- The AHAW Panel considered with 10–33% probability ('unlikely') that AMR *R. equi* meets the criteria as in Section 2 of Annex IV of the AHL, for the application of the disease prevention and control rules referred to in point (b) of Article 9(1) of the AHL.
- The AHAW Panel was uncertain (10–66% probability, from 'unlikely' to 'as likely as not') whether AMR *R. equi* meets the criteria as in Section 3 of Annex IV of the AHL, for the application of the disease prevention and control rules referred to in point (c) of Article 9(1) of the AHL.
- The AHAW Panel was uncertain (10–66% probability, from 'unlikely' to 'as likely as not') whether AMR *R. equi* meets the criteria as in Section 4 of Annex IV of the AHL, for the application of the disease prevention and control rules referred to in point (d) of Article 9(1) of the AHL.
- The AHAW Panel was uncertain (10–66% probability, from 'unlikely' to 'as likely as not') whether AMR *R. equi* meets the criteria as in Section 5 of Annex IV of the AHL, for the application of the disease prevention and control rules referred to in point (e) of Article 9(1) of the AHL.

TOR 3: *For each of the AMR bacteria 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*;

- The animal species that can be considered to be listed for AMR *R. equi* according to Article 8 (3) of the AHL are mainly horses and occasionally other species belonging to Perissodactyla and Artiodactyla, as reported in Table 10 in Section 3.4 of the present document.

The AHAW Panel highlights that monitoring of antimicrobial resistance in opportunistic bacteria could help to assess their impacts. Therefore, even though the assessment on AMR *R. equi* is inconclusive on its eligibility to be listed for Union intervention, specific initiatives (e.g. monitoring or applied research) into various aspects of AMR *R. equi* can be useful to better understand its distribution and to assess its impact on animal health and welfare in the EU.

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Abbreviations

ACVIM	American College of Veterinary Internal Medicine
AHAW	Animal Health and Welfare
AHL	Animal Health Law
AIDS	Acquired immunodeficiency syndrome
AMR	Antimicrobial-resistant
CFSPH	Center for Food Security and Public Health
CI	Current impact
CITES	Convention on International Trade in Endangered Species
DALY	Disability-adjusted life year
DIVA	Differentiation of infected from vaccinated animals
ELISA	Enzyme-linked immunosorbent assay
HIP	Hyperimmune plasma
HIV	Human immunodeficiency virus
IUCN	International Union for Conservation of Nature
MALDI-TOF MS	Matrix-assisted laser desorption ionisation–time-of-flight mass spectrometry
MIC	Minimum inhibitory concentration
MS	Member State
OIE	Office International des Épizooties (World Organisation for Animal Health)
PCR	Polymerase chain reaction
PI	Potential impact
PNAG	Poly-N-acetyl glucosamine
ToR	Term of Reference
Vap	Virulence-associated protein

Annex A – Criteria with certain outcome
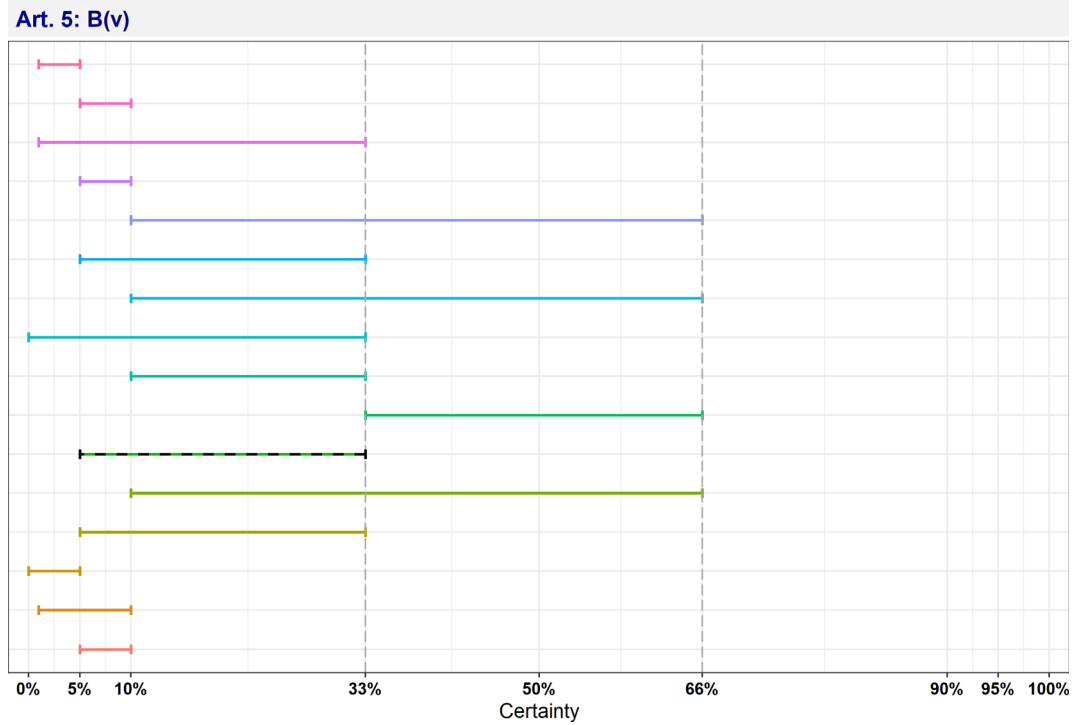
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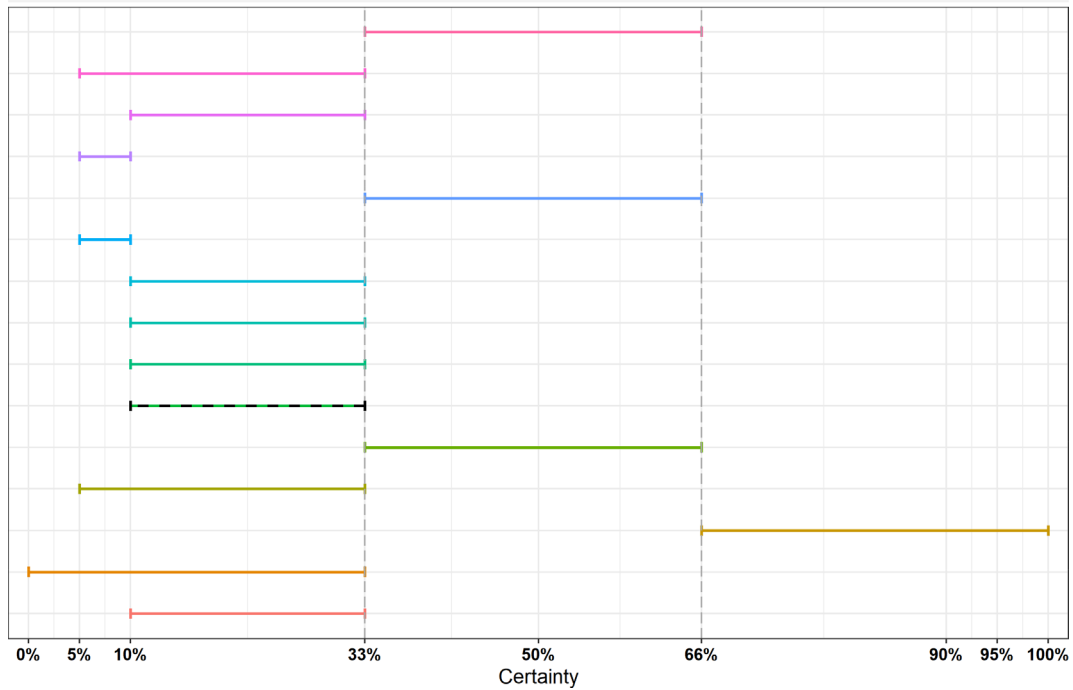
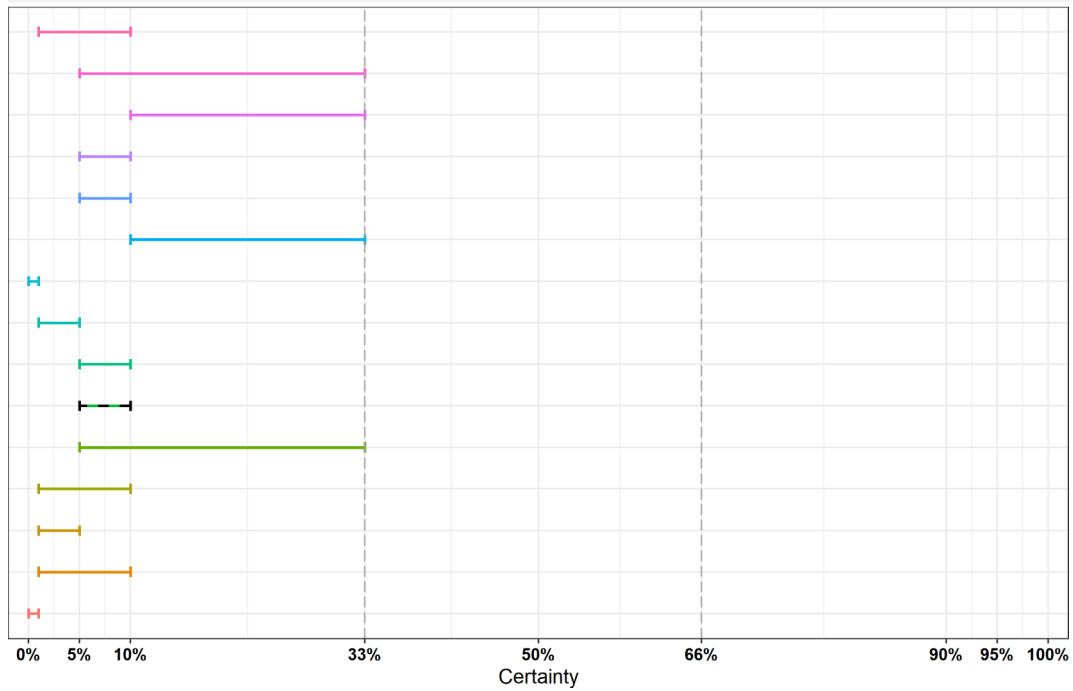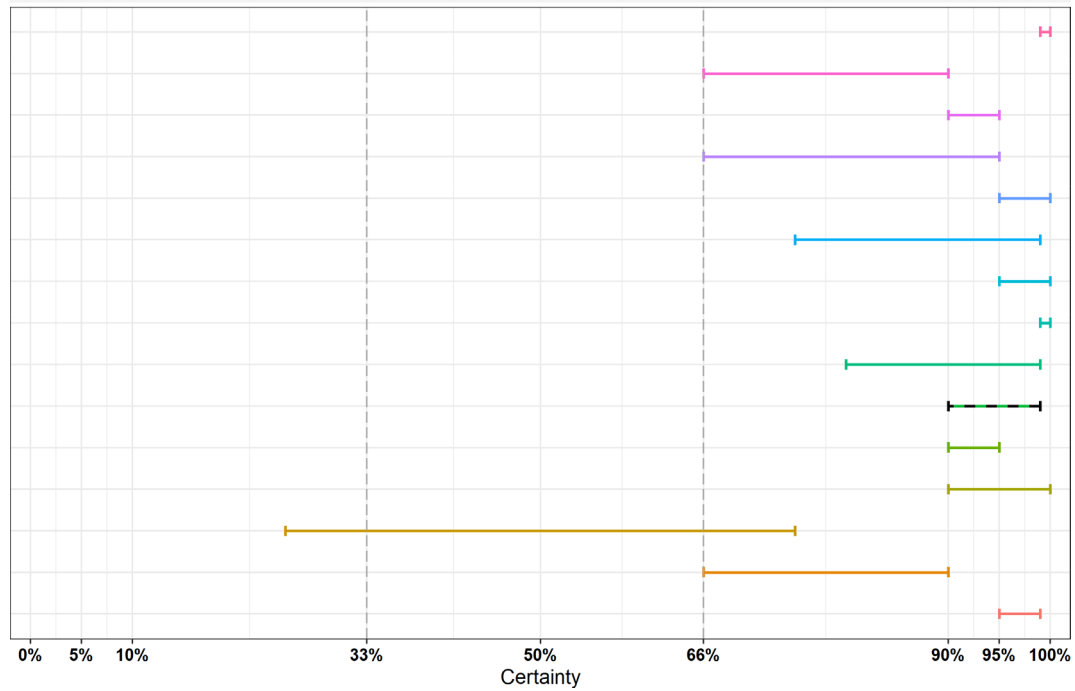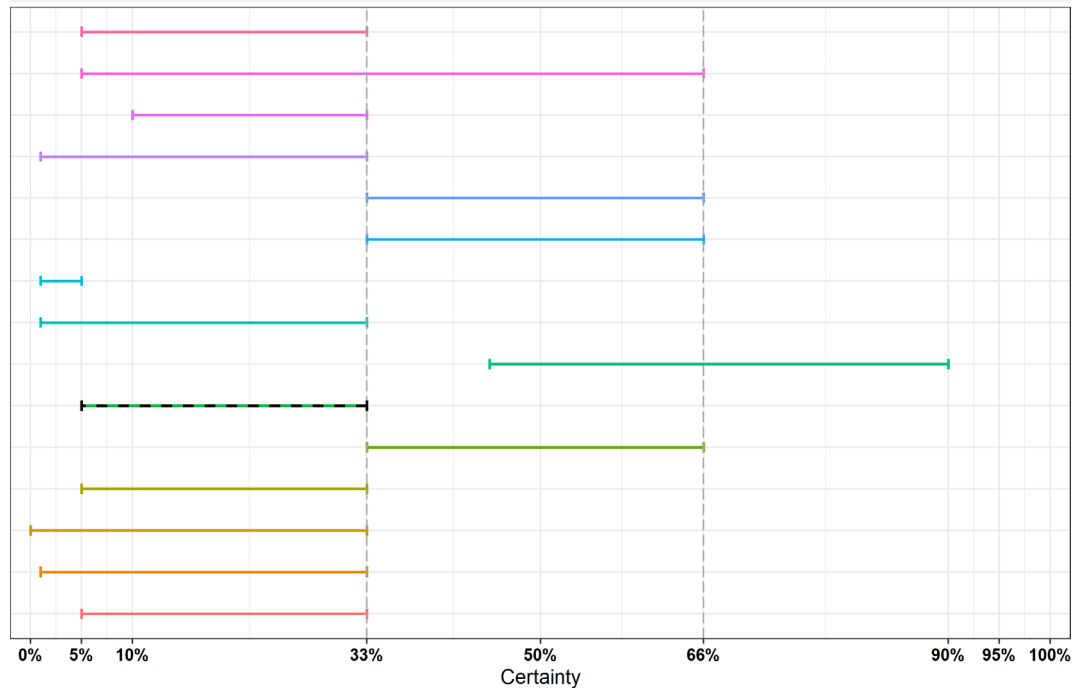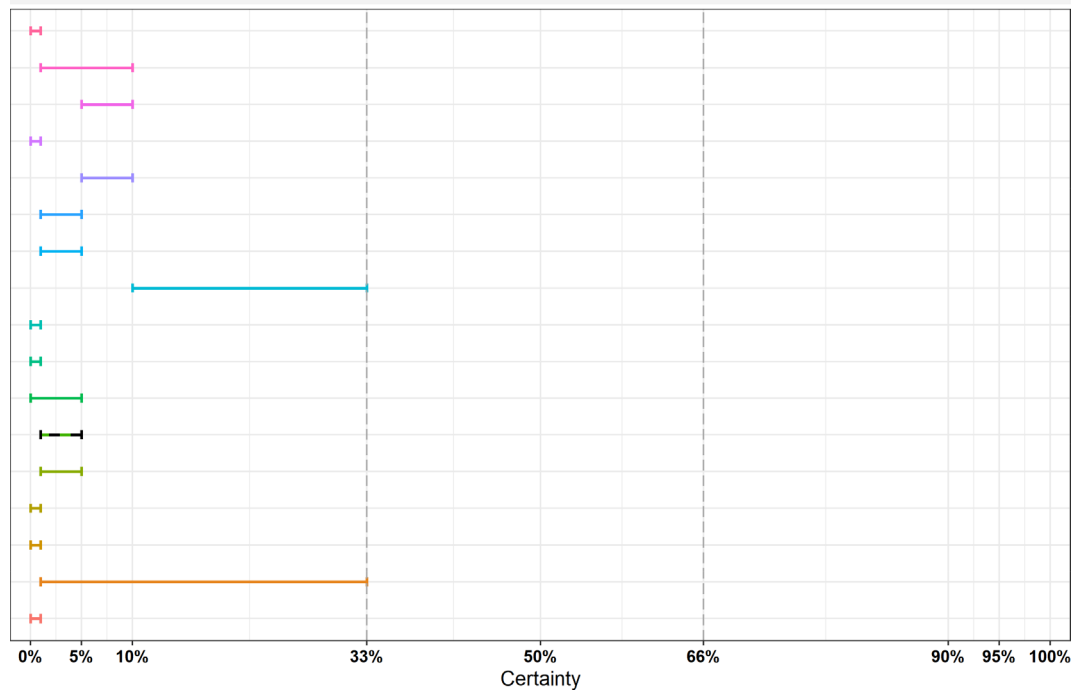**Collective Assessment**
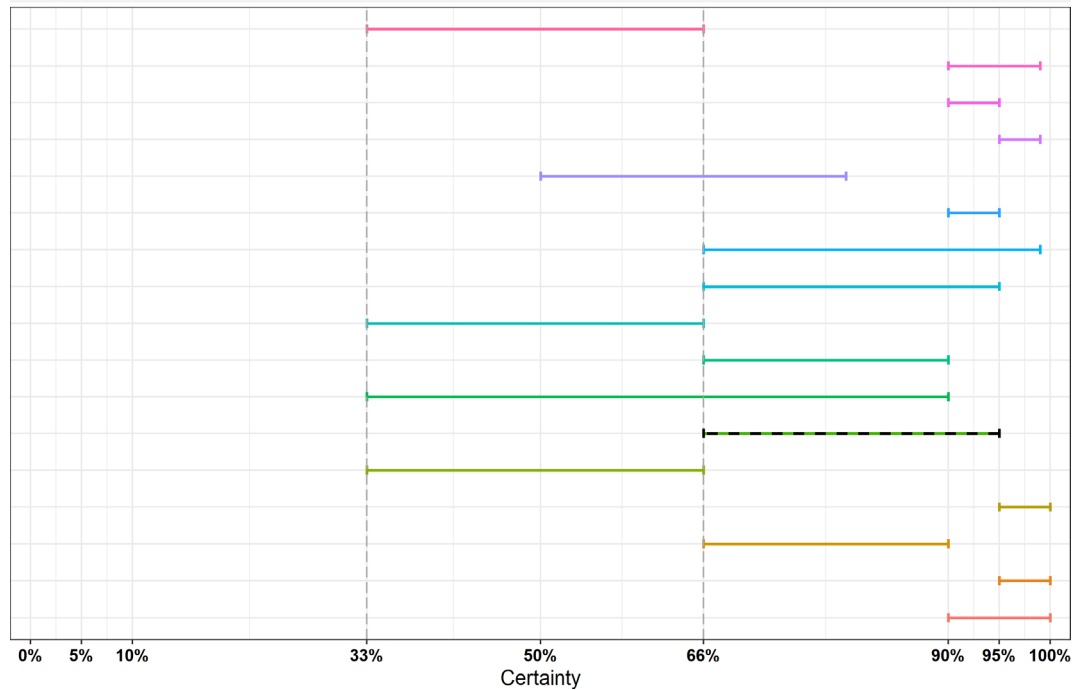
Art. 5: A(i)

The median range is displayed as a dashed line.

Figure A.1: Individual probability ranges reflecting fulfilment of criterion A(i) (the disease is transmissible) after the collective judgement
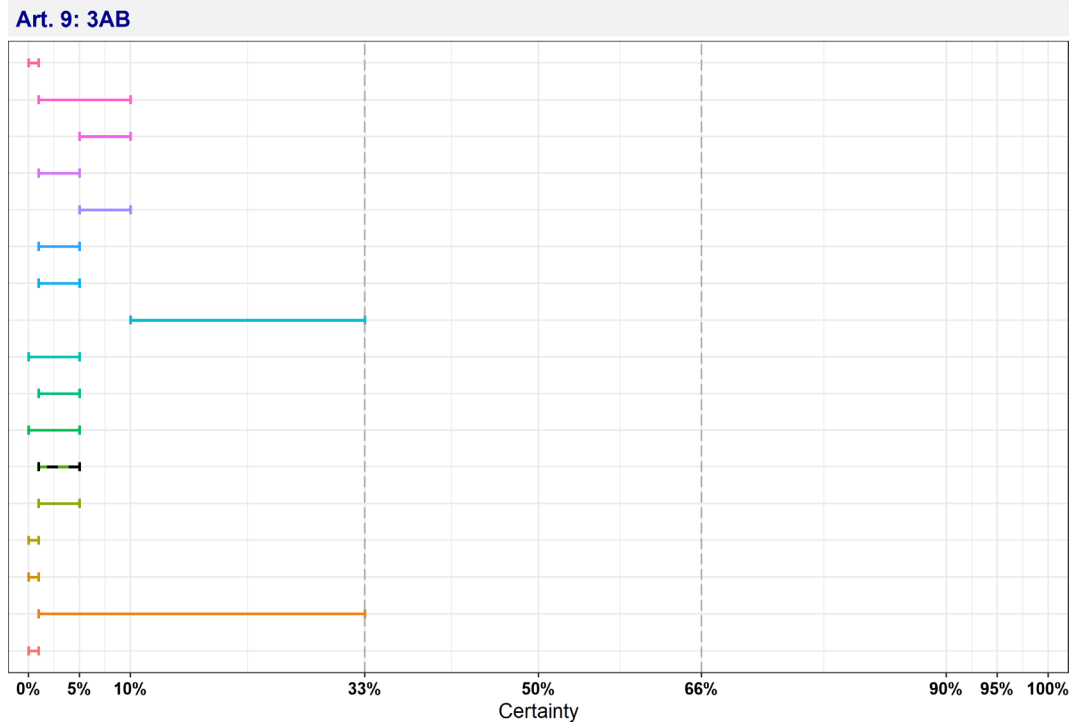
Collective Assessment

Art. 5: A(ii)
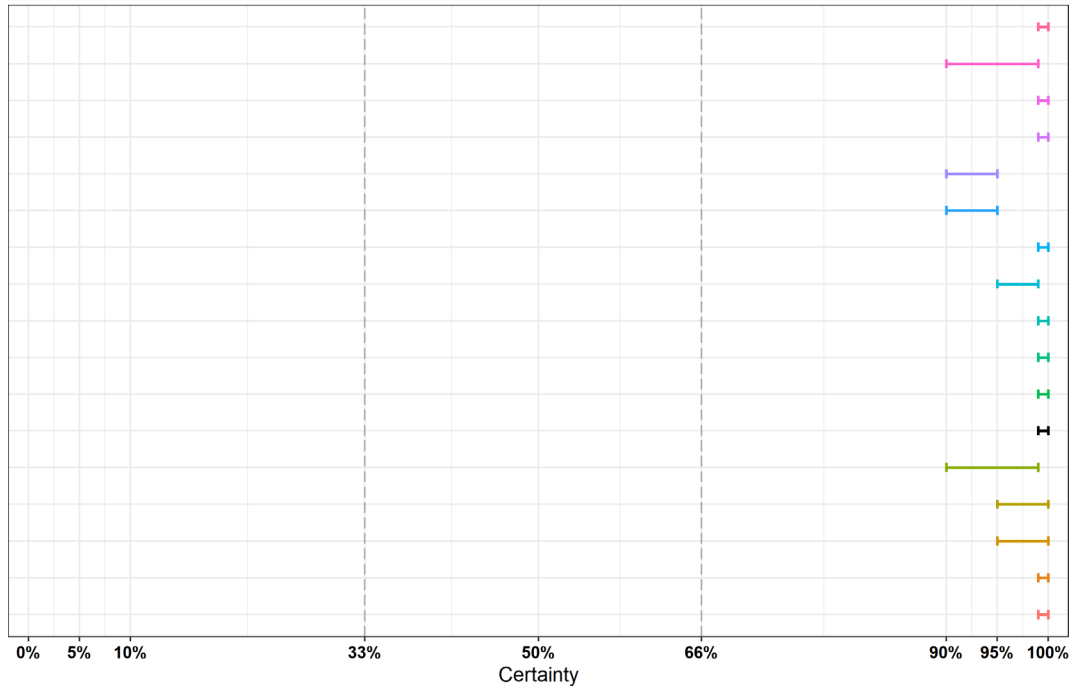
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Figure A.2: Individual probability ranges reflecting fulfilment of criterion A(ii) (animal species are either susceptible to the disease or vectors and reservoirs thereof exist in the Union) after the collective judgement

Collective Assessment

Art. 5: A(iii)
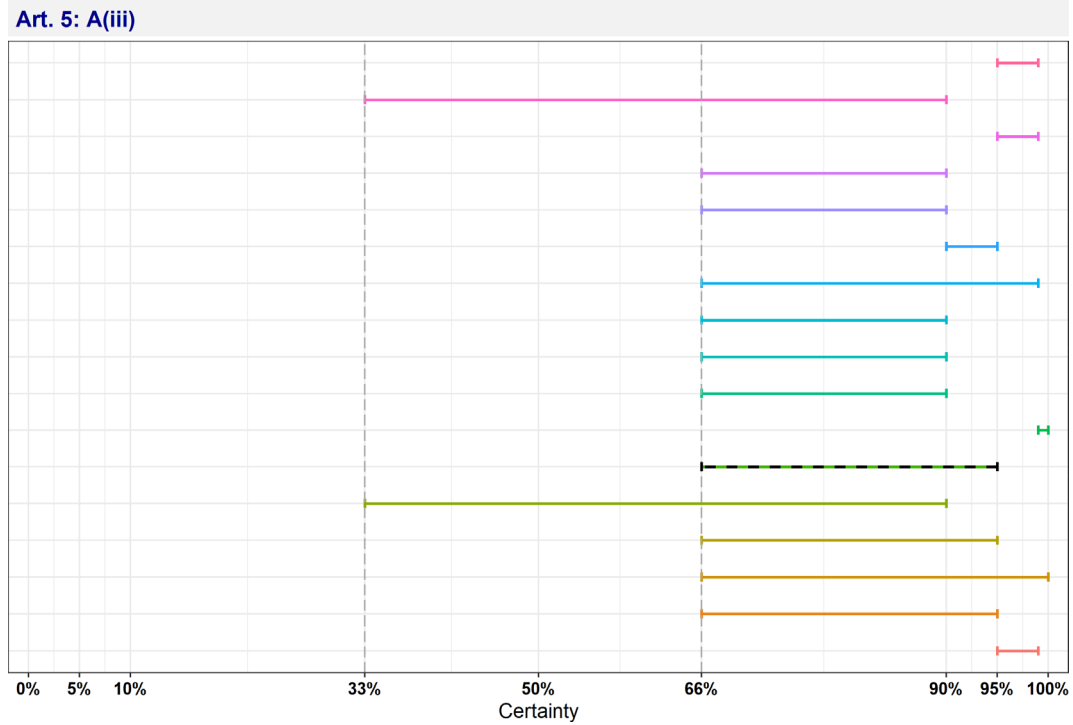
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Figure A.3: Individual probability ranges reflecting fulfilment of criterion A(iii) (the disease causes negative effects on animal health or poses a risk to public health due to its zoonotic character) after the collective judgement

Collective Assessment

Art. 5: A(iv)
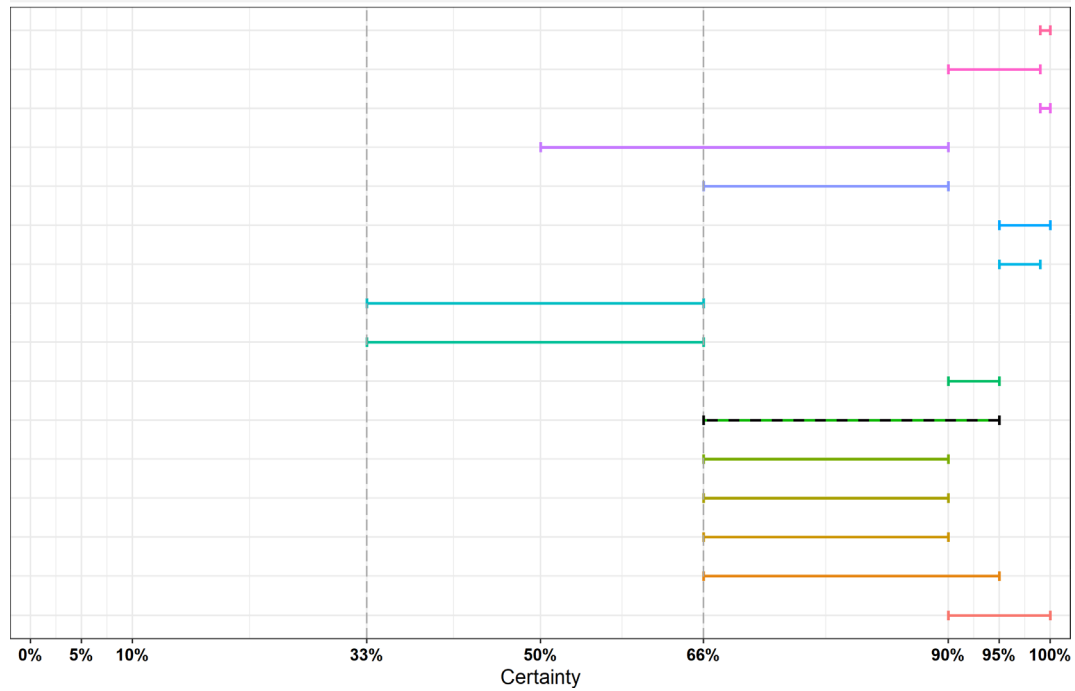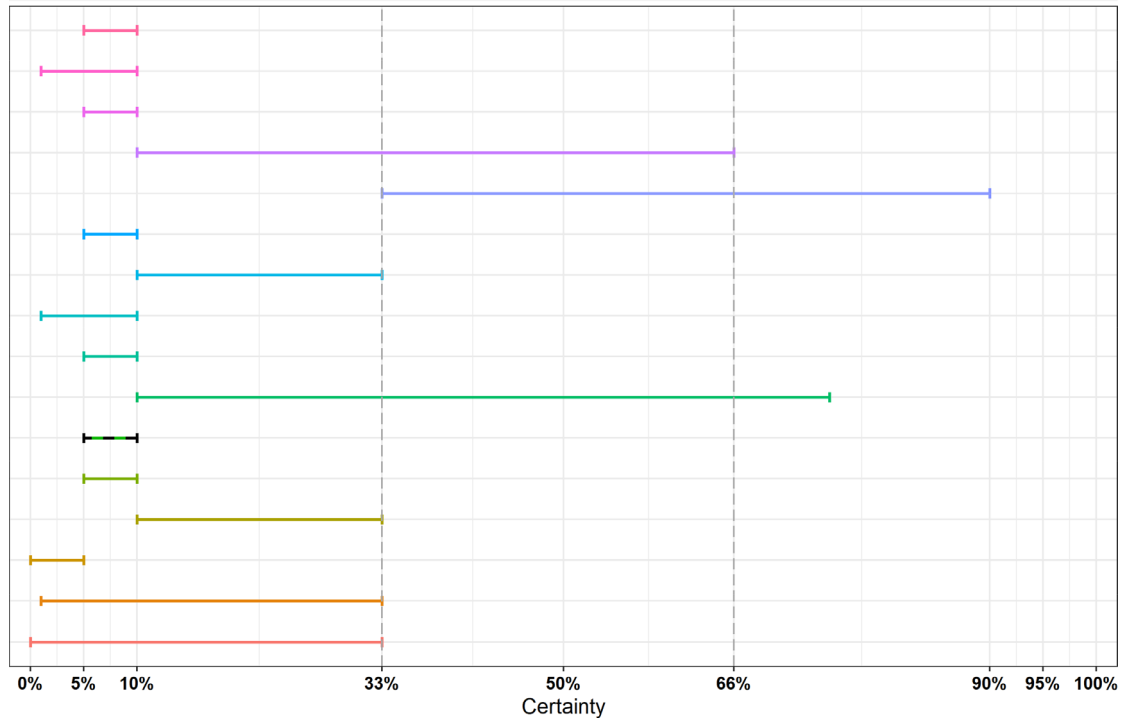

The median range is displayed as a dashed line.

Figure A.4: Individual probability ranges reflecting fulfilment of criterion A(iv) (diagnostic tools are available for the disease) after the collective judgement

Collective Assessment
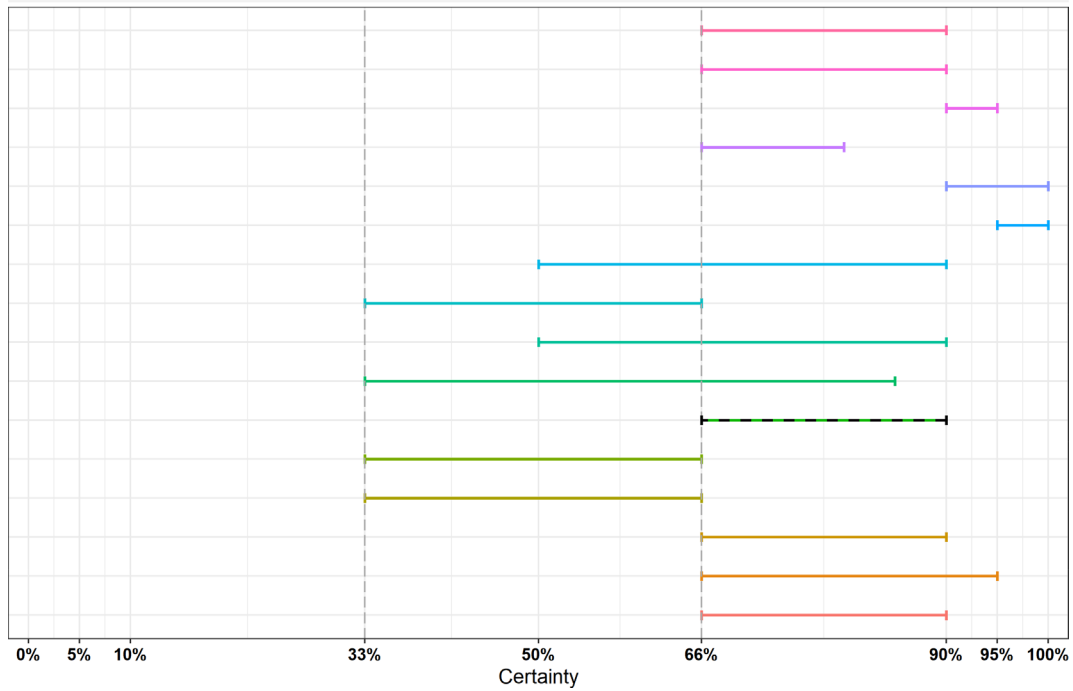
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Figure A.5: Individual probability ranges reflecting fulfilment of criterion B(ii) (the disease agent has developed resistance to treatments which poses a significant danger to public and/or animal health in the Union) after the collective judgement
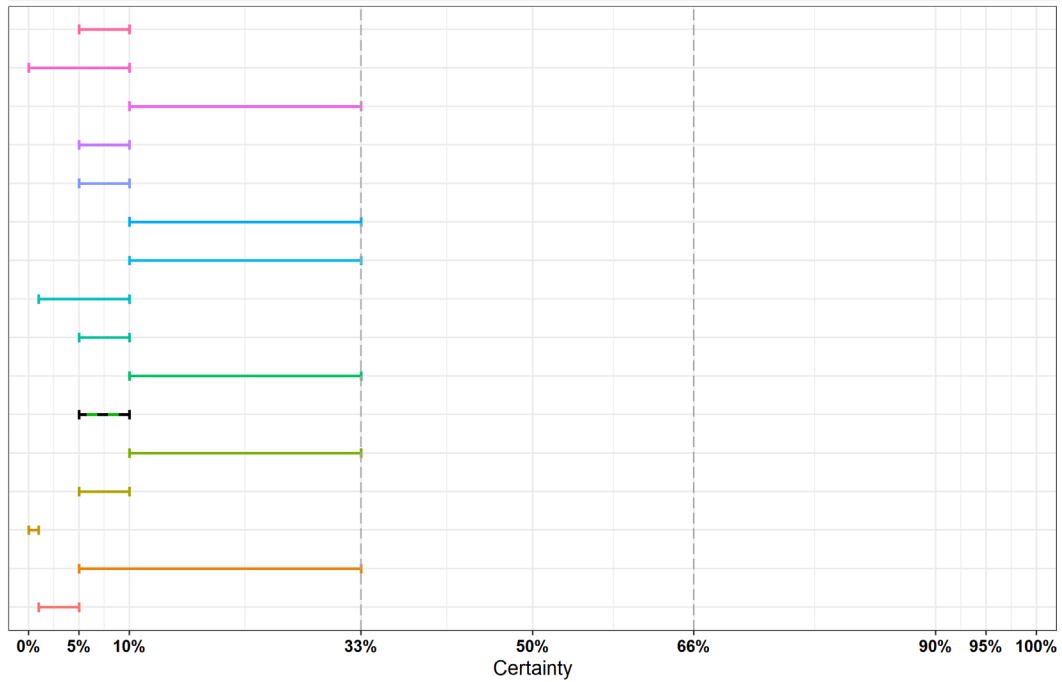
Collective Assessment
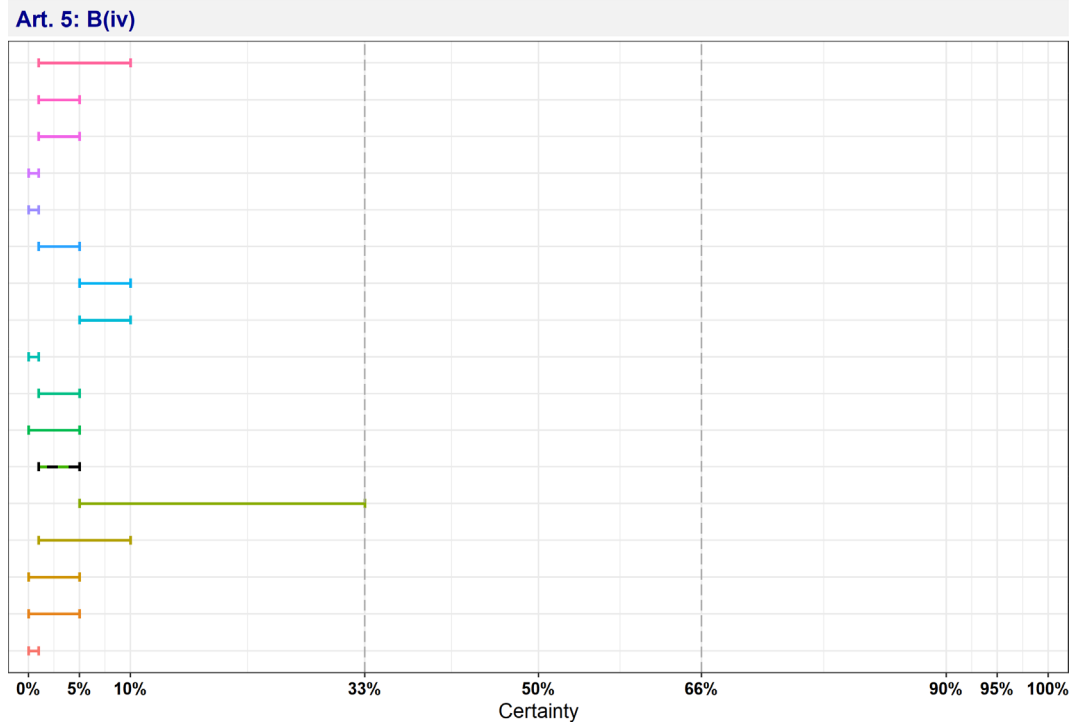
The median range is displayed as a dashed line.

Figure A.6: Individual probability ranges reflecting non-fulfilment of criterion B(iv) (the disease has the potential to generate a crisis or the disease agent could be used for the purpose of bioterrorism) after the collective judgement

Collective Assessment
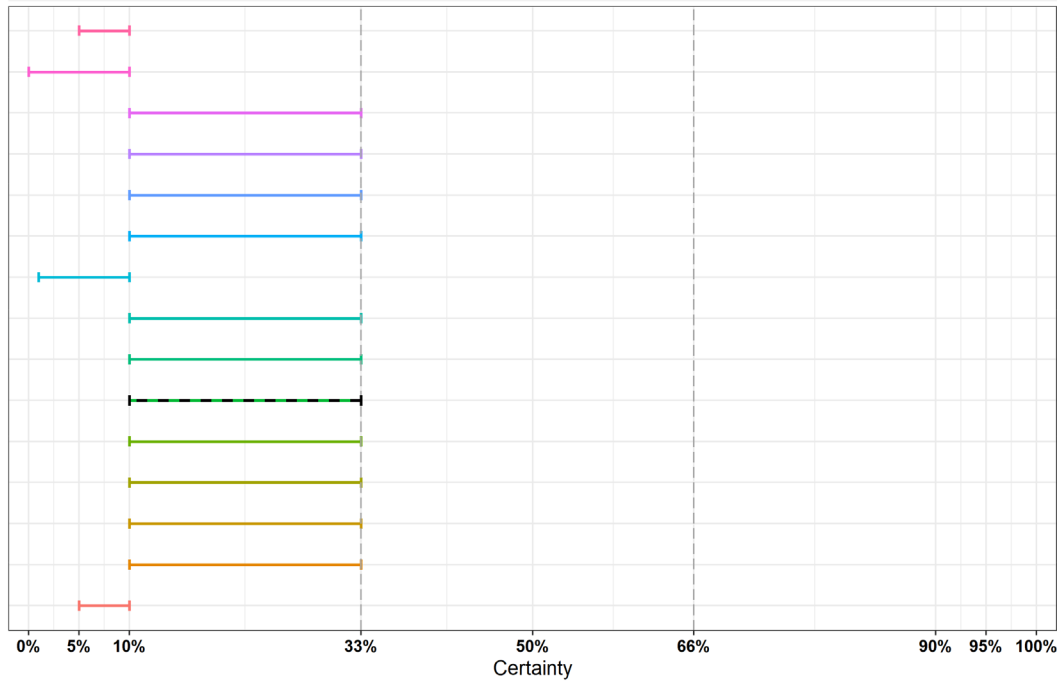

The median range is displayed as a dashed line.

Figure A.7: Individual probability ranges reflecting non-fulfilment of criterion B(v) (the disease has or could have a significant negative impact on the environment, including biodiversity, of the Union) after the collective judgement

A.2 Article 9 criteria
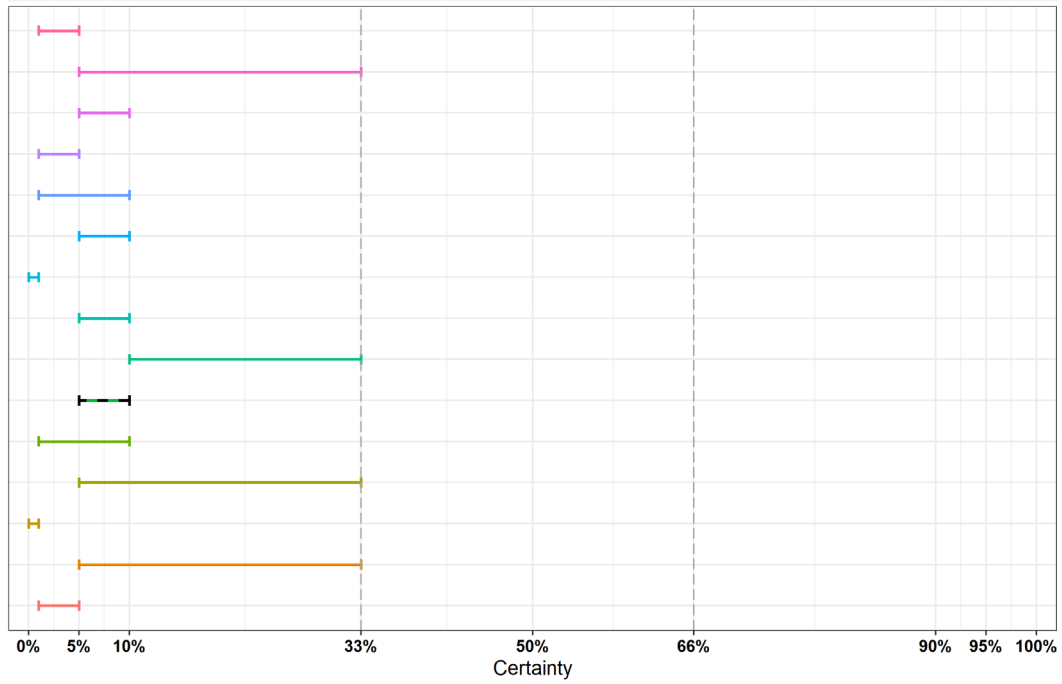

The median range is displayed as a dashed line.

Figure A.8: Individual probability ranges reflecting non-fulfilment of criterion 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) after the collective judgement

Collective Assessment

The median range is displayed as a dashed line.

Figure A.9: Individual probability ranges reflecting non-fulfilment of criterion 2.1A (the disease is highly transmissible) after the collective judgement

Collective Assessment

Art. 9: 2.3A
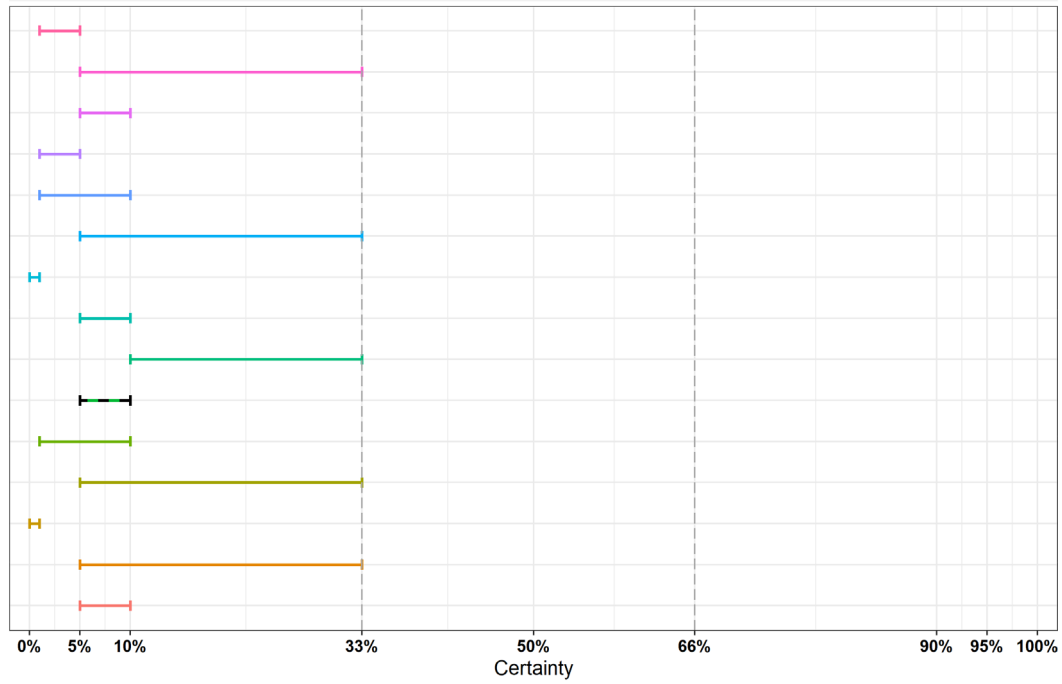

The median range is displayed as a dashed line.

Figure A.10: Individual probability ranges reflecting fulfilment of criterion 2.3A (the disease affects multiple species of kept and wild animals or single species of kept animals of economic importance) after the collective judgement

Collective Assessment

Art. 9: 2.4A

The median range is displayed as a dashed line.

Figure A.11: Individual probability ranges reflecting non-fulfilment of criterion 2.4A (the disease may result in high morbidity and significant mortality rates) after the collective judgement

Collective Assessment
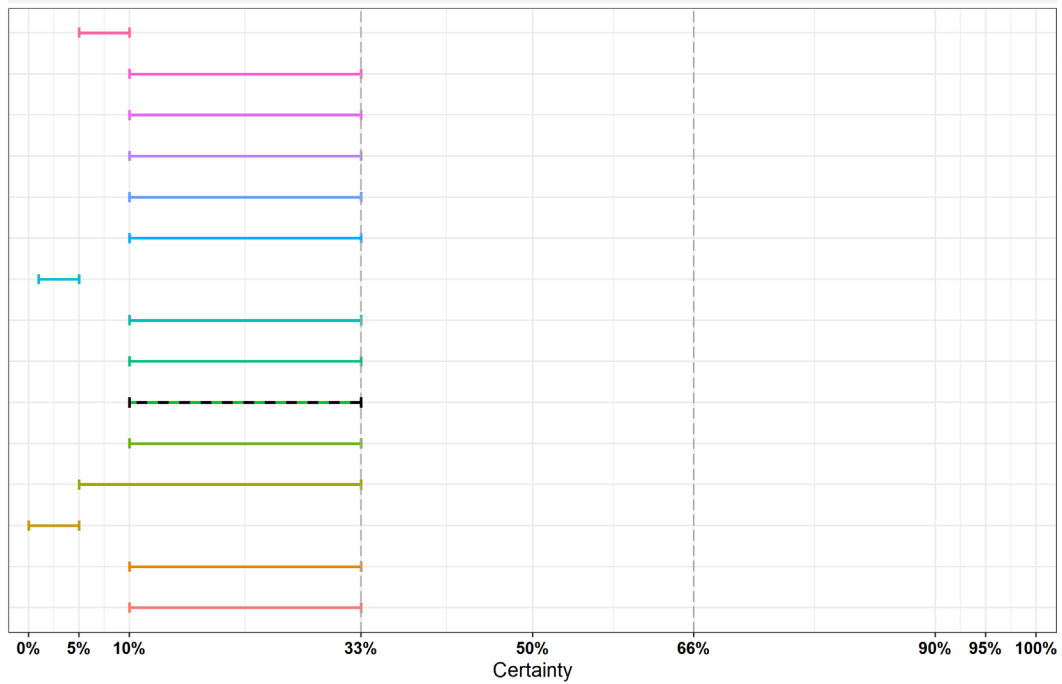

The median range is displayed as a dashed line.

Figure A.12: Individual probability ranges reflecting non-fulfilment of criterion 3A (the disease has a zoonotic potential with significant consequences for public health, including epidemic or pandemic potential or possible significant threats to food safety) after the collective judgement
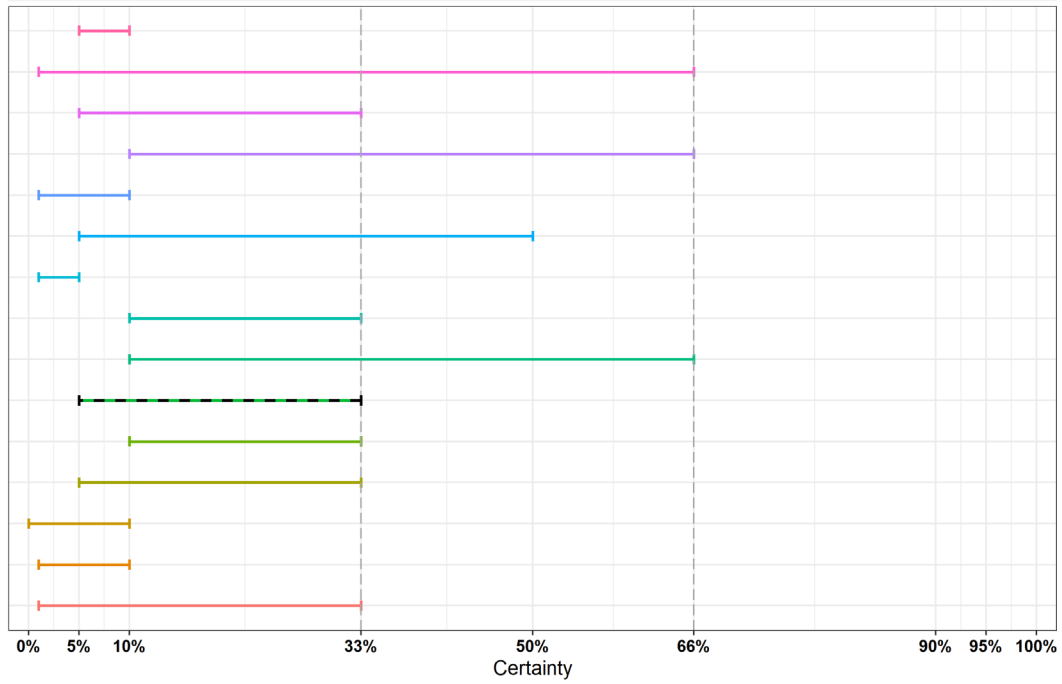
The median range is displayed as a dashed line.

Figure A.13: Individual probability ranges reflecting non-fulfilment of criterion 3AB (the disease has a zoonotic potential with significant consequences for public health, including epidemic potential or possible significant threats to food safety) after the collective judgement

Collective Assessment

Art. 9: 3ABC

The median range is displayed as a dashed line.

Figure A.14: Individual probability ranges reflecting non-fulfilment of criterion 3ABC (the disease has a zoonotic potential with significant consequences for public health or possible significant threats to food safety) after the collective judgement
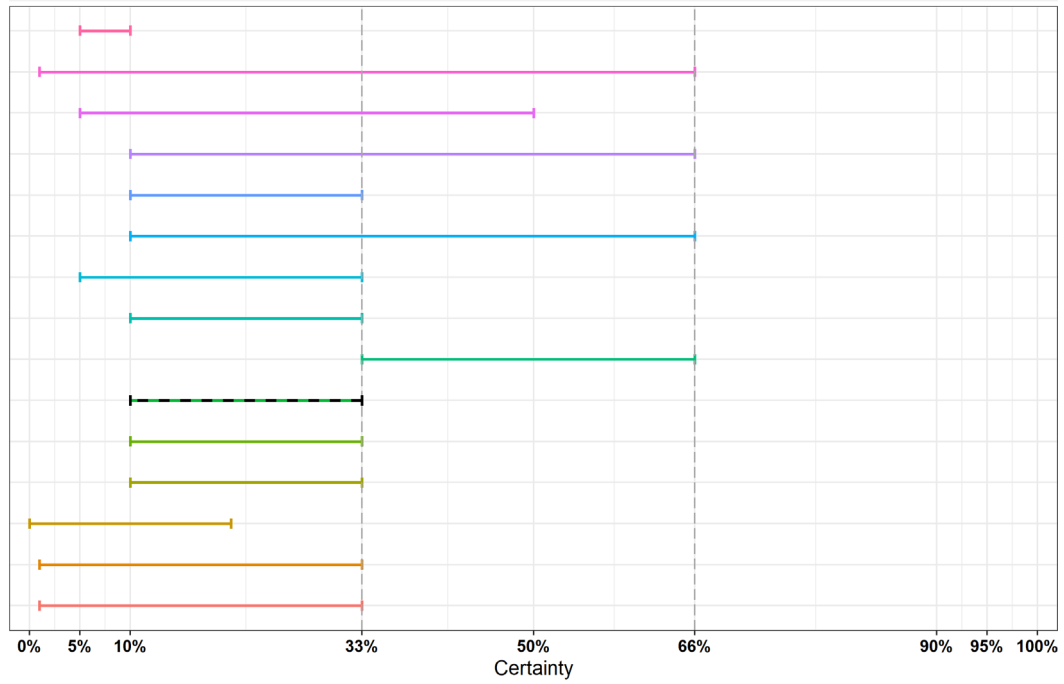
Collective Assessment

Art. 9: 4AB (CI)

CI: current impact

The median range is displayed as a dashed line.

Figure A.15: Individual probability ranges reflecting non-fulfilment of criterion 4AB (current impact) (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) after the collective judgement

Collective Assessment

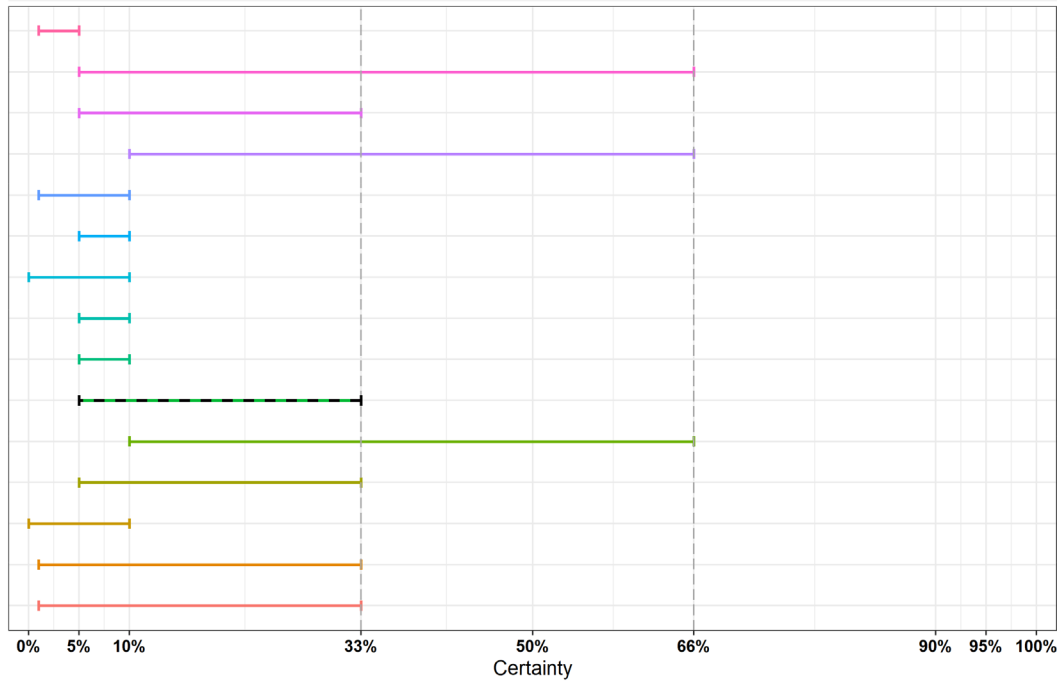CI: current impact

The median range is displayed as a dashed line.

Figure A.16: Individual probability ranges reflecting non-fulfilment of criterion 4C (current impact) (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) after the collective judgement

Collective Assessment

Art. 9: 5(a) (CI)

CI: current impact
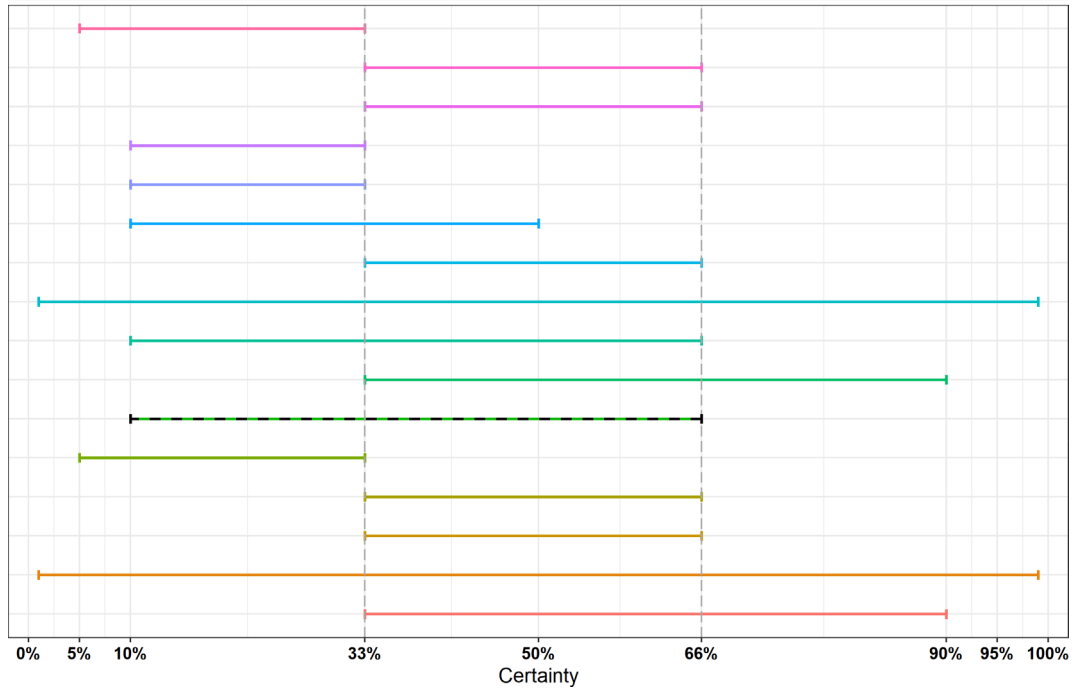
The median range is displayed as a dashed line.

Figure A.17: Individual probability ranges reflecting non-fulfilment of criterion 5(a) (current impact) (the disease has a significant impact on society, with in particular an impact on labour markets) after the collective judgement

Collective Assessment

PI: potential impact

The median range is displayed as a dashed line.

Figure A.18: Individual probability ranges reflecting non-fulfilment of criterion 5(a) (potential impact) (the disease has a significant impact on society, with in particular an impact on labour markets) after the collective judgement

Collective Assessment

Art. 9: 5(b) (CI)

CI: current impact

The median range is displayed as a dashed line.

Figure A.19: Individual probability ranges reflecting non-fulfilment of criterion 5(b) (current impact) (the disease has a significant impact on animal welfare, by causing suffering of large numbers of animals) after the collective judgement

Collective Assessment

Art. 9: 5(c) (CI)

CI: current impact

The median range is displayed as a dashed line.

Figure A.20: Individual probability ranges reflecting non-fulfilment of criterion 5(c) (current impact) (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) after the collective judgement

Collective Assessment

Art. 9: 5(c) (PI)

PI: potential impact

The median range is displayed as a dashed line.

Figure A.21: Individual probability ranges reflecting non-fulfilment of criterion 5(c) (potential impact) (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) after the collective judgement

Collective Assessment

CI: current impact

The median range is displayed as a dashed line.

Figure A.22: Individual probability ranges reflecting non-fulfilment of criterion 5(d) (current impact) (the disease has a significant impact in 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) after the collective judgement

Annex B – Criteria with uncertain outcome

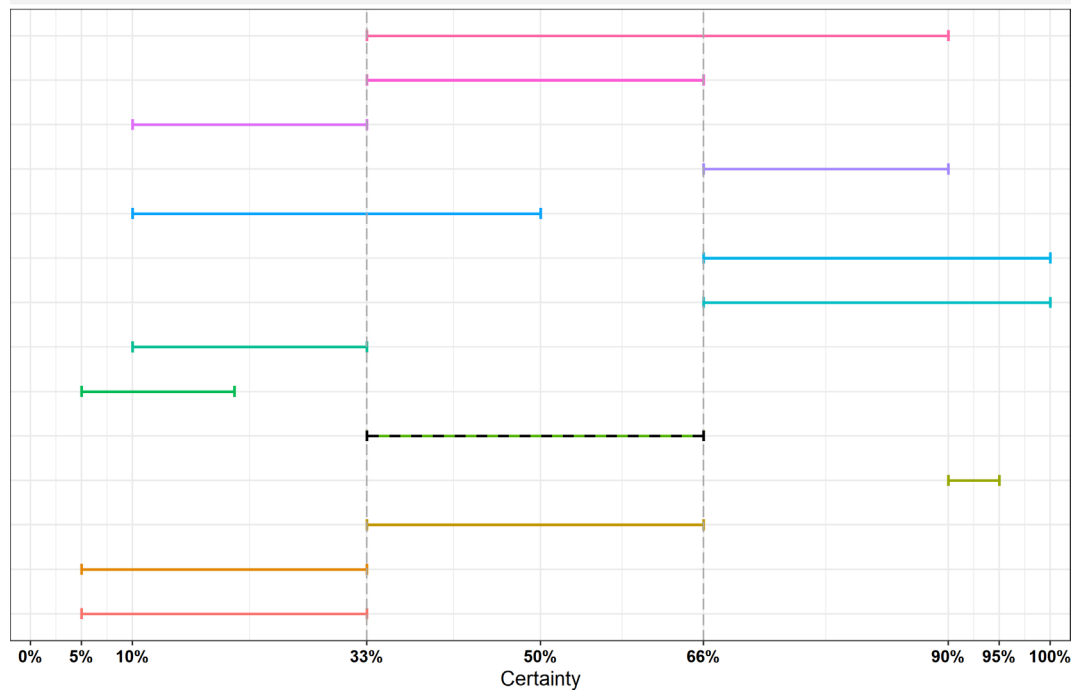## B.1   Article 5 criteria

Collective Assessment

Art. 5: A(v)

The median range is displayed as a dashed line.

Figure B.1: Individual probability ranges reflecting uncertain outcome on criterion 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) after the collective judgement
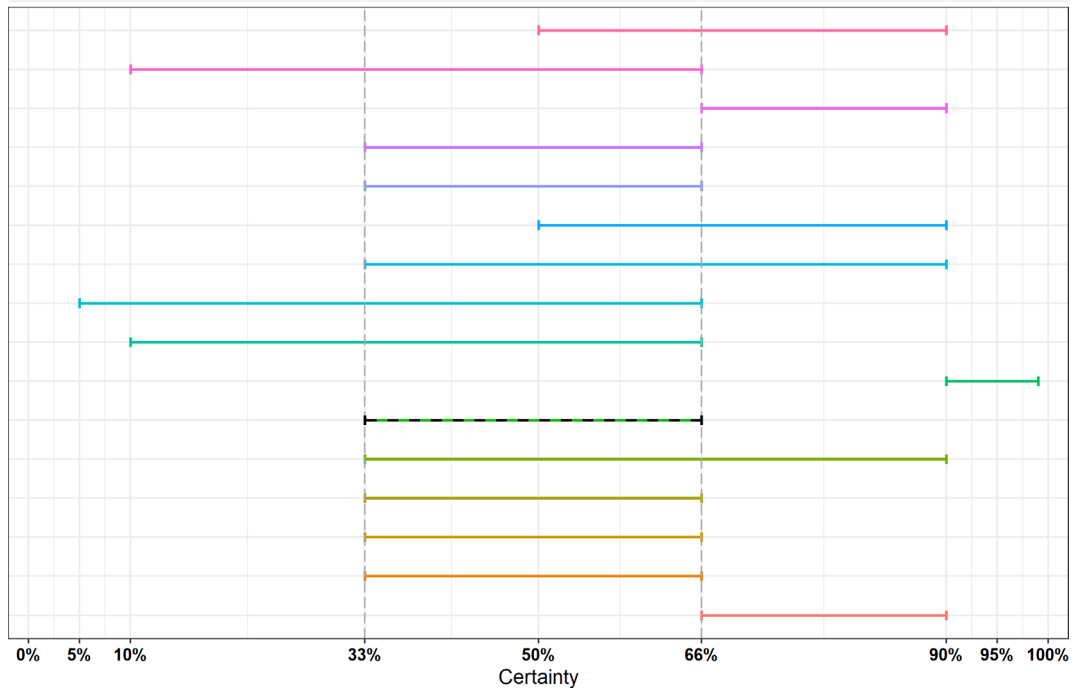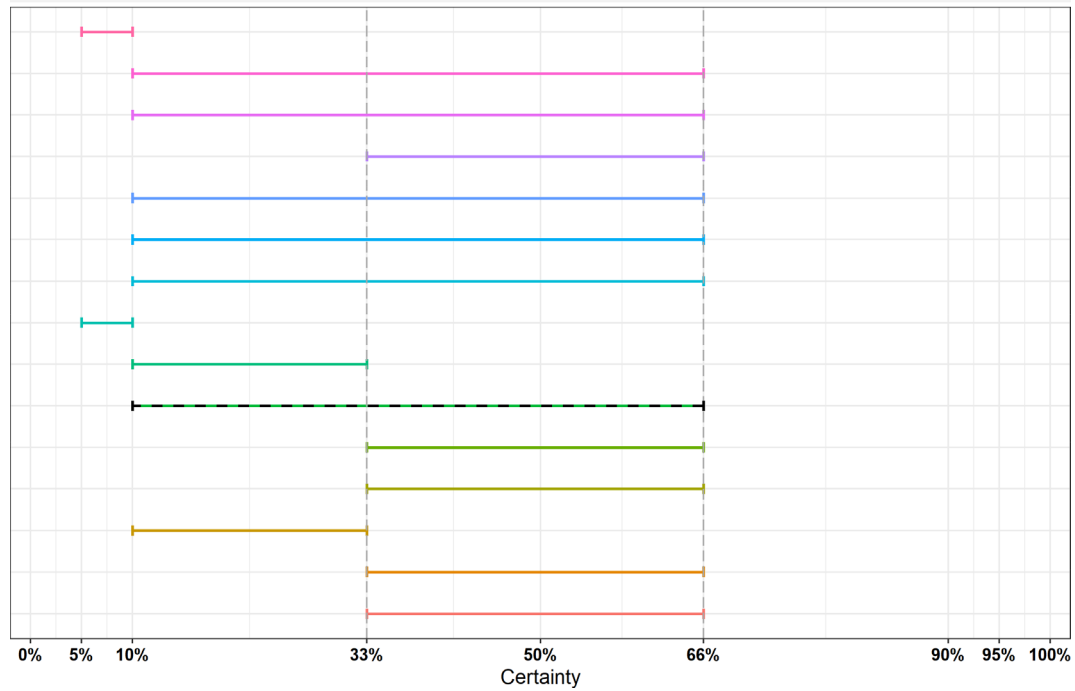
The median range is displayed as a dashed line.

Figure B.2: Individual probability ranges reflecting uncertain outcome on criterion 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) after the collective judgement
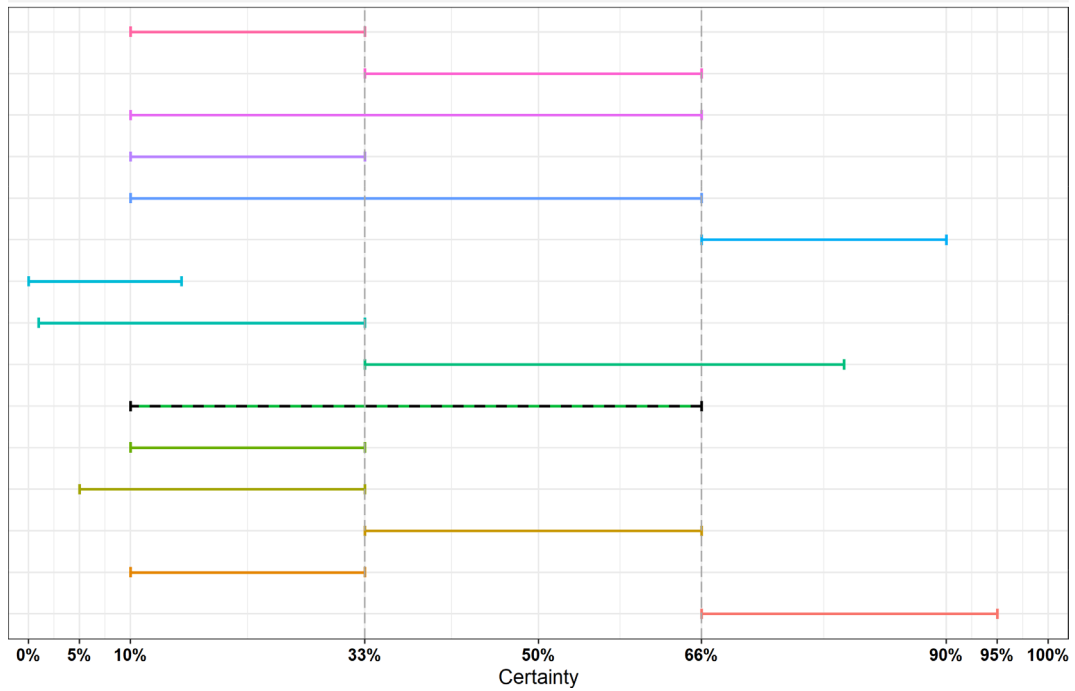
Collective Assessment

Art. 5: B(iii)
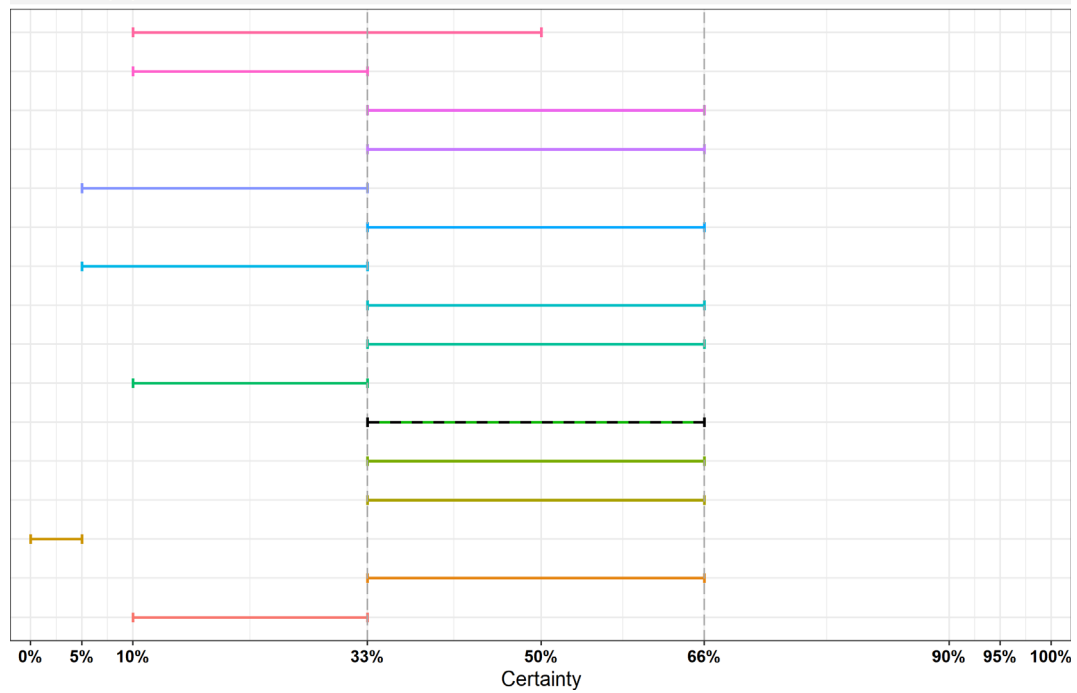
The median range is displayed as a dashed line.

Figure B.3: Individual probability ranges reflecting uncertain outcome on criterion B(iii) (the disease causes or could cause a significant negative economic impact affecting agriculture or aquaculture production in the Union) after the collective judgement

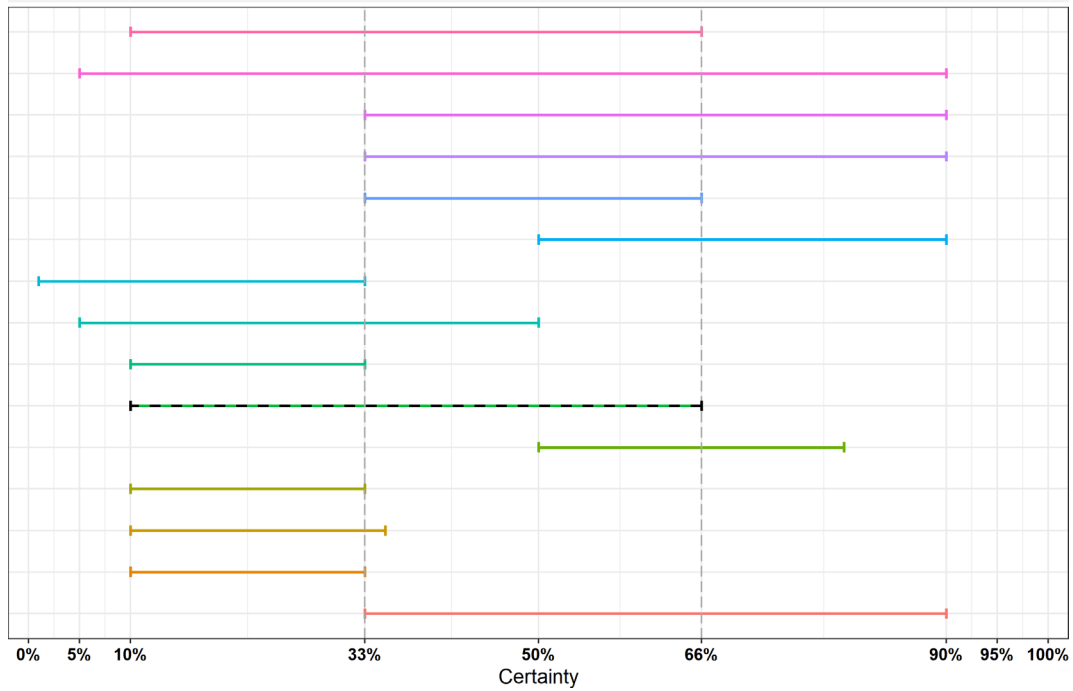## B.2   Article 9 criteria

Collective Assessment

Art. 9: 1A
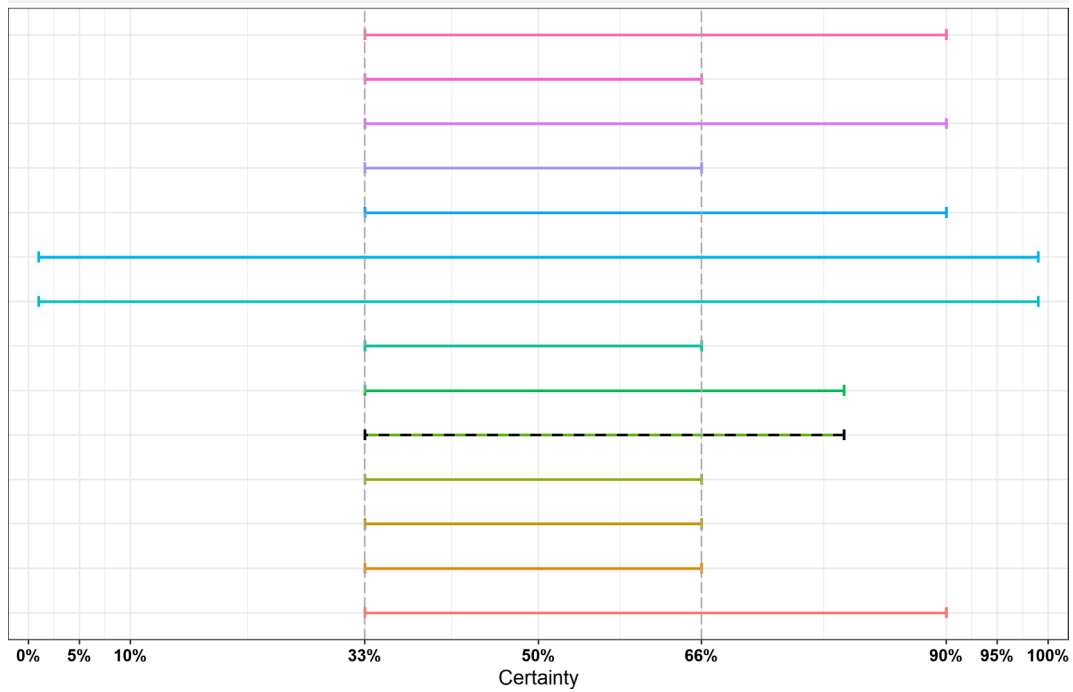
The median range is displayed as a dashed line.

Figure B.4: Individual probability ranges reflecting uncertain outcome on criterion 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) after the collective judgement
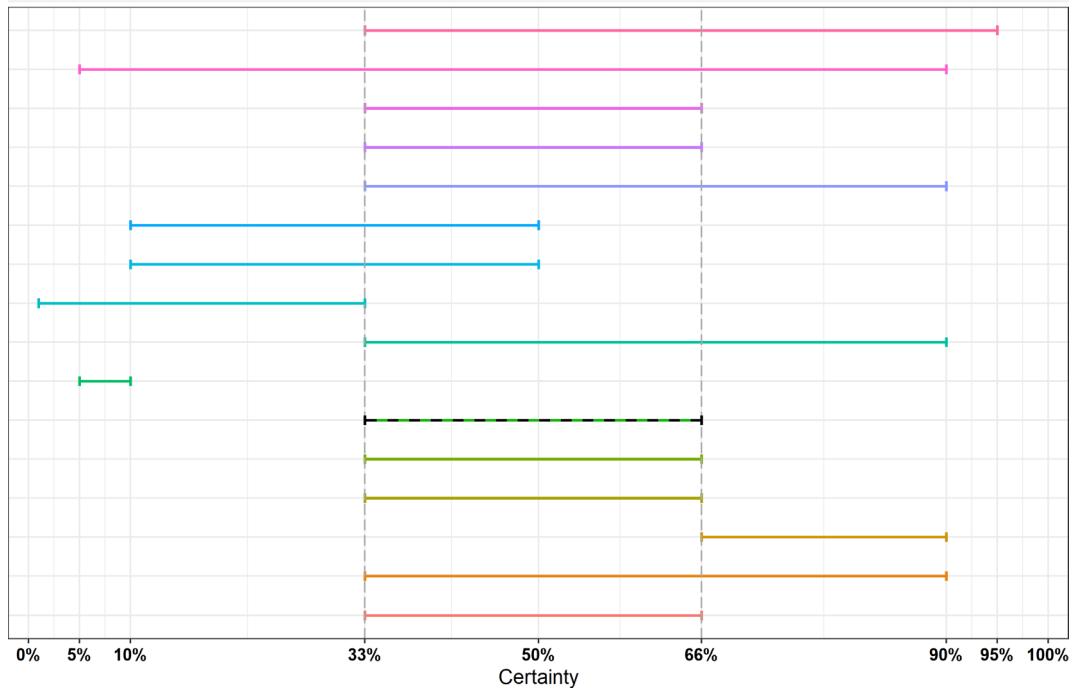
Collective Assessment

Art. 9: 1C

The median range is displayed as a dashed line.

Figure B.5: Individual probability ranges reflecting uncertain outcome on criterion 1C (the disease is present in the whole or part of the Union territory with an endemic character) after the collective judgement

Collective Assessment

Art. 9: 2.1BC

The median range is displayed as a dashed line.

Figure B.6: Individual probability ranges reflecting uncertain outcome on criterion 2.1BC (the disease is moderately to highly transmissible) after the collective judgement

Collective Assessment

Art. 9: 2.2AB

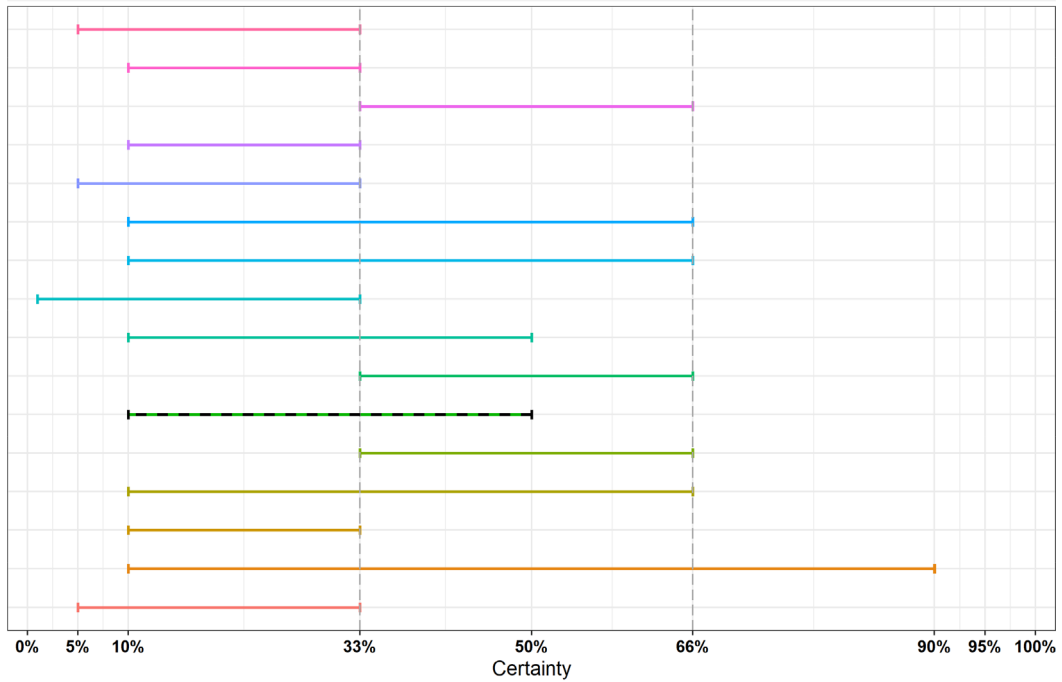

The median range is displayed as a dashed line.

Figure B.7: Individual probability ranges reflecting uncertain outcome on criterion 2.2AB (there are possibilities of airborne or waterborne or vector-borne spread) after the collective judgement

Collective Assessment

Art. 9: 2.4B

The median range is displayed as a dashed line.

Figure B.8: Individual probability ranges reflecting uncertain outcome on criterion 2.4B (the disease may result in high morbidity with in general low mortality) after the collective judgement

The median range is displayed as a dashed line.

Figure B.9: Individual probability ranges reflecting uncertain outcome on criterion 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) after the collective judgement
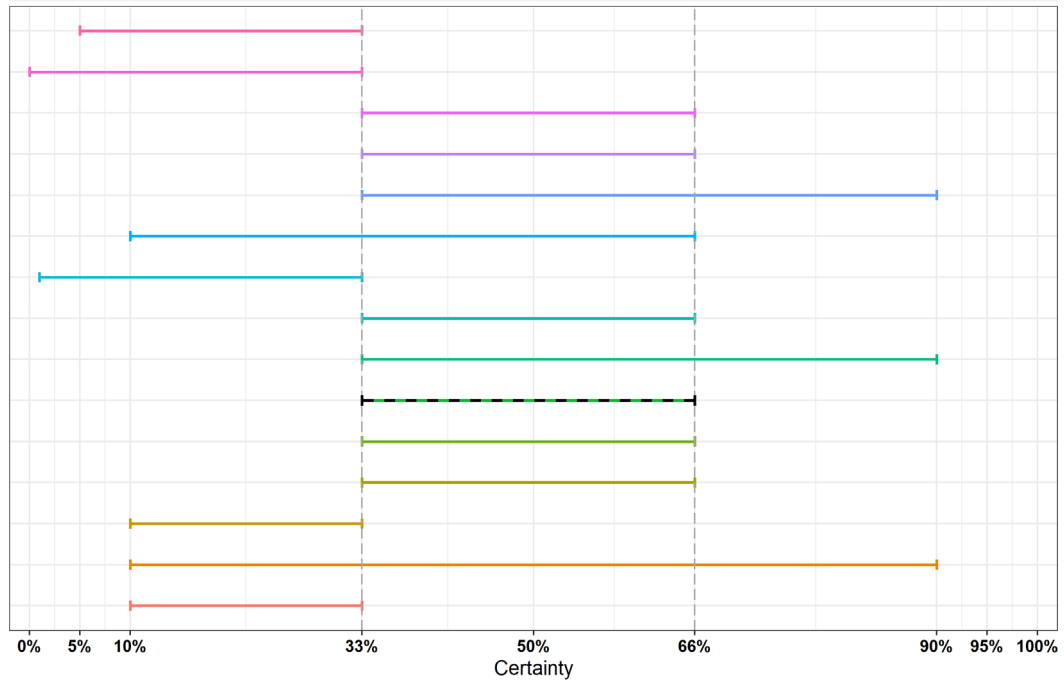
Collective Assessment
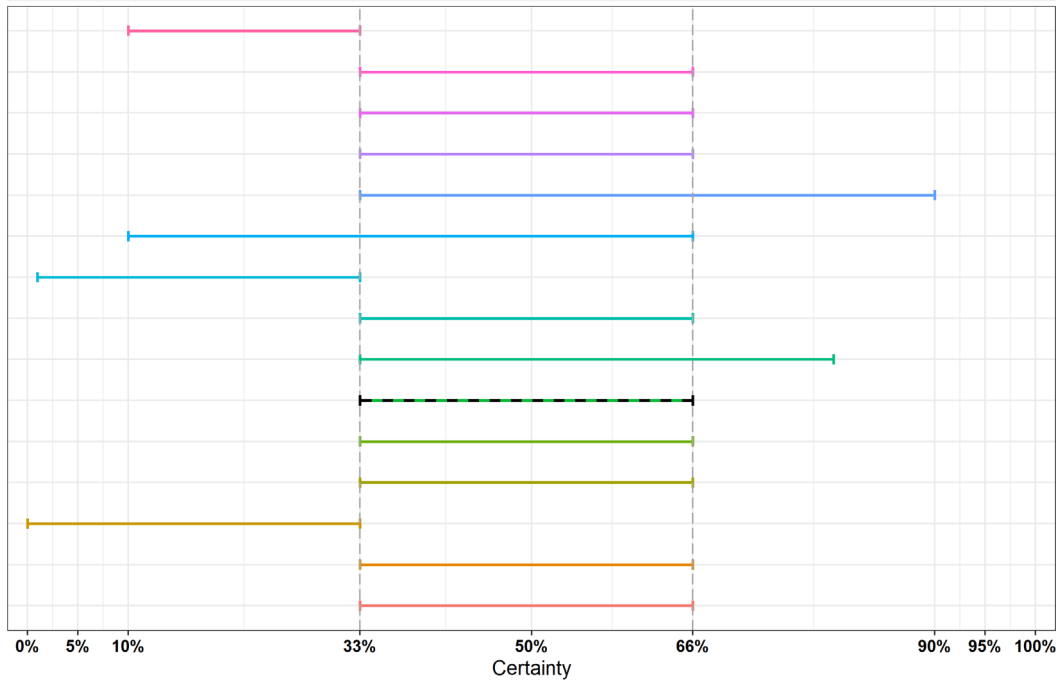
Art. 9: 4AB (PI)

PI: potential impact

The median range is displayed as a dashed line.

Figure B.10: Individual probability ranges reflecting uncertain outcome on criterion 4AB (potential impact) (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) after the collective judgement

Collective Assessment

PI: potential impact

The median range is displayed as a dashed line.

Figure B.11: Individual probability ranges reflecting uncertain outcome on criterion 4C (potential impact) (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) after the collective judgement
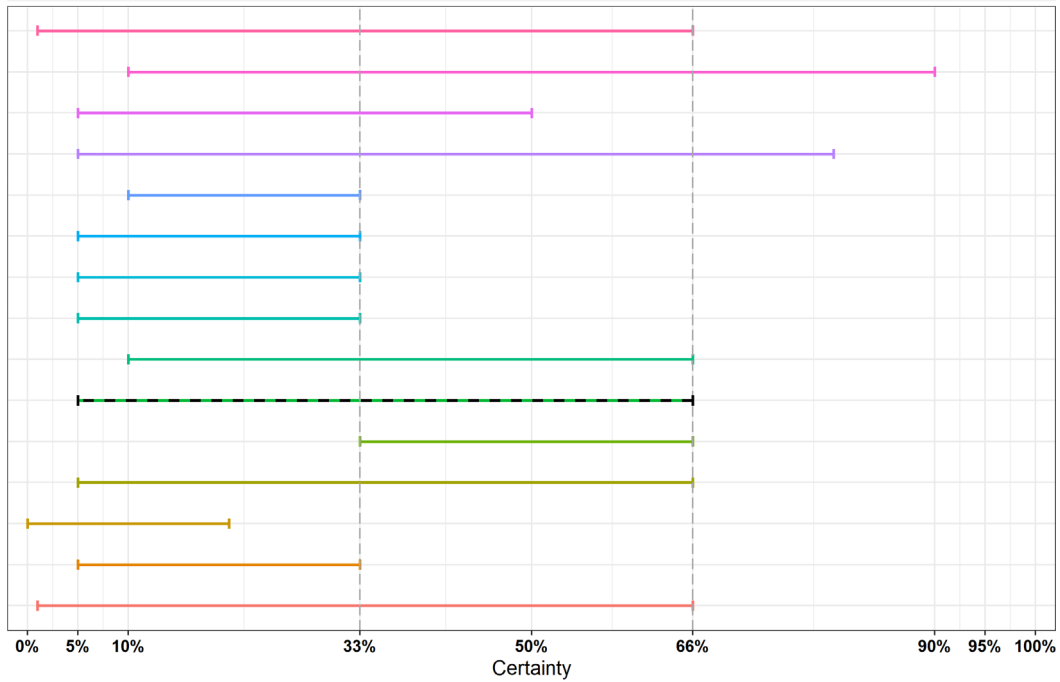
Collective Assessment

PI: potential impact

The median range is displayed as a dashed line.

Figure B.12: Individual probability ranges reflecting uncertain outcome on criterion 5(b) (potential impact) (the disease has a significant impact on animal welfare, by causing suffering of large numbers of animals) after the collective judgement
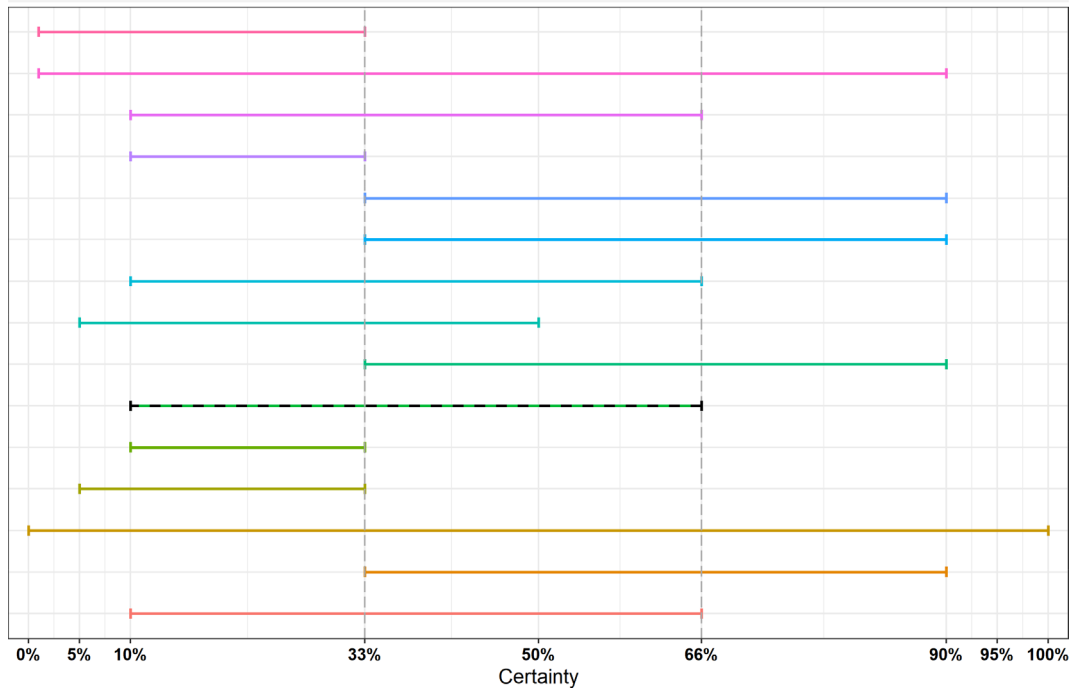
Collective Assessment

Art. 9: 5(d) (PI)

PI: potential impact

The median range is displayed as a dashed line.

Figure B.13: Individual probability ranges reflecting uncertain outcome on criterion 5(d) (potential impact) (the disease has a significant impact in 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) after the collective judgement

Collective Assessment

The median range is displayed as a dashed line.

Figure B.14: Individual probability ranges reflecting uncertain outcome on criterion D (the risk posed by the disease can be effectively and proportionately mitigated by measures concerning movements of animals and products in order to prevent or limit its occurrence and spread) after the collective judgement