SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 30 March 2022

doi: 10.2903/j.efsa.2022.7312

Assessment of listing and categorisation of animal diseases within the framework of the Animal Health Law (Regulation (EU) No 2016/429): antimicrobial-resistant *Staphylococcus aureus* in cattle and horses

EFSA Panel on Animal Health and Welfare (AHAW),
Søren Saxmose Nielsen, Dominique Joseph Bicout, Paolo Calistri, Elisabetta Canali, Julian Ashley Drewe, Bruno Garin-Bastuji, José Luis Gonzales Rojas, Christian Gortázar, Mette Herskin, Virginie Michel, Miguel Ángel Miranda Chueca, Barbara Padalino, Paolo Pasquali, Helen Clare Roberts, Hans Spoolder, Karl Ståhl, Antonio Velarde, Arvo Viltrop, Christoph Winckler, Francesca Baldinelli, Alessandro Broglia, Lisa Kohnle and Julio Alvarez

Abstract

Staphylococcus aureus (*S. aureus*) was identified among the most relevant antimicrobial-resistant (AMR) bacteria in the EU for cattle and horses in previous scientific opinions. 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 $\geq$ 66%) or not (upper bound $\leq$ 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 *S. aureus* can be considered eligible to be listed for Union intervention according to Article 5 of the AHL (60–90% 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, 2 and 4 (Categories A, B and D; 1–5%, 5–10% and 10–33% probability of meeting the criteria, respectively) and the AHAW Panel was uncertain whether it meets the criteria in Sections 3 and 5 (Categories C and E, 33–90% and 60–90% probability of meeting the criteria, respectively). The animal species to be listed for AMR *S. aureus* according to Article 8 criteria include mainly mammals, birds, reptiles and fish.

Keywords: antimicrobial resistance, *Staphylococcus aureus*, Animal Health Law, listing, categorisation, impact

Requestor: European Commission

Question number: EFSA-Q-2022-00094

Correspondence: alpha@efsa.europa.eu

Panel members: Søren Saxmose Nielsen, Julio Alvarez, Dominique Joseph Bicout, Paolo Calistri, Elisabetta Canali, Julian Ashley Drewe, Bruno Garin-Bastuji, José Luis Gonzales Rojas, Christian Gortázar, Mette Herskin, Virginie Michel, Miguel Ángel Miranda Chueca, Barbara Padalino, Paolo Pasquali, Helen Clare Roberts, Hans Spoolder, Karl Ståhl, Antonio Velarde, Arvo Viltrop and Christoph Winckler.

Declarations of interest: The declarations of interest of all scientific experts active in EFSA's work are available at https://ess.efsa.europa.eu/doi/doiweb/doisearch.

Acknowledgments: The AHAW Panel wishes to thank Wannes Vanderhaeghen from AMCRA for conducting the extensive literature review under the contract PO/EFSA/ALPHA/2021/04. The AHAW Panel also wishes to thank Verena Oswaldi from EFSA for the support provided for this scientific output.

Suggested citation: EFSA AHAW Panel (EFSA Panel on Animal Health and Welfare), Nielsen SS, Bicout DJ, Calistri P, Canali E, Drewe JA, Garin-Bastuji B, Gonzales Rojas JL, Gortázar C, Herskin M, Michel V, Miranda Chueca MÁ, Padalino B, Pasquali P, Roberts HC, Spoolder H, Ståhl K, Velarde A, Viltrop A, Winckler C, Baldinelli F, Broglia A, Kohnle L and Alvarez J, 2022. Scientific Opinion on the assessment of listing and categorisation of animal diseases within the framework of the Animal Health Law (Regulation (EU) No 2016/429): antimicrobial-resistant *Staphylococcus aureus* in cattle and horses. EFSA Journal 2022;20(5):7312, 103 pp. https://doi.org/10.2903/j.efsa.2022.7312

ISSN: 1831-4732

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

Table of contents

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 cattle and horses were published in separate EFSA scientific opinions (EFSA AHAW Panel, 2021a,b).

According to the results of the assessment already conducted, *Staphylococcus aureus* (*S. aureus*) was identified among the most relevant AMR bacteria in the EU for cattle and horses due to their frequent involvement in a variety of infections in both species (and especially mastitis in the case of cattle) and the high levels of phenotypic resistance to commonly used antimicrobials (particularly β-lactams) found in strains of animal origin.

This scientific opinion presents the results of the assessment on AMR *S. aureus* in cattle and horses on its eligibility to be listed and categorised within the AHL framework. Special focus is placed on the animal health impact of AMR *S. aureus* in cattle and 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, 2021c).

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, 2021c).

The present document reports the results of the assessment on AMR *S. aureus* in cattle and horses according to the criteria of the AHL articles as follows:

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

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

[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.

document. The outcome is the median of the probability ranges provided by the experts, which are accompanied by verbal interpretations only when they fall within the ranges 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 *Staphylococcus aureus* according to Article 7 criteria of the AHL

3.1.1. Article 7(a) Disease profile

This fact sheet summarises current knowledge on the presence, importance, control and prevention of AMR *S. aureus* in cattle and horses.

For cattle, the focus of the fact sheet is on resistance against antimicrobials used for dry cow therapy and treatment of mastitis (cefoperazone, oxacillin, neomycin, penicillin, penicillin–novobiocin, pirlimycin) and other infections such as of the respiratory and digestive system, metritis and skin/soft tissue infections (ceftiofur, enro-/ciprofloxacin, erythromycin, sulfa-TMP) (EFSA AHAW Panel, 2021a). For these antimicrobials, geographically varying levels of resistance have been described, predominantly in *S. aureus* isolates from the udder or milk and with highest levels in Asia and Africa (EFSA AHAW Panel, 2021a). The *mecA* gene, responsible for methicillin resistance in *S. aureus* (MRSA), is specifically mentioned. The presence of the *mecA* gene is considered as conferring resistance to all β-lactam antibiotics, even though heterogeneous and borderline resistance phenotypes exist (Chambers, 1997). Attention is also granted to MRSA carrying the *mecC* gene, a more recently described variant of the *mecA* gene (García-Álvarez et al., 2011). Beta-lactam resistance caused by non-*mec* genes (e.g. due to penicillinases) are mentioned where relevant.

For horses, the focus is on *S. aureus* associated with skin and soft tissue infections (SSTIs) and exhibiting resistance to fusidic acid, methicillin, sulfa-TMP, gentamicin, tetracyclines and enro-/ciprofloxacin (EFSA AHAW Panel, 2021b).

S. aureus are Gram-positive, non-motile, facultative anaerobic, typically coagulase-positive cocci that live as commensals on the skin, in the nose and on diverse mucous membranes of humans and animals (Kluytmans et al., 1997; Haag et al., 2019). They behave as opportunistic pathogens causing SSTIs and a range of other infections in virtually all hosts, animals and humans, with in the latter frequent lethal outcomes, especially due to MRSA in, e.g. bacteraemia, endocarditis and pneumonia (Lee et al., 2018). In animals, it is best known as a cause of mastitis in dairy cattle, being one of the major mastitis pathogens (Reyher et al., 2012; Rainard et al., 2018), of SSTI in various animal species, including horses (Devriese et al., 1985; Sieber et al., 2011), and of skin and skeletal disorders in poultry (Heidemann Olsen et al., 2018; Szafraniec et al., 2022).

Mastitis is an inflammation of the mammary gland, and in general, the vast majority of mastitis cases are due to an intramammary infection (IMI) caused by a microorganism. The latter starts with the penetration into the mammary gland and proliferation in milk, followed by the dissemination in the cisterns and throughout the duct system, triggering an inflammatory reaction with an influx of leucocytes, leading to elevated somatic cell counts (SCC). The host response may be varied but in *S. aureus* mastitis typically involves an initial clinical stage with visual clinical signs (swelling, firmness, warmth, tenderness of the udder, clotted milk, elevated body temperature, etc.) that may disappear in

a few days with the condition evolving into a subclinical stage, with sometimes more or less intense flare-up episodes (Rainard et al., 2018). In this context, a distinction will be made between infection with (AMR) *S. aureus*, leading to disease (inflammation) of the infected tissue, hence comprising both clinical and subclinical mastitis in dairy cows and clinical horse SSTI, and (healthy) presence of (AMR) *S. aureus*, with isolates originating from typical carriage sites such as the nose.

Literature on AMR *S. aureus* in animals, including cattle and horses, in the last two decades is dominated by MRSA. This is due to the emergence of livestock-associated (LA-)MRSA capable of causing human infections (Voss et al., 2005), hence considered a third type of MRSA relevant for human healthcare – along with hospital-associated (HA-)MRSA and community-associated (CA-)MRSA (van Alen et al., 2017; Lee et al., 2018).

The general construction of the sections below is that facts about 'LA-MRSA (of clonal complex 398)' in cattle and horses are described first, including other resistances of interest (RoI) for this fact sheet when available. Secondly, facts about (some) 'other MRSA' strains in cattle and horses (including other RoIs when available) are presented. Thirdly, 'non-MRSA' in cattle and horses exhibiting other RoIs are discussed. When *S. aureus* is mentioned in general, results are described not linked to particular resistant strains.

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

It is accepted that *S. aureus* shows host specificity; this was originally based on phenotypic traits and has since been confirmed with molecular data (Fitzgerald, 2012; Haag et al., 2019). Host adaptation might occur frequently and quickly, in various lineages and to several host species, including cattle and horses (Lowder et al., 2009; Spoor et al., 2013; Akkou et al., 2018; Grunert et al., 2018; Magro et al., 2018; Wang et al., 2018). Cattle is considered a major exchange host with humans (Haag et al., 2019). Yet, contamination and spill-over events from other hosts also occur commonly (Boss et al., 2016). From the multitude of recent studies offering typing results, the enormous diversity of *S. aureus* strains and complexity of *S. aureus* lineages become more and more apparent (Boss et al., 2016), but actual host adaptation is not always investigated.

Moreover, many studies do not conclude on the type of non-infection related presence (contamination, intermittent carriage or true colonisation) the isolation of (AMR) *S. aureus* in animals implies (Magro et al., 2018). Hence, isolation of *S. aureus* from an animal provides, as such, little evidence about the degree to which the animal species is affected by it (e.g. whether it can be considered a reservoir or a natural host species).

Furthermore, it is difficult to say whether all animals apparently 'susceptible' for non-AMR *S. aureus* (= where *S. aureus* has been isolated from) are also 'susceptible' to AMR *S. aureus* or vice versa, and if the isolation of AMR *S. aureus* pertains to a real reservoir or a temporary presence due to a spill-over event or a selection pressure (e.g. use of antimicrobials).

To deal with this complexity, the tables, lists or texts below, pertaining to the subsequent parameters, have been drafted as follows:

- 'Naturally susceptible' species (wildlife/domestic) include those species where natural (= not experimentally caused) presence of *S. aureus* – resistant or not – has been demonstrated. This can include isolates from infections or healthy presence.
- 'Experimentally susceptible' species (wildlife/domestic) include those species where the presence of *S. aureus* – resistant or not – has been experimentally induced. This can include isolates from infections or healthy presence.
- The sections on 'reservoir species' (wildlife/domestic) focus on (AMR) *S. aureus* lineages that have been suggested or shown to be adapted to a certain host species or might be suspected to have a reservoir in a certain species due to frequent detection in that species.
- A 'wildlife species' has been considered free-living or living in captivity but without being bred for the purpose of living alongside humans (held in zoos or parks, or as exotic pets); 'domestic species' as living in captivity and having been bred for the purpose of living alongside humans.

Susceptible animal species

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

S. aureus has been isolated from a huge variety of animal species, ranging from mammals (terrestrial and aquatic) to birds, reptiles, fish and insects. Table 2 lists those species from which *S. aureus* with one or more RoIs for this fact sheet have been isolated. If available in the referenced study, the Latin name is provided in the table; if not, the common name is given.

The mentioned resistances can pertain to different studies or different isolates in one study; no distinction is made between pheno- and genotypic resistance; MRSA might have been determined genotypically (*mecA*) or phenotypically (oxacillin and/or cefoxitin resistance); *mecC* is specifically mentioned.

The review of Heaton et al. (2020) provides the most extensive summary to date of the presence of (AMR) *S. aureus* in wildlife, including the species, molecular types and antibiotic resistances identified – if available. When a species (group) was included in any of the referenced studies, it was not systematically investigated whether there could be additional references for the same species or additional species from that group.

Table 2: List of wildlife species (groups) where *S. aureus* with RoIs for this fact sheet has been isolated

Species (group)	Antimicrobial resistance	Reference
Mammals		
Small mammals		
Hammer-headed bat (*Hypsignathus monstrosus*)	MRSA, TET	Loncaric et al. (2019)
Indian flying fox (*Pteropus giganteus*)	*mecC*	Heaton et al. (2020)
Straw-coloured fruit bat (*Eidolon helvum*)	CIP, CLI, ERY, FUS, PEN, TET	Heaton et al. (2020)
Black-flanked rock wallaby (*Petrogale lateralis*)	PEN	Heaton et al. (2020)
Common vole (*Microtus arvalis*)	PEN	Heaton et al. (2020)
European brown hare (*Lepus europaeus*)	BLA, *mecC*, MRSA	Heaton et al. (2020)
European hedgehog (*Erinaceus europaeus*)	CLI, ERY, FUS, GEN, *mecC*, MRSA, PEN, TET	Heaton et al. (2020)
European otter (*Lutra lutra*)	BLA, *mecC*, MRSA	Heaton et al. (2020)
European pine marten (*Martes martes*)	CLI, ERY, MRSA, TET	Heaton et al. (2020)
Mara (*Dolichotis patagonum*)	*mecC*	Heaton et al. (2020)
Naked mole rat (*Heterocephalus glaber*)	PEN, TET	Heaton et al. (2020)
Norway/Brown rat (*Rattus norvegicus*)	MRSA, PEN, TET	Heaton et al. (2020)
Eastern cottontail rabbit (*Sylvilagus floridanus*)	ERY, MRSA, TET	Heaton et al. (2020)
European rabbit (*Oryctolagus cuniculus*)	*mecC*, PEN	Heaton et al. (2020)
Red fox (*Vulpes vulpes*)	MRSA	Heaton et al. (2020)
Red squirrel (*Sciurus vulgaris*)	PEN, FQ	Heaton et al. (2020)
Rodents and shrews (various)	MRSA	Heaton et al. (2020)
Wood mouse (*Apodemus sylvaticus*)	*mecC*, MRSA, PEN	Heaton et al. (2020)
Large mammals		
African elephant (*Loxodonta africana*)	MRSA	Heaton et al. (2020)
Alpine chamois (*Rupicapra rupicapra*)	CIP, FQ, MRSA, PEN	Heaton et al. (2020)
Fallow deer (*Dama dama*)	*mecC*, MRSA, PEN	Heaton et al. (2020)
Red deer (*Cervus elaphus*)	*mecC*, MRSA, PEN, TET, T/S	Heaton et al. (2020)
Eurasian lynx (*Lynx lynx*)	BLA, FQ	Heaton et al. (2020)
Iberian ibex (*Capra pyrenaica*)	MRSA, PEN, TET, T/S	Heaton et al. (2020)
Wild boar (*Sus scrofa*)	CLI, CIP, ERY, GEN, LIN, *mecC*, MRSA, PEN, TET, T/S	Heaton et al. (2020)
Non-human primates/monkeys		
Chimpanzee (*Pan troglodytes*)	CLI, ERY, MRSA, PEN, TET, T/S	Heaton et al. (2020)
Gorilla (*Gorilla gorilla gorilla*)	PEN	Heaton et al. (2020)
Rhesus macaque (*Macaca mulatta*)	CIP, CLI, ERY, GEN, MRSA, PEN, TET, T/S	Heaton et al. (2020)
Singaporean long-tailed macaque (*Macaca fascicularis*)	CIP, ERY, GEN, KAN, MRSA, PEN, TET	Heaton et al. (2020)
Southern pig-tailed macaque (*Macaca nemestrina*)	CIP, ERY, GEN, MRSA, PEN, TET	Heaton et al. (2020)

Species (group)	Antimicrobial resistance	Reference
Red-fronted lemur (*Eulemur rufifrons*)	PEN	Heaton et al. (2020)
Verraux's sifaka (*Propithecus verreauxi*)	PEN	Heaton et al. (2020)
Marine mammals		
Common seal (*Phoca vitulina*)	*mecC*	Paterson et al. (2012)
Risso's dolphin (*Grampus griseus*)	MRSA, PEN	Mazzariol et al. (2018)
Bottlenose dolphin (*Tursiops truncatus*)	MRSA, PEN	Mazzariol et al. (2018)
Short-finned pilot whale (*Globicephala macrorhynchus*)	MRSA	Hower et al. (2013)
Walrus (*Odobenus rosmarus*)	MRSA	Heaton et al. (2020)
Birds		
Common buzzard (*Buteo buteo*)	PEN, TET	Heaton et al. (2020)
Common chaffinch (*Fringilla coelebs*)	*mecC*	Paterson et al. (2012)
Canada goose (*Branta canadensis*)	CLI, ERY, MRSA, PEN	Heaton et al. (2020)
Lesser yellowlegs (*Tringa flavipes*)	CLI, ERY, MRSA	Heaton et al. (2020)
Magpie (*Pica pica*)	MRSA, PEN	Heaton et al. (2020)
Northern bald ibis (*Geronticus eremita*)	CIP, MRSA, PEN, TET	Loncaric et al. (2019)
African grey parrot (*Psittacus erithacus*)	FQ, MRSA	Rankin et al. (2005)
Peregrine (*Falco peregrinus*)	CIP	Vidal et al. (2017)
Rook (*Corvus frugilegus*)	MRSA	Heaton et al. (2020)
Rock pigeon (*Columba livia*)	TET	Heaton et al. (2020)
Screech owl (*Megascops* spp.)	TET	Heaton et al. (2020)
Cinereous vulture (*Aegypius monachus*)	CLI, ERY, MRSA, PEN, TET	Heaton et al. (2020)
Eurasian griffon vulture (*Gyps fulvus*)	MRSA, TET	Heaton et al. (2020)
White-face whistling duck (*Dendrocygna viduata*)	TET	Heaton et al. (2020)
White stork (*Ciconia ciconia*)	ERY, FUS, *mecC*, MRSA, PEN, TET	Heaton et al. (2020)
Reptiles		
Turtle	MRSA	Walther et al. (2008)
Fish		
Tilapia (*Oreochromis niloticus*)	MRSA	Heaton et al. (2020)
Insects		
House flies (*Musca domestica*) and stable flies (*Stomoxys calcitrans*)	MRSA	Stelder et al. (2021)

BLA: β-lactams; CIP: ciprofloxacin; CLI: clindamycin; ERY: erythromycin; FQ: fluoroquinolones; FUS: fusidic acid; GEN: gentamicin; KAN: kanamycin; LIN: lincomycin; MRSA: methicillin-resistant *S. aureus* with the *mecA* gene or phenotypic resistance (oxacillin and/or cefoxitin); PEN: penicillin; TET: tetracycline; T/S: trim-sulfa antimicrobials.

In addition, the lists below include animal species (groups) from which *S. aureus* has also been isolated but where either resistances not of interest were found, either no resistances at all were found or resistance data were not determined or unclear from the respective studies. It is hence unclear whether these species are susceptible for AMR *S. aureus* with RoIs, but they were considered potentially relevant. It must be noted that some of the studies referenced in Heaton et al. (2020) did not determine antimicrobial resistance in species where RoIs had been described in other studies (e.g. in one study penicillin resistance in common vole (*Microtus arvalis*) was identified, but in another study antimicrobial resistance was not determined in the same species). In those cases, the species is included in Table 2 but is excluded from the lists below. If available in the referenced study, the Latin name is provided; if not, the common name is given.

Mammals:

- Banded mongoose (*Mungos mungo*) (Heaton et al., 2020);
- Bats (Nathusius pipistrelle (*Pipistrellus nathusii*), Egyptian fruit bat (*Rousettus aegyptiacus*), Peters's dwarf epauletted fruit bat (*Micropteropus pusillus*)) (Heaton et al., 2020);

- Black bear (*Ursus americanus*) (McBurney et al., 2000);
- Black rhinoceros (*Diceros bicornis*) (Clausen and Ashford, 1980);
- Capybara (*Hydrochoerus hydrochaeris*) (Heaton et al., 2020);
- Chinchilla (*Chinchilla* sp.) (Walther et al., 2008);
- Colobuses (King colobus (*Colobus polykomos*), Western red colobus (*Piliocolobus badius*)) (Heaton et al., 2020);
- Deer (Roe deer (*Capreolus capreolus*), Silka deer (*Cervus nippon*)) (Heaton et al., 2020);
- Dromedary camel (*Camelus dromedaries*) (Heaton et al., 2020);
- European badger (*Meles meles*) (Heaton et al., 2020);
- European beaver (*Castor fiber*) (Heaton et al., 2020);
- European marmot (*Marmota marmota*) (Heaton et al., 2020);
- Fox squirrel (*Sciurus niger*) (Heaton et al., 2020);
- Gabon talapoin (*Miopithecus ogouensis*) (Heaton et al., 2020);
- Grey-cheeked mangabey (*Lophocebus albigena*) (Heaton et al., 2020);
- Harbour porpoise (*Phocoena phocoena*) (Heaton et al., 2020);
- Killer whale (*Orcinus orca*) (Power and Murphy, 2002);
- Lion (*Panthera leo*) (Heaton et al., 2020);
- Macaques (Japanese macaque (*Macaca fuscata*), Barbary macaque (*Macaca sylvanus*)) (Heaton et al., 2020);
- Malayan tapir (*Tapirus indicus*) (Heaton et al., 2020);
- Mandrill (*Mandrillus* sp.) (Heaton et al., 2020);
- Mice (Yellow-necked mouse (*Apodemus flavicollis*), House mouse (*Mus musculus*) (Heaton et al., 2020);
- Mongolian sheep (*Ovis ammon f. aries*) (Heaton et al., 2020);
- Monkeys (Greater spot-nose monkey (*Cercopithecus nictitans*), Red-tailed monkey (*Cercopithecus ascanius*)) (Heaton et al., 2020);
- Moose (*Alces alces*) (Heaton et al., 2020);
- Mouflons (European mouflon, Mouflon (*Ovis orientalis*)) (Heaton et al., 2020);
- Moustached guenon (*Cercopithecus cephus*) (Heaton et al., 2020);
- Northern white-breasted hedgehog (*Erinaceus roumanicus*) (Heaton et al., 2020);
- Pygmy goat (*Capra hircus*) (Heaton et al., 2020);
- Raccoon (*Procyon lotor*) (Plommet and Wilson, 1969);
- Reindeer (*Rangifer tarandus*) (Heaton et al., 2020);
- Voles (Bank vole (*Myodes glareolus*), Field vole (*Microtus agrestis*)) (Heaton et al., 2020);
- White-eared opossum (*Didelphis albiventris*) (Siqueira et al., 2010);
- Wild cats (European wildcat (*Felis silvestris*), African wildcat (*Felis lybica*)) (Heaton et al., 2020);
- Yellow-footed rock wallaby (*Petrogale xanthopus*) (Heaton et al., 2020).

Birds:

- Bustards (Heaton et al., 2020);
- Eagles (Golden eagle (*Aquila chrysaetos*), White-tailed eagle (*Haliaeetus albicilla*)) (Heaton et al., 2020);
- Great blue heron (*Ardea herodias*) (Heaton et al., 2020);
- Great tit (*Parus major*) (Heaton et al., 2020);
- Green woodpecker (*Picus viridis*) (Heaton et al., 2020);
- Grey partridge (*Perdix perdix*) (Heaton et al., 2020);
- Herring gull (*Larus argentatus*) (Monecke et al., 2016);
- Japanese quail (*Coturnix coturnix japonica*) (Monecke et al., 2016);
- Red kite (*Milvus milvus*) (Heaton et al., 2020);
- Swans (Black swan (*Cygnus atratus*), Mute swan (*Cygnus olor*)) (Heaton et al., 2020);
- Owls (Great horned owl (*Bubo virginianus*), Tawny owl (*Strix aluco*)) (Heaton et al., 2020);
- Teals (Baikal teal (*Sibirionetta formosa*), Blue-winged teal (*Spatula discors*)) (Heaton et al., 2020).

Reptiles:

- Komodo dragon (*Varanus komodoensis*) (Montgomery et al., 2002).

From these numerous susceptible animal species, an enormous diversity of molecular types of (AMR) *S. aureus* has been identified, some less common or unique and other associated with humans and animals, with some having a likely reservoir in certain wildlife species (see Parameter 5 in this section).

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

S. aureus of various AMR types, including most RoIs for this fact sheet, has been isolated from virtually all major and some less common domestic animal species. It is not feasible to list all references per species or per resistance. A recent review by Schwarz et al. (2018) provides an overview of antimicrobial resistance (genes) in staphylococci of animal origin, including *S. aureus*. A selection of other studies providing pheno- or genotypical resistance data allowed to establish Table 3, with susceptible domestic animal species for *S. aureus* and its RoIs; note that when animal species are in the table that could be considered wildlife as well (e.g. guinea pigs and rabbits), the referenced studies do pertain to domesticated animals of the species.

Table 3: List of domestic species where *S. aureus* with RoIs for this fact sheet has been isolated

Species	Antimicrobial resistance	Reference
Mammals		
Companion animals		
Cat	FQ, GEN, LS, *mecC*, ML, MRSA, NEO, PEN, TET, T/S	Schwarz et al. (2018), Loncaric et al. (2019), Chueahiran et al. (2021)
Dog	FUS, FQ, GEN, LS, *mecC*, ML, MRSA, NEO, PEN, TET, T/S	Schwarz et al. (2018), Frosini et al. (2019), Loncaric et al. (2019), Chueahiran et al. (2021)
Horse	FQ, GEN, LS, *mecC*, ML, MRSA, NEO, PEN, TET, T/S	Haenni et al. (2015), Schwarz et al. (2018), Loncaric et al. (2019), Sekizuka et al. (2020)
Rabbit	GEN, LS, *mecC*, ML, MRSA, NEO, PEN, TET, T/S	Vancraeynest et al. (2004), Schwarz et al. (2018), Loncaric et al. (2019)
Livestock and farmed animals		
Cow	FUS, GEN, LS, *mecC*, ML, MRSA, NEO, PEN, TET, T/S	Khemiri et al. (2018), Schwarz et al. (2018)
Goat	FUS, FQ, GEN, LS, *mecC*, ML, MRSA, NEO, PEN, TET, T/S	Schwarz et al. (2018), Lima et al. (2020), Quraishi et al. (2021)
Guinea pig	FQ, LS, *mecC*, ML, MRSA, TET, T/S	Schwarz et al. (2018), Zambrano-Mila et al. (2020)
Mink	FQ, GEN, LS, ML, MRSA, NEO, PEN, TET, T/S	Hansen et al. (2017, 2020), Nikolaisen et al. (2017)
Pig	FQ, GEN, LS, *mecC*, ML, MRSA, NEO, PEN, TET, T/S	Feltrin et al. (2016), Schwarz et al. (2018)
Sheep	FUS, LS, *mecC*, ML, MRSA, PEN, TET, T/S	Carfora et al. (2016a), Schwarz et al. (2018)
Birds		
Chicken	FQ, GEN, LS, ML, MRSA, NEO, PEN, TET, T/S	El-Adawy et al. (2016), Schwarz et al. (2018)
Canary	FQ, GEN, MRSA, PEN, TET	Loncaric et al. (2019)
Pigeon	GEN, LS, ML, MRSA, TET	Chobrak-Chmiel et al. (2021)
Turkey	FQ, GEN, LS, ML, MRSA, NEO, PEN, TET, T/S	El-Adawy et al. (2016), Schwarz et al. (2018)

FQ: fluoroquinolones; FUS: fusidic acid; GEN: gentamicin; LS: lincosamides; ML: macrolides; MRSA: methicillin-resistant *S. aureus* with the *mecA* gene or phenotypic resistance; NEO: neomycin; PEN: penicillin; TET: tetracycline; T/S: trim-sulfa antimicrobials.

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

No literature was found on the experimental infection of wildlife with (AMR) *S. aureus*.

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

Many studies have experimentally applied (AMR) *S. aureus* or MRSA (of human origin) in common laboratory animals, typically to study its pathology or test new strategies for battling its infections:

mice (Kim et al., 2014; Marra, 2020), guinea pigs (Baldoni et al., 2009; Tatar et al., 2017), rabbits (Castañeda et al., 2021; Long et al., 2021) and rats (Marra, 2020; Valente et al., 2021). Even *Drosophila melanogaster* models have repeatedly been deployed (Wu et al., 2012; Thomsen et al., 2016).

S. aureus osteomyelitis appears to be of particular interest; a review from Reizner et al. (2014) shows that various animal species have been used to develop models exploring this disease: mostly rabbits and rats, but also mice, sheep, dogs, goats, pigs, guinea pigs and hamsters, leading to a list of 93 references, the earliest one from 1973.

Mice have also been used as a model for bovine *S. aureus* mastitis (Brouillette and Malouin, 2005). In general, *S. aureus* mastitis is a frequent subject of experimental studies, in small and large ruminants (Le Maréchal et al., 2009; Kerro-Dego et al., 2012, 2020; Capoferri et al., 2021) and rabbits (Penadés et al., 2020).

The spread of livestock-associated MRSA CC398 has been investigated in several experimental studies in pigs (Broens et al., 2012; Crombé et al., 2013; Rosen et al., 2018; Sørensen et al., 2018) and mink (Fertner et al., 2019).

Reservoir animal species

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

Compared to livestock or domestic animals, true host adaptation of *S. aureus* to wildlife species has been sparsely studied. Clues to the reservoir potential of wildlife species for certain lineages of *S. aureus*, including AMR isolates, therefore generally come from frequent detection of these lineages in wildlife or, in contrast, from detection of new, not previously reported lineages (van Elk et al., 2012; Monecke et al., 2016). Remarkably, several of the main cattle lineages are also widely found in wildlife and might in fact be animal-adapted rather than cattle- or livestock-adapted.

In addition to its major reservoir in livestock (see below), CC398 has repeatedly been detected in wildlife, including in mammals (deer, hares, ibexes, rats, wild boar) and birds (geese, storks, vultures) (Heaton et al., 2020). This is mostly but not always MRSA, containing various additional RoIs. While MRSA CC398 appears to be particularly adapted to pigs (Fitzgerald, 2012; Aires-de-Souza et al., 2017), it is less frequently found in wild boar (Monecke et al., 2016; Silva et al., 2020; Plaza-Rodríguez et al., 2021). It is unclear whether CC398 has a true reservoir in any wildlife species but due to its proven low host specificity, making it prone to colonise various host species, it has been suggested that CC398 was originally a human methicillin-susceptible *S. aureus* (MSSA) that has adapted to livestock, acquiring methicillin and several other resistances (Price et al., 2012), and is now spreading to wildlife (Silva et al., 2020).

An especially interesting MRSA lineage is CC130, not only because it is one of the most common found MRSA lineages among wildlife but it also typically carries the *mecC* gene, instead of the common *mecA* gene conferring methicillin resistance (Monecke et al., 2016; Silva et al., 2020), and it is furthermore considered a cattle-adapted lineage (Fitzgerald, 2012; Aires-de-Souza et al., 2017; see also Parameter 6 in this section). CC130 has been described in birds (stork, magpies, vultures, teals) and large mammals (deer, wild boar, ibexes); however, it appears to be of particular importance in small mammals, having been found in otters and foxes, yet finding its likely main wildlife reservoir in rodents (rats, wild mice, maras), lagomorphs (hares, rabbits) and hedgehogs (Monecke et al., 2016; Heaton et al., 2020; Silva et al., 2020; Dube et al., 2021). Interestingly, the lineage seems limited to (Western) Europe (Monecke et al., 2016).

In addition, the CC425 lineage appears to be shared among wildlife and cattle. It has been described as a cattle lineage (Fitzgerald, 2012) and in wildlife ST425 strains have been found in deer, wild boar, foxes, badgers, ibexes, rabbits and vultures (Heaton et al., 2020), typically as MSSA, with occasional RoIs (against penicillin, erythromycin, lincosamides, co-trimoxazole/trimethoprim and tetracycline). *mecC*-MRSA ST425 isolates have been reported in wild boar and fallow deer (Heaton et al., 2020).

It has been suggested that *mecC*-MRSA is a general wildlife rather than livestock-associated MRSA, with a main reservoir in European hedgehogs (Becker et al., 2014; Monecke et al., 2016; Dube et al., 2021). Recently, it has even been suggested that *mecC*-methicillin resistance in *S. aureus* has evolved in hedgehogs in the pre-antibiotic era, possibly as a co-evolutionary adaptation of *S. aureus* to colonisation of dermatophyte-infected hedgehogs (Larsen et al., 2022).

A potential wildlife reservoir of *S. aureus* CC133 is noteworthy. CC133 is considered a ruminant- (Fitzgerald, 2012) or even ungulate-associated lineage (Smyth et al., 2009). In wildlife, it typically appears as MSSA with occasional RoIs (penicillin, erythromycin, tetracycline, co-trimoxazole/

trimethoprim) and has been found in various mammals (maras, capybaras, wild boar, deer, mouflon, tapirs, wild goats and lions) and birds (vultures, stork, teals, ducks). In Tunisia, CC133 appeared to be the predominant lineage in donkeys; the isolates were all identified as MSSA with various RoIs, including against fusidic acid (Gharsa et al., 2012).

Several other *S. aureus* lineages might have a wildlife reservoir: most relevant are CC97, of which isolates phenotypically related to cattle isolates have been found in roe deer and wild Norway rats; ST8, considered as typically human but having adapted to horses and repeatedly isolated from wildlife such as chimpanzee (captive), European pine marten, Norway rats, red fox, semi-captive short-finned pilot whales and Canada goose; and ST5, also considered typically human but having adapted to poultry and apparently spreading in wild fowl (Hower et al., 2013; Monecke et al., 2016; Nowakiewicz et al., 2016; Heaton et al., 2020).

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

In 2012, Fitzgerald published an overview of livestock-associated *S. aureus* sequence types and their host species (including humans). This is reproduced in Table 4.

Table 4: *S. aureus* genetic lineages and reservoir domestic animal species

ST	Host species
ST1	Human, cow, horse, chicken
CC5	Human, chicken, turkey
ST8	Human, horse, cow
ST9	Pig, chicken
CC97	Cow, human
ST121	Human, rabbit
CC126	Cow
CC130	Cow, sheep
CC133	Sheep, goat, cow
CC385	Chicken, wild birds
ST398	Pig, human, cow, chicken, horse
ST425	Cow
CC705, including ST151	Cow
ST1464	Sheep

CC: clonal complex; ST: sequence type.

Since then, multiple publications have largely confirmed these findings, and it still represents the major *S. aureus* lineage–host relations known of in domestic animals (Smith, 2015; Feltrin et al., 2016; Wang et al., 2018; Leijon et al., 2021). Note that little added value is to be expected from including information on antimicrobial resistance to this list, since it is focussing on host specificity and antimicrobial resistance as such is not associated with host specificity, the latter being rather determined by genetic adaptations in terms of host–bacteria interaction (Haag et al., 2019). Antimicrobial resistance in host-specific lineages is to be considered the result of a selection pressure, suggesting that all possible resistances might at some point be found in isolates of that lineage in that host species under the 'right' circumstances (Haag et al., 2019), and the host at that moment functioning as a reservoir. Indeed, in most of the lineages in the list, various resistance profiles have been described and virtually all have been found as MRSA as well as MSSA in the suggested host species (see the references provided below).

A notable exception might be CC398, which is the predominant MRSA in domestic animals, with several additional RoIs. Carriage rates are particularly high in pigs and veal calves generally without causing infections (Vandendriessche et al., 2013; Tenhagen et al., 2014; Haag et al., 2019). A subclone ('the equine clinic clade'), epidemiologically associated with infections in horses and typically gentamicin-resistant, has been described (Abdelbary et al., 2014; Cuny and Witte, 2017; Islam et al., 2017). It has been suggested that MRSA CC398 is replacing the CC8 lineage in horses (Cuny and Witte, 2017). AlUNMRSA CC398 might be emerging (Aires-de-Sousa et al., 2017).

MRSA CC8 itself is assumed to have originated from humans and adapted to horses quite recently (Cuny and Witte, 2017). There might also be a cattle-adapted CC8 lineage (Boss et al., 2016).

As noted, CC130 is considered an archetypical ruminant lineage, sharing a common ancestor with CC705, a lineage typical for cattle (Boss et al., 2016; Grunert et al., 2018). Yet, it might need to be considered general animal-associated rather than livestock- (or bovine-) associated. CC130 is one of the most typical MRSA lineages harbouring *mecC*, also in domestic animals (Paterson et al., 2014a).

CC97 is one of the most common bovine lineages, and is found sometimes as MRSA (Luini et al., 2015; Feltrin et al., 2016; Locatelli et al., 2017) but might be mostly MSSA (Akkou et al., 2018; Wang et al., 2018). MRSA-CC97 appears also to be of importance in pigs in certain countries (Feltrin et al., 2016).

Some additional lineages might be emerging in specific hosts: CC22-MRSA in cattle (Akkou et al., 2018; Magro et al., 2018) and possibly also horses (Cuny and Witte, 2017), and ST612-MRSA in horses (Murphy et al., 2019). CC9 is a genotype predominant among MRSA from pigs in Asia (Haag et al., 2019) but has recently been found as an MSSA subtype with a high within-herd prevalence, persisting for years in dairy herds with notable resistances to pirlimycin, erythromycin and marbofloxacin (Grunert et al., 2018).

Finally, ST1 and ST5 are also frequently detected in animals, including dairy cattle where they are mostly suggested to have originated from human contacts (Schnitt and Tenhagen, 2020). Notably, a poultry ST5 clade has been described to have evolved from a human-to-poultry jump several decades ago (Lowder et al., 2009).

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

Morbidity

Parameter 1 – Prevalence/incidence

For this parameter, non-infection related presence (referred to in the table as 'carriage') is differentiated from presence in subclinical or clinical infections ('disease'); for the latter for cows, a distinction is made between presence in 'milk/subclinical mastitis/clinical mastitis' (which are in practice milk samples originating from the udder or from the bulk tank) and 'other infections'.

Results on 'carriage' and '(other) infections' in cattle and horses are presented at animal level (% cows/horses with AMR *S. aureus* among all cows/horses sampled) or farm/clinic level (% farms/clinics with AMR *S. aureus* among all farms/clinics sampled). Results on 'milk/subclinical mastitis/clinical mastitis' can additionally be presented at quarter level (% quarter milk samples with AMR *S. aureus* in all quarter milk samples taken). Almost all results are prevalence data; incidence data of AMR *S. aureus* were found only in horses (incidence rates, IR). Prevalence data mostly are point prevalence data; this is important as e.g. Graveland et al. (2012) illustrated that MRSA (CC398) prevalence in white veal calves (nasal and rectal carriage) on three farms ranged from 9% to 14% directly after arrival on the farm to 63–96% at the end of the study period (± 126 days later), with even 100% carriers in between in one farm.

Table 5: Prevalence/incidence of AMR *S. aureus* with RoIs for this fact sheet in cattle, ranked per country and year of the publication

Prevalence/ incidence	Type	Geographical area	Time period	RoI[(a)]	Population remarks	Reference
Carriage (nose/skin/udder)						
AL: 64%/FL: 90%	NA	Belgium	August 2009–May 2011	MRSA	200 veal calves from 20 herds	Vandendriessche et al. (2013)
AL: 5%/FL: 30%	NA	Belgium	August 2009–May 2011	MRSA	100 beef cows from 10 herds	Vandendriessche et al. (2013)
AL: 1%/FL: 10%	NA	Belgium	August 2009–May 2011	MRSA	100 dairy cows from 10 herds	Vandendriessche et al. (2013)
FL: 9.9%	NA	Belgium	2012	MRSA	141 dairy farms	Nemeghaire et al. (2014)
FL: 10.2%	NA	Belgium	2012	MRSA	187 beef farms	Nemeghaire et al. (2014)
FL: 46.1%	NA	Belgium	2012	MRSA CC398	104 veal calf farms	Nemeghaire et al. (2014)

Prevalence/ incidence	Type	Geographical area	Time period	RoI[(a)]	Population remarks	Reference
AL: 35.1% (2009)/ 45.0% (2012)	NA	Germany	2009–2012	MRSA	350/320 veal calves at slaughter	Tenhagen et al. (2014)
AL: 8.7%	NA	Germany	2009–2012	MRSA	288 beef cows at slaughter	Tenhagen et al. (2014)
AL: 22.7%	NA	Germany	November 2018–December 2020	MRSA CC398	20 herds previously MRSA-positive, 201 milk-fed calves	Schnitt et al. (2020)
AL: 9.1%	NA	Germany	November 2018–December 2020	MRSA CC398	20 herds previously MRSA-positive, 187 post-weaning calves	Schnitt et al. (2020)
AL: 8.9%	NA	Germany	November 2018–December 2020	MRSA CC398	20 herds previously MRSA-positive, 191 pre-fresh heifers' nose	Schnitt et al. (2020)
AL: 6.5%	NA	Germany	November 2018–December 2020	MRSA CC398	20 herds previously MRSA-positive, 170 pre-fresh heifers' udder	Schnitt et al. (2020)
AL: 3.9%	NA	Netherlands		MRSA CC398	411 cows at slaughterhouse	van Duijkeren et al. (2014)
Milk/subclinical mastitis/clinical mastitis						
AL: 0–7.4%	SCM	Belgium	February–April 2008	MRSA CC398, AG, LS, ML, TMP	All lactating cows in 5 herds	Vanderhaeghen et al. (2010a)
IRCM: 0.5	CM	Belgium (Flanders)	2012–2013	*S. aureus*	42 randomly selected dairy herds	Verbeke et al. (2014)
FL: 2.2%	BTM	England and Wales	November 2011–October 2012	*mecC* MRSA	BTM samples, 465 farms	Paterson et al. (2014b)
FL: 4.4%	BTM	Germany	2009–2010	MRSA CC398	28/635 farms, part of national monitoring	Kreausukon et al. (2012)
AL: 28.6%	SCM	Germany (Bavaria)	Not specified	*mecC* MRSA	16/56 lactating cows, single farm	Schlotter et al. (2014)
AL: 1.4%–16.7%	SCM	Germany	June 2008–April 2009	MRSA CC398	3 farms, sampled twice, 40–162 animals	Spohr et al. (2011)
FL: 10% (2010)	BTM	Germany	2009–2010	MRSA	30 BTM samples from certified dairy farms, allowed to sell raw milk to consumers but required to take additional hygienic measures	Tenhagen et al. (2014)

Prevalence/ incidence	Type	Geographical area	Time period	RoI[(a)]	Population remarks	Reference
FL: 4.1% (2009)/ 4.7% (2010)	BTM	Germany	2009–2010	MRSA	338/297 BTM samples from conventional dairy farms	Tenhagen et al. (2014)
QL: 2.9%	SCM	Germany	November 2018–December 2020	MRSA CC398	20 herds previously MRSA-positive, 2,347 QMS from 597 cows	Schnitt et al. (2020)
AL: 7.9%	SCM	Germany	November 2018–December 2020	MRSA CC398	20 herds previously MRSA-positive, 2,347 QMS from 597 cows	Schnitt et al. (2020)
FL: 8.3%–10%	BTM	Greece (North)	2016–2017	MRSA, ERY, TRIM	1/12 and 1/10 dairy farms	Papadopoulos et al. (2018, 2019)
FL: 7%	BTM	Italy (North)	March 2010	MRSA	27 dairy farms	Locatelli et al. (2016)
FL: 3.8%	BTM	Italy (North)	July 2012–October 2013	MRSA	32/844 farms out of total of 7,008 dairy farms in Lombardy	Cortimiglia et al. (2016)
AL: 4.8%–60%						
QL: 2.1%–28.2%	SCM	Italy (North)	April–July 2010	MRSA, ENR, ERY, CLI, GEN	(Part of) lactating cows on 2 farms, close pig contact	Locatelli et al. (2017)
AL: 16.7%	SCM	Italy (Lombardy)	Not specified	MRSA, FQ, KAN	4/24 lactating cows in single farm	Magro et al. (2018)

AG: aminoglycosides; AL: animal level; BTM: bulk tank milk; CC: clonal complex; CLI: clindamycin; CM: clinical mastitis; ENR: enrofloxacin; ERY: erythromycin; FL: farm level; FQ: fluoroquinolones; GEN: gentamicin; IRCM: incidence rate of clinical mastitis; KAN: kanamycin; LS: lincosamides; ML: macrolides; MRSA: methicillin-resistant *S. aureus*; NA: not applicable; NOR: norfloxacin; QL: quarter level; SCM: subclinical mastitis; TMP: trimethoprim.
(a): When no MRSA ST/CC is indicated, another type than CC398 was detected (along with CC398).

Table 6: Prevalence/incidence of AMR *S. aureus* with RoIs for this fact sheet in horses, ranked per country and year of the publication

Prevalence/ incidence	Geographical area	Time period	RoI[(a)]	Population remarks	Reference
Carriage (nose/skin)					
AL: 10.9%	Belgium, France, Luxembourg, Netherlands	March–July 2007	MRSA CC398, TET, GEN	110 horses upon submission, Veterinary Teaching Hospital	van den Eede et al. (2009)
AL: 0.5%	Belgium (East/ West Flanders)	January–March 2008	MRSA CC398, TET	Convenience sample, 189 horses from 10 farms (15–21 animals per farm)	van den Eede et al. (2012)

Prevalence/ incidence	Geographical area	Time period	RoI[(a)]	Population remarks	Reference
AL: 2.7%	Canada	October 2002 – June 2004	MRSA	2,283 horses upon submission, Veterinary Teaching Hospital	Weese et al. (2006)
Nosocomial IR: 23/1,000 admissions	Canada	October 2002 – June 2004	MRSA	Horses during hospitalisation, Veterinary Teaching Hospital	Weese et al. (2006)
AL: 4.2%/FL: 9.5%	Denmark (Funen and Zealand)	April–August 2015	MRSA, GEN	17/401 horses from 7/74 farms	Islam et al. (2017)
AL: 0.9%/FL: 8.7%	Germany (Northwest)	May 2015–March 2016	MRSA, GEN, TET, T/S	223 horses from 23 farms	Kaspar et al. (2019)
AL: 50%	Israel	September 2012	MRSA, CIP, GEN	14 hospitalised horses, single hospital, Veterinary Teaching Hospital	Steinman et al. (2015)
AL: 7.2%	Israel	November 2007–April 2009	MRSA ST5, CIP, GEN	83 hospitalised horses, single hospital, Veterinary Teaching Hospital	Tirosh-Levy et al. (2015)
AL: 54%	Pakistan	Not specified	MRSA, CIP	150 horses from a race club (100), a hospital (35) and a farm (15)	Waqar et al. (2019)
Infections					
Nosocomial IR: 1.8/1,000 admissions	Canada	October 2002–June 2004	MRSA	Horses during hospitalisation, Veterinary Teaching Hospital	Weese et al. (2006)
AL: 13.6%	Germany	October 2015–September 2016	MRSA, TET, GEN, FQ, T/S	44 horses with clinical signs of conjunctivitis/ blepharitis (n = 8), keratitis (n = 9) or uveitis (n = 29)	Soimala et al. (2018)
AL: 6.3%	UK	January 2011–May 2016	CC 398 MRSA	Surgical site infections, one equine clinic	Bortolami et al. (2017)

AL: animal level; CC: clonal complex; CIP: ciprofloxacin; FL: farm level; FQ: fluoroquinolones; GEN: gentamicin; IR: incidence rate; MRSA: methicillin-resistant *S. aureus*; TET: tetracycline; T/S: trim-sulfa antimicrobials.
(a): When no MRSA ST/CC is indicated, another type than CC398 was detected.

Noteworthy, a recent meta-analysis estimated the global, pooled point prevalence of MRSA in bovine subclinical/clinical mastitis as 4.3% (95% CI: 3.2–5.5), with the highest prevalence in Asia (6.5%, 95% CI: 4.3–9.0) and the lowest prevalence in Europe (1.2%, 95% CI: 0.2–2.8) as well as a significantly higher prevalence in clinical mastitis (5.9%, 95% CI: 3.1–9.4) compared with subclinical mastitis (2.85, 95% CI: 1.6–4.4), and in cases published between 2016 and 2020.

(5.3%, 95% CI: 3.6–7.3) compared with between 2012 and 2015 (3.8%, 95% CI: 1.8–6.5), and between 2005 and 2011 (1.8%, 95% CI: 0.6–4.9) (Zaatout and Hezil, 2021).

It should also be noted that several studies from various countries worldwide have reported a lack of MRSA colonisation in horses outside the hospital setting (Yasuda et al., 2002; Baptiste et al., 2005; Busscher et al., 2006; Vengust et al., 2006; Burton et al., 2008; Tirosh-Levy et al., 2015). Yet, Baptiste et al. (2005) suggested that MRSA should be present in the general horse population in the UK, based on the diversity of MRSA isolates found in hospitalised horses. Moreover, a point prevalence study of MRSA colonisation of horses on farms in Ontario, Canada and New York state, USA reported isolation of MRSA from 46/391 (12%) of horses from farms with a history of MRSA infection or colonisation, including one farm where 45% of horses were colonised (Weese et al., 2005b).

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

For this parameter, morbidity was understood as 'causing clinical signs' and cases as 'the number of animals where AMR *S. aureus* was present' (hence, including healthy carriage, non-clinically infected and clinically infected). Rates all pertain to animal level.

It appears such case morbidity data of AMR *S. aureus* pertaining to mastitis (hence: number of cows with clinical mastitis due to AMR *S. aureus* out of the total number of cows with *S. aureus* IMI and/or *S. aureus* carriage) are extremely rare. Several studies describe resistance profiles of only a selection of clinical mastitis *S. aureus* isolates, or provide inadequate denominator data to calculate the case morbidity rate, and/or lack data about resistance (e.g. Waage et al., 1999; Gröhn et al., 2004; Pitkälä et al., 2004; Bradley et al., 2007; Bengtsson et al., 2009; Verbeke et al., 2014; de Jong et al., 2018). No other data were found allowing assessment of case morbidity rates associated with mastitis or other bovine infections.

Table 7: Case morbidity rates of AMR *S. aureus* with RoIs for this fact sheet in infections of horses

Case morbidity rate	Geographical area	Time period	Resistances	Population remarks	Reference
8.3%	Belgium, France, Luxembourg, Netherlands	March–July 2007	MRSA CC398, TET, GEN	1/12 carriers with infected wound	van den Eede et al. (2009)
16%	Canada	October 2002–June 2004	MRSA	10/61 horses	Weese et al. (2006)

CC: clonal complex; GEN: gentamicin; MRSA: methicillin-resistant *S. aureus*; TET: tetracycline.

Mortality

Parameter 3 – Case fatality rate

Very little data are available to assess the case fatality rates associated with AMR *S. aureus* infections in cattle or horses. In dairy cows, culling is often applied in chronic *S. aureus* IMI (see Parameter 1 in Section 3.1.1.4) but that type of 'fatality' was not considered as applicable to include in Table 8 (besides, there are little quantitative data available on the rate of culling due to *S. aureus* in general and for AMR *S. aureus* in particular). Fatal *S. aureus* mastitis cases are known on an anecdotic basis (Rainard et al., 2018), which does not fit the purpose of assessing rates. No other data were found allowing assessment of case fatality rates associated with mastitis or other bovine infections.

To get some insight, it should be noted that *S. aureus* mastitis is commonly subclinical and when clinical cases occur, clinical signs are varying but generally mild (Rainard et al., 2018). However, (very) severe, peracute cases can occur, as gangrenous mastitis causing necrosis of the udder quarter and severe systemic signs, requiring euthanasia (Rüegsegger et al., 2014; Rainard et al., 2018; Åvall-Jääskeläinen et al., 2021). In Finland, among *S. aureus* isolates from very severe bovine mastitis cases (of which 11 died or were euthanised) during the years 2011–2018 in the Ambulatory Production Animal Clinic of the Faculty of Veterinary Medicine, University of Helsinki, 14 isolates associated with the most severe clinical signs were selected for a genomic analysis study comparing with isolates from less severe clinical and subclinical mastitis cases (Åvall-Jääskeläinen et al., 2021). None of the isolates harboured the *blaZ*, *mecA* or *mecC* genes responsible for β-lactam resistance, but the *norA* gene conferring quinolone resistance and the *tet*(38) gene encoding tetracycline resistance were found in all isolates.

With respect to culling, in a field evaluation of sanitation approaches for 19 Swiss farms selected as positive for a specific *S. aureus* genotype dubbed genotype B (GTB), Sartori et al. (2018) found culling rates (defined as total number of cows culled – because *S. aureus* GTB-positive – divided by the total number of cows tested *S. aureus* GTB-positive over all samplings, with cows sampled positive several times being counted only once) between 0% and 71%, with a median culling rate of 17%. Antimicrobial resistance data for the strains involved on the different farms were not provided, although an overall very high cure rate of 93% was found for the recommended treatment protocol, suggested to be the result of the use of aminoglycoside antimicrobials because aminoglycoside resistance was known to be low (Sartori et al., 2018). In a single Italian herd, of 4/24 animals with MRSA IMI, two of the animals were culled 7–8 weeks after first detection (Magro et al., 2018).

For the table below, 'case' was understood as the presence (hence, including healthy carriage, non-clinically infected and clinically infected) of AMR *S. aureus*.

Table 8: Case fatality rates of AMR *S. aureus* with RoIs for this fact sheet in horses

Case-fatality rate	Geographical area	Time period	Resistances	Population and infection remarks	Reference
1.3%	Canada	2000, 2002	MRSA	79 horses from hospital and farms; 1 dead horse due to severe osteomyelitis	Weese et al. (2005a)
1.5%	USA	2007–2017	MRSA	Convenience sample of 65 *S. aureus* isolates from horses, Texas A&M University Veterinary Medical Teaching Hospital; secondary infection at site of previous erythema multiforme and bronchopneumonia, synovitis, abscesses	Little et al. (2021)

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

Parameter 1 – Report of zoonotic human cases (anywhere)

In a recent systematic review and meta-analysis, human exposure to livestock was significantly associated with an increased risk of MRSA carriage (pooled odds ratio of 7.03), with a cattle-specific OR of 5.66 and a horse-specific OR of 2.28 (Liu et al., 2020). With increasing frequency of livestock exposure, risk of MRSA carriage increased (Liu et al., 2020). A similar study found a pooled OR for LA-MRSA carriage among livestock workers and veterinarians of 9.80, with an OR of 11.62 for cattle workers and of 7.45 for horse workers specifically (Chen and Wu, 2021). In addition, slaughterhouse workers are at increased risk of carriage (Becker et al., 2017; Chen and Wu, 2021).

There are indeed numerous reports of (suspected) zoonotic cases of AMR *S. aureus* from cattle or horses. In some cases, similar strains of suspected animal origin were detected in humans and in cattle or horses that had (direct) contact (van Duijkeren et al., 2011; van den Eede et al., 2013; Vandendriessche et al., 2013; Krukowski et al., 2020). Other studies looked at population level, with assumed animal AMR *S. aureus* strains found in people, without investigating the (suspected) reservoir animals (Deiters et al., 2015; Alekish et al., 2020). It is unfeasible to give a comprehensive overview of all the existing reports here, but in several papers, zoonotic cases of AMR *S. aureus*, including cases originating from horses and cattle, are reviewed (Smith and Wardyn, 2015; Cuny et al., 2016; Cuny and Witte, 2017; Goerge et al., 2017; Haag et al., 2019; Dong et al., 2021).

The bulk of reports involve *S. aureus* CC398, predominantly MRSA. When present in horses, it is often found in human contacts and it poses a risk for veterinary personnel working in equine clinics (Cuny and Witte, 2017). Remarkably, although MRSA CC398 has in several studies been detected in cow (mastitis) milk (Schnitt and Tenhagen, 2020) and it is in general considered primarily an occupational health risk to farm workers and veterinarians, transfer of MRSA CC398 from dairy cows to humans is infrequently described (Goerge et al., 2017; Krukowski et al., 2020). Among cattle, veal calves seem to pose the greatest risk for transmission (Graveland et al., 2010; Vandendriessche et al., 2013), with even higher antimicrobial resistance levels in veal calf-related MRSA CC398 strains than in strains from pigs (Vandendriessche et al., 2013).

Zoonotic cases involving other AMR *S. aureus* lineages have also been reported (Spoor et al., 2013; Cuny and Witte, 2017; Wang et al., 2018; Tomao et al., 2020). However, with both animals and humans being natural hosts of various, sometimes overlapping lineages of *S. aureus*, the direction of transfer is not always obvious (Juhász-Kaszanyitzky et al., 2007; Murphy et al., 2019; Tomao et al., 2020). In addition, MRSA CC398 might actually be introduced in cattle or horses as a spillover event mostly from pigs, through the veterinarian (Krukowski et al., 2020) or owner (Locatelli et al., 2016, 2017).

Zoonotic cases of MRSA in humans, including from horses and cattle, mostly result in asymptomatic and possibly intermittent carriage (Cuny et al., 2016; Cuny and Witte, 2017; Goerge et al., 2017; Chen and Wu, 2021). Yet, there are several reports of infections with CC398 and other types of MRSA after suspected zoonotic transfer from cattle or horses, sometimes very serious and even fatal (Becker et al., 2017; Goerge et al., 2017). A dairy cattle farmer was identified with necrotising fasciitis

(Soavi et al., 2010). Cases of wound and urinary tract infection by MRSA CC398 from horses were described in the Netherlands (van Duijkeren et al., 2011; Overbeek et al., 2017). In livestock-dense regions, CC398 take in a high proportion of MRSA in screening samples upon hospital admission or in infections (Cuny and Witte, 2017; van Alen et al., 2017). A CC130 *mecC*-MRSA strain with suspected cow origin was found causing an invasive bone infection in a French man (Barraud et al., 2013). Also in Denmark, ST130 *mecC*-MRSA strains from cows and sheep were identified from human infections (Harrison et al., 2013).

A longer-term risk of zoonotic transfer is the development of host adaptation, with the potential to introduce new clones with the capacity for pandemic spread in humans. This has been described from MSSA/MRSA CC97 that originated from bovines (Spoor et al., 2013).

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

Due to the presence of *mecA*, MRSA CC398 is per definition resistant to all β-lactam antibiotics, a widely used antimicrobial class in treatment of cattle IMI and horse SSTI (Boyen et al., 2013; Rainard et al., 2018). In addition, MRSA CC398, regardless of animal species and isolation from healthy or diseased animals, carriage or infection sites, is typically resistant to tetracyclines, often to macrolides, lincosamides, streptogramins, aminoglycosides and in part to cotrimoxazole (trimethoprim), fluoroquinolones and phenicols; MRSA CC398 are typically susceptible to other antimicrobials, including fusidic acid and mupirocin (Vanderhaeghen et al., 2010b; Haenni et al., 2014; Tenhagen et al., 2014; Haag et al., 2019; Krukowski et al., 2020). Resistance levels appear to be particularly high in isolates from veal calves (Vandendriessche et al., 2013; Tenhagen et al., 2014). The equine clade of MRSA CC398 appears typically resistant to gentamicin (Cuny and Witte, 2017).

Resistance of other MRSA strains found in cattle and horses is varying. *mecC*-MRSA strains appear to have little additional antimicrobial resistance to β-lactams (Paterson et al., 2014b; Haenni et al., 2014, 2015; Lozano et al., 2020). Tetracycline resistance appeared common among non-CC398 MRSA in veal calves, dairy and beef cattle (Tenhagen et al., 2014). ST8 MRSA in horses is typically multiresistant, including to gentamicin (Cuny and Witte, 2017). Tirosh-Levy et al. (2015) found a multidrug-resistant MRSA clone, ST5-SCCmec V, in 6 of 83 nasal samples of horses hospitalised in a veterinary teaching hospital, displaying resistance to ciprofloxacin. It has been suggested that fluoroquinolone resistance in MRSA from horses is rising in recent years compared to earlier studies, as a possible result from selective pressure by use of fluoroquinolones in equine clinics (Cuny et al., 2016).

Such a wide variety of resistance types among other AMR *S. aureus* strains from cattle and horses has been described that it is unfeasible to list it. As noted in EFSA AHAW Panel (2021a), resistance levels for *S. aureus* from IMI appear particularly high in Asia and Africa. However, pan-resistance of AMR *S. aureus* from mastitis has not been described, meaning that some options remain for the treatment of AMR *S. aureus*, e.g. penicillin–novobiocin and pirlimycin (EFSA AHAW Panel, 2021a). Notably, resistance to treatment of *S. aureus* IMI is often not (only) due to antimicrobial resistance but also results from factors like immune evasion, cell internalisation, biofilm formation and the forming of small colony variants (Grunert et al., 2018; Rainard et al., 2018). Therefore, *in vitro* susceptibility not necessarily results in *in vivo* treatment success. Also in horses, pan-resistant AMR *S. aureus* has not been described.

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 dominant pattern in *S. aureus* IMI is persistent infection with relatively low bacterial shedding, with the majority of the IMIs going clinically unnoticed (Schukken et al., 2011; Rainard et al., 2018). Most infections are chronic, frequently persisting over the ongoing lactation and possibly the following lactations, with more or less intense clinical flare-up episodes, with sometimes an acute clinical phase at the start. Alternatively, infections may colonise udders without clinical signs and spread furtively in the herd (Rainard et al., 2018).

In a study of both experimentally induced and natural *S. aureus* IMI, a duration of at least 20 days was found (Sears et al., 1990). It was not specified whether the IMI was resolved with antimicrobial

treatment. In a Dutch herd, an overall median duration of *S. aureus* IMI, including chronic and transient cases but excluding samples within 14 days after antimicrobial treatment for mastitis, of 30 (95% CI: 20–45) days was found, but specifically for chronic *S. aureus* IMI the median duration was found to be 95 (95% CI: 72–125) days (Deng et al., 2021); the authors however stated that it was likely that they underestimated the duration of IMI due to biased data (left truncation and right censoring). Indeed, other studies reported durations of *S. aureus* IMI of 64–91 days, with cured animals comprising both spontaneously cured animals and treated animals (Kirkeby et al., 2019), 128 days including only untreated subclinical IMI (Dalen et al., 2019) and 136–178 days (Lam et al., 1996; information on antimicrobial treatment unclear). The definition of IMI (taking transient IMI along with chronic IMI into account), the duration of the study and the type of milking system are factors that can contribute to the differences among these results (Deng et al., 2021). In all these studies, it was not elucidated whether the *S. aureus* strains involved were AMR or not.

Clearly, *S. aureus* IMI can have a very long duration. In a single herd in Brazil with Jersey and Holstein Friesian dairy cows, a CC133 MSSA strain resistant to ciprofloxacin persisted for 9 months (Rossi et al., 2019). Another fully susceptible SA CC126 strain persisted for 4 months. However, in an Austrian farm, MSSA CC705 and CC9 strains with (phenotypical) resistance to marbofloxacin, erythromycin and pirlimycin were found to persist over several years (Grunert et al., 2018). While it is generally poorly understood to what extent duration of IMI is driven by host or pathogen, antimicrobial resistance is an obvious pathogen factor (Rainard et al., 2018). It has been shown that the cure rate of *S. aureus* IMI is lower for penicillin-resistant isolates regardless of the antimicrobial molecule used for treatment, but the mechanisms underlying this association remain unknown (Rainard et al., 2018).

Little is known on the duration of and shedding of AMR *S. aureus* from SSTI in horses. A study testing honeybee lactic acid as treatment for chronic SSTI included several horses with SSTI lasting for over 1 year that were infected with *S. aureus*, among other pathogens (Olofsson et al., 2016).

Parameter 2 – Presence and duration of latent infection period

It is unclear whether there is a real latent infection period after contracting (AMR) *S. aureus*. Experimentally induced *S. aureus* IMI in cows exhibit short incubation periods (12–48 h) with most strains, even with low inoculum (< 1,000 colony forming units), before *S. aureus* is detectable in milk samples (Rainard et al., 2018). Shedding is almost continuous but with irregular, cyclical patterns and low numbers in many subclinical cases. Consequently, the sensitivity of a single milk sample to allow determination of the infection status of a gland is not perfect, particularly when employing a typical sample volume of 10 μl. A second or third sample for bacterial culture is necessary to reach a high sensitivity of > 95%, owing to the irregular pattern of *S. aureus* A shedding (Rainard et al., 2018). Hence, these low-shedding periods might be considered latent infection periods but appear to be irregular and unpredictable.

A latent infection period for MRSA CC398 in cattle or horses has not been reported.

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

Little is known about the period in which healthy animals carrying AMR *S. aureus* can shed the bacteria, in both cattle and horses, and what is known comes from MRSA CC398, which may not be representative for other AMR *S. aureus* strains due to its elevated host promiscuity. In a longitudinal study of MRSA CC398 carriage in Dutch veal calves, Graveland et al. (2012) found a small number of source animals rapidly affecting the rest of the calves, especially after releasing from their individual housing. Yet, there were large numbers of intermittent carriers, suggesting the infectious period of a single animal carrying MRSA CC398 is probably short but due to high level of shedding, especially from rectal colonisation, a heavily contaminated environment, including air, contributes to frequent re-infection events.

Also in the Netherlands, it was shown that a girl, only after avoiding contact with her foal suspected as source of her CC398 infectious MRSA strain, kept a negative status; the horse itself had been hospitalised at a horse clinic 2 months prior to the detection of the MRSA strain from the girl, where it probably contracted MRSA. It became – without treatment – negative after 3 months (van Duijkeren et al., 2011). This carriage duration is in line with the median carriage time (143 days, IQR: 111–172 days) observed in a small longitudinal study on MRSA carriage in horses with healed wounds previously infected with MRSA (Bergström et al., 2013).

Environment

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

MRSA CC398 can be heavily present in the direct environment of cows on a farm including air and dust (Fessler et al., 2012; Graveland et al., 2012; Locatelli et al., 2017) and of horses in clinics (Bortolami et al., 2017). It is, however, unclear how long it can survive there. In pigs, experimental exposition of piglets to air containing MRSA at high doses led to persistent colonisation (Rosen et al., 2018). In experimental studies in pigs, strains could be found 42 days post-infection on the barn walls and feeders (Crombé et al., 2013). MRSA CC398 has also been found in various water samples in relation to slaughterhouses and wastewater treatment facilities (Savin et al., 2020a,b).

mecC-MRSA of CC425 and CC130 and several MSSA lineages with variable RoIs types have been found in surface waters, of which some had a possible cattle or horse origin (Silva et al., 2021). A study by Porrero et al. (2014) found *mecC*-positive *S. aureus* in river water after the area had been found to be positive for ST425-*mecC* in wild boar and fallow deer at the same location (Porrero et al., 2013), suggesting a shared source of exposure or transmission between the various animal species and/or the environment.

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)

Horizontal transmission is the main type of transmission of (AMR) *S. aureus* in cattle as well as in horses.

When (AMR) *S. aureus* is predominantly found in the nose or the rectum and young animals with frequent contact are involved, as is the case in veal calves with MRSA CC398, both direct contact and spread through exposure to a contaminated environment are important transmission routes (Graveland et al., 2012). Air and/or dust might play a particularly important role (Graveland et al., 2012; Bos et al., 2016).

When direct contact occurs less frequently, like in adult cattle or horses in veterinary clinics, indirect animal-to-animal transmission and circulation through the contaminated environment, abiotic as well as biotic, appears to be more important (van Duijkeren et al., 2010; van Balen et al., 2014; Steinman et al., 2015; Rainard et al., 2018). In dairy cattle, chronically infected mammary glands represent the main reservoir of *S. aureus* in herds and the pathogen is primarily transmitted during the milking process as the bacteria are spread to uninfected quarters by teat cup liners, milkers' hands and wash cloths (fomites). There is no reason to assume this typical pattern would be absent for AMR *S. aureus*, e.g. for MRSA. Yet, to understand the transmission pattern in a herd, hygiene practices as well as the pathogen and host characteristics are also important (Rainard et al., 2018). The frequent occurrence of multiple strains with low prevalence or incidence in infected herds indicates that not all infections are the result of cow-to-cow transmission (Klaas and Zadoks, 2018; Rainard et al., 2018). These environmental reservoirs may include bedding material, faeces and dust (Locatelli et al., 2017; Klaas and Zadoks, 2018), although the latter might be less contaminated compared to veal calf farms (Dahms et al., 2014).

In dairy farms as well as veterinary clinics, AMR *S. aureus* might frequently be introduced through indirect transmission from other animals (Brennan et al., 2016; Schnitt et al., 2020).

Indirect vertical transmission through feeding mastitis 'waste milk' (containing pathogens or residues) to calves has been suggested to represent a risk for heifer mastitis but few data support this (De Vliegher et al., 2012; Abb-Schwedler et al., 2014; Schnitt et al., 2020).

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

Both direct and indirect transmission of AMR *S. aureus* between cattle and horses and humans occurs, but direct transmission is of greater importance. Numerous reports have described similar AMR *S. aureus* strains in cattle and horses and human contacts, of various genetic lineages, including but certainly not limited to CC398. As noted, there are several interesting reviews providing further references (Cuny and Witte, 2017; Goerge et al., 2017; Chen and Wu, 2021; Liu et al., 2020; Dong et al., 2021). Noteworthy, transmission can go in both ways and the direction is often difficult to be determined.

Indirect transmission through contaminated surfaces or dust and air might also occur (van Cleef et al., 2011; Bisdorff et al., 2012; Deiters et al., 2015; Bos et al., 2016).

Contact with and consumption of contaminated food products (carcasses, meat, milk) have been described as possible sources of MRSA in humans (Larsen et al., 2016), but in general, it is perceived that this poses only a minor risk (Wendlandt et al., 2013; Larsen et al., 2016; Cuny et al., 2019).

Speed of transmission

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

A few studies provide data on the occurrence of new IMIs of *S. aureus* in dairy cows (Lam et al., 1996; Zadoks et al., 2002; Barlow et al., 2013; Schukken et al., 2014; van den Borne et al., 2017; Kirkeby et al., 2019). However, except for Barlow et al. (2013), these studies do not note anything about antimicrobial resistance. It is unclear whether antimicrobial resistance would be related to incidence, but considering that many other factors are involved in the transmission dynamics of *S. aureus* IMI (hygiene practices, host factors, pathogen virulence) (Rainard et al., 2018), it seems unlikely that any such relationship would be 'universal'.

Lam et al. (1996) studied an *S. aureus* outbreak over a 20-month study period on a single dairy farm during a split-udder trial where all right teats were disinfected post-milking and all left teats were left as untreated controls. They found the incidence density rate (IDR), expressed as the number of new *S. aureus* IMIs per number of susceptible quarter-days, was 13 of 71,129 for dipped quarters and 40 of 65,509 for control quarters, revealing a crude IDR of 0.30 (95% CI of 0.16–0.56). In a study investigating a model for control of *S. aureus* mastitis in three endemically infected herds, the number of new IMIs over 3-week intervals ranged between 0 and 7 over the herds and in time (Zadoks et al., 2002). The other studies do not mention (single) incidence rates.

No other data were found on the incidence of (AMR) *S. aureus* in cattle or horses, nor on the transmission of (AMR) *S. aureus* from animals to humans.

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

A few studies provide data on the transmission rate of *S. aureus* IMI in dairy cows, but again, these studies do not include resistance data. Here as well, it is unclear whether 'resistance' would have a 'universal' impact on transmission. Some studies have investigated the transmission of MRSA CC398 experimentally in pigs and mink (e.g. Crombé et al. (2013) and Fertner et al. (2019)), but similar studies have not been performed in cattle or horses. Transmission rates from (AMR) *S. aureus* from cattle or horses to humans are also unknown.

In their split-udder trial for estimating efficacy of post-milking teat disinfection, Lam et al. (1996) found transmission rates of 0.0032 per day for dipped quarters and 0.011 per day for control non-dipped quarters. Zadoks et al. (2002) estimated transmission rates for new infections in uninfected quarters of 0.007, 0.014 and 0.014 cases/quarter-day at risk in three different herds, and rates for new infections in recovered-uninfected quarters of 0.042, 0.052 and 0.041 cases/quarter-days at risk in those same herds. In a field trial that evaluated a diagnosis-driven treatment programme targeting subclinical *S. aureus* IMI, Barlow et al. (2013) estimated the transmission rate for *S. aureus* at 0.00804 cases/quarter-day and 0.00448 cases/quarter-day for two different herds. In a trial assessing the Startvac vaccine (Hipra), Schukken et al. (2014) estimated a monthly quarter-level transmission rate at 0.295, corresponding to 0.009 per quarter-day. Van den Borne et al. (2017) quantified transmission of a specific *S. aureus* genotype (B) among Swiss dairy cows in nine communal pasture-based operations and over the seven positive farms involved estimated a cow-level transmission rate of 0.0232 per day. Kirkeby et al. (2019) investigated the transmission dynamics of *S. aureus* in two Danish dairy herds – one with low prevalence and one with high prevalence of *S. aureus* IMI – and estimated daily quarter-level transmission rates of 0.0132 and 0.0077 cases/quarter-day in the two herds, respectively. Finally, Deng et al. (2021) studied transmission dynamics of *S. aureus* and *S. agalactiae* in a Dutch dairy herd using an automated milking system. Using three different definitions of IMI, they estimated the transmission rate for *S. aureus* to be within the range of 0.002 cases/quarter-days to 0.019 cases/quarter-days.

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

Considering that *S. aureus* has a highly clonal population structure and that several lineages worldwide, and so in several European countries, have adapted to bovine (e.g. CC97, CC130, CC151, etc.) or equine (CC8, CC398, etc.) hosts, it might appear that *S. aureus* has a rather pandemic occurrence (Keane, 2019). However, from an ecological point of view, this may be questioned, since *S. aureus* is a normal coloniser of skin and mucous membranes, from where it can cause opportunistic infections. Furthermore, it is a heterogeneous organism with a high degree of adaptability (Monistero et al., 2020), resulting in adaptations within the same lineage to different host species, e.g. CC8 (Boss et al., 2016; Cuny and Witte, 2017) or environments (Rainard et al., 2018). Moreover, in numerous studies, sublineages of the common lineages or several uncommon, local or sporadic lineages have been detected in cattle or horses (Nemeghaire et al., 2014; Guérin et al., 2017; Locatelli et al., 2017; Mama et al., 2019). Hence, it might make more sense to describe the occurrence of (AMR) *S. aureus* in cattle and horses in Europe and worldwide as endemic. Indeed, as shown in Section 3.1.2.1 later on, AMR *S. aureus* with RoIs has been described from most European countries. The presence of antimicrobial resistance makes in this sense no difference. In theory, as will be the case for most of the RoIs of this fact sheet, antimicrobial resistance in *S. aureus* should be considered an adaptation to a selection pressure, occurring in the locally residing strains (Price et al., 2012). The emergence of methicillin-resistant strains, and specifically MRSA CC398, might seem different with an apparent clonal spread over various animal species as colonisers and occasional infection-causing agents. However, even if it would be assumed that its emergence and rapid spread over various species, countries and continents was due to a limited number of genetic variants, recent studies show in reality an enormous variety of sublineages exists (Glasner et al., 2013; Bosch et al., 2015; van Alen et al., 2017), likely endemically associated with specific reservoirs, regions or even farms and clinics (Lienen et al., 2021).

Risk of introduction

MRSA CC398 and numerous other (AMR) *S. aureus* (sub)lineages reside and can cause infections in cattle and horses virtually all over Europe. Therefore, this section is not applicable.

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

Diagnostic tools

Parameter 1 – Existence of diagnostic tools

To investigate carriage of (AMR) *S. aureus* in cattle and horses requires, as in other animals, samples from the nose, skin, mucous membranes or other exterior body locations, like the guttural pouch or the rectum (Graveland et al., 2012; Boyle et al., 2017). Van den Eede et al. (2013) investigated three nasal locations from horses (the left nasal vestibulum, the diverticulum and the ventral meatus) and found the likelihood of detecting an MRSA-positive animal was highest following sampling of the vestibulum. Deep sampling, of the ventral meatus, has not significantly worse results, but the more proximal sampling technique is easily accessible, well-tolerated by the patient and delivers results at least as good as the deep sampling method indicating that the nasal vestibulum is the optimum sampling location for equine MRSA screening.

To isolate (AMR) *S. aureus* from infections, tissue samples of infection sites are required. For detection of IMI, milk samples are required. Due to the typical shedding pattern of *S. aureus* IMI, two or three consecutive milk samples are preferable (Rainard et al., 2018). Samples require standard treatment for preservation and transport to the lab.

Diagnosis of mastitis (the inflammation resulting from the IMI of the pathogen) is based on SCC, bacteriological results and view of the udder and milk, as well as temperature of udder and animal (Dohoo et al., 2011; Ruegg, 2017; Rainard et al., 2018).

Standard bacteriological culturing and identification methods should be applied. *S. aureus* is a typically coagulase-positive organism, allowing to differentiate it from the large group of coagulase-negative staphylococci which are the most important pathogens in bovine subclinical mastitis (Vanderhaeghen et al., 2015). It has characteristic small white-yellow β-haemolytic colonies on blood

agar. Recently, selective chromogenic culture media for rapid identification of microorganisms, including *S. aureus*, specifically from samples of bovine mastitis have been tested (Garcia et al., 2021; Granja et al., 2021). Also for selective growth of MRSA, chromogenic agars are commercially available (Pletinckx et al., 2013). In general, increased sensitivity is obtained when using selective liquid enrichment methods. In recent decades, identification of *S. aureus* is commonly confirmed by gene detection (PCR or micro-array) for genus-specific (16S rRNA) and species-specific sequences (e.g. *spa*, *nuc*, *rpoB*) (Maes et al., 2002; Spanu et al., 2011; EFSA, 2012). Some other molecular identification techniques are more and more used, e.g. matrix-assisted laser desorption ionisation–time-of-flight mass spectrometry (MALDI-TOF MS) (Spanu et al., 2011; Hansen et al., 2019).

Determination of antimicrobial resistance can be done pheno- and genotypically. The standard phenotypical methods (disk diffusion, minimum inhibitory concentration (MIC) determination, E-tests) are available. Automated systems can be used, e.g. VITEK 2 (bioMérieux) (Felten et al., 2002; Schmitt et al., 2020). To identify methicillin resistance, testing for cefoxitin resistance is the current phenotypical standard. Another phenotypic test is the latex agglutination test, for detection of pbp2a (Felten et al., 2002). Detection of the *mecA* gene can be done for confirmation and is nowadays often performed as a standard. Care must be taken as methicillin resistance can also be caused by the *mecC* gene (Becker et al., 2014).

A multitude of resistance and virulence genes have been described for which PCR or micro-arrays have been developed (Monecke et al., 2007; Kadlec et al., 2012; Schmitt et al., 2020). Whole genome sequencing (WGS) is also more and more used as a tool to scan for resistance (and virulence) genes (e.g. Hansen et al., 2019).

Parameter 2 – Existence of control tools

Epidemiological typing tools are an essential starting point for a well-founded control of (AMR) *S. aureus*. A multitude of typing tools for (AMR) *S. aureus* has been described, with various resolution power (Zadoks et al., 2011). Fingerprinting methods such as pulsed-field gel electrophoresis, amplified fragment length polymorphism, restriction fragment length polymorphism, random amplification of polymorphic DNA and multiple-locus variable number tandem repeat analysis have a high discriminatory power, allowing for small-scale epidemiological research (Rasschaert et al., 2009; Sakwinska et al., 2011; Zadoks et al., 2011; Gurjar et al., 2012). *spa* typing and multilocus sequence typing (MLST) (used for distinguishing sequence types, grouped in clonal complexes) are used to identify (sub)lineages, and in combination with typing of the methicillin resistance determinant SCCmec form a basic typing set for LA-MRSA (EFSA, 2012). In addition, micro-array and WGS can be used for typing and epidemiological analyses (Zhou et al., 2018; Lienen et al., 2021).

To prevent *S. aureus* mastitis, vaccines are available in Europe (STARTVAC, Hipra SA) as well as Northern America (the Lysigin vaccine, Boehringer Ingelheim Vetmedica, Inc.). Other preventive measures relate to hygienic, biosecurity and health management practices, adapted to the specific farm or clinic setting. In dairy cattle, *S. aureus* is considered a major contagious pathogen, for control of which mastitis control programmes have been developed (see Section 3.1.4.4), to good success (Ruegg, 2017; Rainard et al., 2018). Yet, it can also have an environmental origin, requiring adapted control measures, such as managing bacterial load in bedding material or choosing appropriate bedding and housing to avoid injury (Klaas and Zadoks, 2018; Leuenberger et al., 2019). Within a farm, multiple epidemiological types of *S. aureus* might be present (Leuenberger et al., 2019; Rainard et al., 2018). The roles of extra-mammary colonisation of healthy persistent carriers and of environmental sources as a reservoir for IMI are not well defined, and the drivers of the shift from colonisation to IMI still need to be investigated using modern molecular epidemiological methods (Rainard et al., 2018).

S. aureus mastitis is known to be difficult to treat and can become chronic; this might be due to antimicrobial resistance but more typically is considered to be due to factors like immune-evasion, cell internalisation, biofilm formation and the forming of small colony variants (Grunert et al., 2018; Rainard et al., 2018). Culling is advised for chronic infections, especially in multiparous cows (Rainard et al., 2018).

In horse clinics, typical nosocomial (surgery) hygienic and hospital sanitation measures are applied in order to limit the spread of (AMR) *S. aureus* (Boyen et al., 2013; Steinman et al., 2015).

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 the presence of the disease in the Union

Parameter 1 – Number of MSs where the disease is present

It is virtually certain that *S. aureus* with one or multiple of the RoIs is present in both cattle and horses in all of the MSs of the EU, even if this would not yet have been described in literature. As noted, *S. aureus* is a natural coloniser and opportunistic pathogen in both animal species and antimicrobial treatment is broadly applied in both species. Table 9 gives examples per animal species and MS of studies that illustrate the presence of AMR *S. aureus* (with a RoI). This list is exemplary, with hyphens indicating no references were found.

Table 9: Examples of studies in MSs of the EU that illustrate the presence of AMR *S. aureus* with (any of) the RoIs for this fact sheet

Country	Cattle	Horses
Austria	Firth et al. (2022)	Cuny et al. (2008)
Belgium	Vanderhaeghen et al. (2010a)	van den Eede et al. (2012)
Bulgaria	–	–
Croatia	Cvetnić et al. (2021)	–
Cyprus	–	–
Czech Republic	Tegegne et al. (2019)	–
Denmark	Ronco et al. (2018)	Islam et al. (2017)
Estonia	–	–
Finland	Gindonis et al. (2013)	–
France	Haenni et al. (2014)	Guérin et al. (2017)
Germany	Lienen et al. (2021)	Walther et al. (2009)
Greece	Papadopoulos et al. (2019)	–
Hungary	Juhász-Kaszanyitzky et al. (2007)	Albert et al. (2019)
Ireland	Anjum et al. (2019)	Brennan et al. (2016)
Italy	Antoci et al. (2013)	Carfora et al. (2016b)
Latvia	–	–
Lithuania	–	–
Luxembourg	–	–
Malta	–	–
Netherlands	Graveland et al. (2010)	van Duijkeren et al. (2014)
Poland	Krukowski et al. (2020)	–
Portugal	Couto et al. (2015)	Couto et al. (2015)
Romania	Pascu et al. (2022)	–
Slovakia	–	–
Slovenia	–	–
Spain	–	Gómez-Sanz et al. (2014)
Sweden	Unnerstad et al. (2013)	Bergström et al. (2012)

–: No references were found.

The loss of production due to the disease

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

Mastitis in general is considered the most important cause of economic losses in the dairy sector, mostly due to a reduced milk yield and quality, but also because of treatment and veterinary costs, costs of culling (cattle replacement, impact on the herd's ability to genetically improve, etc.), investment in mastitis management protocols and infrastructure, diagnostic testing and even fertility effects (Ruegg, 2017; Rainard et al., 2018). In a UK study, the estimated annual output losses,

treatment costs and costs of prevention for mastitis were £197.9 million, £79.8 million and £9.3 million, respectively (Rainard et al., 2018). According to a comprehensive review on the overall economic effects of bovine mastitis and mastitis management, the cost per case of clinical mastitis and subclinical mastitis was estimated at €287 and €102, respectively (Halasa et al., 2007). Also Huijps et al. (2008) presented a model estimating economic losses due to clinical and subclinical mastitis. It is clear, however, that the cost depends on a great number of factors. That also explains why the proportion of *S. aureus* and specifically AMR *S. aureus* in these losses is difficult to estimate (Swinkels et al., 2005; Rainard et al., 2018). Although considered one of the major mastitis pathogens, *S. aureus* mastitis is commonly subclinical. Most infections are chronic, frequently persisting over the ongoing lactation and possibly the following lactations, with more or less intense clinical flare-up episodes (Rainard et al., 2018). *S. aureus* appears to mostly circumvent the host immune response and IMI typically result in a very moderate host response, milk production losses and risks of culling and death (Schukken et al., 2011). Nonetheless, Huijps et al. (2008) assumed by default in their model that *S. aureus* clinical mastitis caused more production losses than other pathogens. If the number of *S. aureus* clinical mastitis cases was higher than default (20%), the production losses were estimated to be 1% higher. If the number of *S. aureus* clinical mastitis cases was lower, the production losses were estimated to be 1% lower. However, a calculated loss due to (AMR) *S. aureus* (sub)clinical mastitis was not found in literature.

For other cattle types, production losses are unknown but are likely low, since *S. aureus* is not considered an important pathogen in these species, even though carriage rates of MRSA CC398 can be very high in veal calves (Vandendriessche et al., 2013).

In horses, no estimates are available for the production losses due to (AMR) *S. aureus*. Cases of AMR *S. aureus* infections in, e.g. race horses have been described (Sekizuka et al., 2020), but the economic impact has not been systematically investigated.

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

As evidenced by numerous studies, direct contact is the most important transmission route for transmission of AMR *S. aureus*, including MRSA CC398, *mecC*-MRSA and several other MRSA lineages, from cattle and horses to humans (Bisdorff et al., 2012; Graveland et al., 2012; Vandendriessche et al., 2013; Deiters et al., 2015; Cuny and Witte, 2017; Alekish et al., 2020; Lozano et al., 2020). Recent reviews and meta-analyses found that people (e.g. farm workers, veterinarians, slaughterhouse workers, etc.) with frequent direct contact with livestock, including cattle and horses, had an increased risk for MRSA carriage (Goerge et al., 2017; Chen and Wu, 2021; Liu et al., 2020; Dong et al., 2021).

Indirect transmission in the close environment of animals, through contaminated surfaces or dust and air, might also occur (Wendlandt et al., 2013). Bos et al. (2016) found that exposure to MRSA CC398 in veal calf barn air was an important determinant for nasal carriage, especially in the group of farmers that had frequent or long contact with the animals. Dorado-García et al. (2013) described a positive association between the level of MRSA prevalence in veal calves, barn dust and MRSA carriage in veal calf famers and household members. Single visits to MRSA CC398-positive veal calf barns (lasting a few hours but with intensive contact with animals and dust) led to the isolation of MRSA CC398 in the fieldworkers, up to 24 h after the visit (van Cleef et al., 2011). Similarly, private farm visits without or with only rare animal contact were identified as risk factors for colonisation with MRSA (Bisdorff et al., 2012). Transmission might also be possible through contaminated equipment or surfaces or equipment in farms and (equine) veterinary clinics (Bortolami et al., 2017).

Transmission through dissemination of (AMR) *S. aureus* in the further environment appears to be less likely (Bisdorff et al., 2012; Deiters et al., 2015). Even though MRSA (CC398) has been described from carcasses and (retail) meat, especially pork and poultry meat, and has been suggested as a possible source of transmission to people further without livestock contact (Larsen et al., 2016; Sergelidis and Angelidis, 2017; Anjum et al., 2019; ECDC, EFSA and EMEA, 2009), food-borne colonisation or infection seems in general to be of minor importance in the epidemiology of LA-MRSA in humans (ECDC, EFSA and EMEA, 2009; Deiters et al., 2015; Cuny et al., 2019). The main risk might be the potential for food poisoning due to the consumption of raw foods, like milk, harbouring enterotoxigenic (AMR) *S. aureus*. In that sense, the presence of enterotoxins in AMR *S. aureus* from milk has been occasionally described (Argudín et al., 2011; Sergelidis and Angelidis, 2017; El-Ashker et al., 2020) and so is likely of minor concern (Lienen et al., 2021).

Parameter 2 – Incidence of zoonotic cases

Although zoonotic cases of AMR *S. aureus* from cattle and horses have been extensively documented (see Section 3.1.1.3), the incidence of zoonotic transmission cases has not yet been estimated.

Transmissibility between humans

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

Clearly, most cases of (AMR) *S. aureus* from animals being present in humans originate from animal-to-human transmission (Deiters et al., 2015). With respect to MRSA CC398, secondary cases in humans occur but are less common and often have a link to another person with direct occupational contact, for example in the household (Bosch et al., 2015; Deiters et al., 2015; Walter et al., 2017; Krukowski et al., 2020).

Several cases of MRSA CC398 carriage or infections in humans reporting no (direct) animal contact have been described (van Rijen et al., 2014; Larsen et al., 2015; Becker et al., 2017). These infections can be very severe (Becker et al., 2017). Wulf et al. (2008) described an outbreak of MRSA CC398 with a possible pig origin in a Dutch hospital, involving 10 cases in total, patients as well as healthcare workers, possibly introduced by one of the latter.

Human-to-human transmission has also been described for *mecC*-MRSA from cattle but these strains are considered even less able to colonise and spread among humans than CC398 (Lozano et al., 2020). Long-term colonisation with *mecC*-MRSA appears unlikely (Barraud et al., 2013; Lozano et al., 2020).

It appears that the potential to lead to community-level outbreaks of human-to-human transmission of (AMR) *S. aureus* with a direct link to the source animals is limited. Yet, considering the potential of *S. aureus* to be able to quickly adapt to new hosts, zoonotic transmission might lead to human-pathogenic *S. aureus* with the capacity for pandemic spread among its new hosts (Spoor et al., 2013).

Parameter 4 – Sporadic, epidemic or pandemic potential

Just as MRSA CC398 might appear to behave as an epidemic or even pandemic in animals, having been described in livestock worldwide, its transmission to humans in close contact might be considered an epidemic or pandemic. However, MRSA CC398 is currently more likely being present endemically in various regions. Due to the necessity of direct contact and the likeliness of transmission, MRSA CC398 should be considered to behave endemic in human populations in close contact with animal populations where MRSA CC398 resides endemically. This might lead to the increased representation of MRSA CC398 among human clinical cases in regions with high livestock density, especially when numbers of healthcare-associated MRSA infections are low (Becker et al., 2017; Schnitt et al., 2020). However, after dramatic increases in the past decade, numbers of MRSA CC398 in human surveillance data seem to have stabilised in recent years (van Alen et al., 2017).

Other AMR *S. aureus* strains from cattle or horses, e.g. *mecC*-MRSA, seem to have rather a sporadic potential (Barraud et al., 2013; Lozano et al., 2020). In Australia, MRSA ST612 might have a reservoir in horses, leading to colonisation of veterinarians and sporadic infections (Murphy et al., 2019).

The severity of human forms of the disease

Parameter 5 – Disability-adjusted life year (DALY)

The DALY in humans is unknown for AMR *S. aureus* strains originating from cattle and horses. Recently, it was reported that the global burden of MRSA in humans in 2019 included 3.5 million DALYs attributable to resistance (Antimicrobial Resistance Collaborators, 2022).

The availability of effective prevention or medical treatment in humans

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

Presence of AMR *S. aureus*, just as for regular *S. aureus*, in itself is not cause for medical treatment. However, upon hospital admission, decolonisation of MRSA (CC398) might be attempted, especially in those countries where hospital-prevalence of MRSA is low, e.g. the Netherlands and Northern European countries (George et al., 2017). Mupirocin ointment and chlorhexidine washing is often applied for decolonisation (Wulf et al., 2008).

Treatment of human infections with AMR *S. aureus* from cattle and horses has been done using different strategies, depending on the type and severity of the infection and the antimicrobial resistances present. In the Netherlands, a girl was infected with an MRSA ST398 strain transmitted from a foal that was resistant to clindamycin, ciprofloxacin, erythromycin, gentamicin, kanamycin, tetracycline and trimethoprim/sulfonamide, and susceptible to rifampin and fusidic acid. The girl's wound healed after application of mupirocin ointment to the nares and perineum (3×/day for 5 days), washing of the body with chlorhexidine shampoo (1×/day for 5 days) and oral administration of fusidic acid and rifampin for 7 days.

In France, a patient infected with a *mecC*-MRSA strain possibly originating from cows was initially treated with cloxacillin, gentamicin and metronidazole for only 3 days and then switched to vancomycin, gentamicin and fosfomycin. After 2 weeks of this intravenous treatment, he was prescribed oral ofloxacin and rifampicin for 8 weeks. The infection was considered cured at the end of treatment (Barraud et al., 2013).

In general, treatment of a human MSSA infection would start with administration (orally for less severe infections or intravenously for more severe infections) of a penicillinase-resistant penicillin or a cephalosporin, with various possible substances for step-down treatment (see for example references provided on https://www.uptodate.com/contents/clinical-approach-to-staphylococcus-aureus-bacteremia-in-adults).

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

There are no human vaccines for (AMR) *S. aureus* with a cattle or horse origin.

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

S. aureus IMI in dairy cattle is typically chronic and subclinical. Chronic, persistent IMI cases are difficult to treat and prone to resurgence, and often accompanied by long-lasting cost-intensive antibiotic treatment and premature culling (Rainard et al., 2018). It can last one or even several lactations (Grunert et al., 2018; Deng et al., 2021).

S. aureus is among the most common causes of clinical bovine mastitis as well (Verbeke et al., 2014; Åvall-Jääskeläinen et al., 2021). Occasionally, the severity of clinical *S. aureus* mastitis can go to peracute gangrenous mastitis causing necrosis of the affected udder quarter, severe systemic signs and even death of the cow (Rainard et al., 2018; Åvall-Jääskeläinen et al., 2021).

In horses, several types of infections with (AMR) *S. aureus*, with variable seriousness and duration of infection, occur (Weese et al., 2005a; Guérin et al., 2017; Soimala et al., 2018). Infections might last over a year (Olofsson et al., 2016). In the latter study, honeybee lactic acid was successfully applied for treatment of long lasting wound in 7 out of 10 treated horses. Weese et al. (2005a) reported a number of horses infected, sometimes seriously ill and requiring prolonged hospitalisation, with MRSA implicated directly in the death of one horse as a result of severe osteomyelitis.

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

Table 10: List of wildlife species where *S. aureus* with RoIs for this fact-sheet has been isolated and that are included in the CITES and/or IUCN lists

Species (group)	Antimicrobial resistance	CITES	IUCN
Mammals			
Small mammals			
Indian flying fox (*Pteropus giganteus*)[(a)]	*mecC*	Appendix II	
Straw-coloured fruit bat (*Eidolon helvum*)	CIP, CLI, ERY, FUS, PEN, TET		Near threatened
Black-flanked rock wallaby (*Petrogale lateralis*)	PEN		Vulnerable
European otter (*Lutra lutra*)[(a)]	BLA, *mecC*, MRSA	Appendix I	Near threatened
Mara (*Dolichotis patagonum*)	*mecC*		Near threatened
Large mammals			
African elephant (*Loxodonta africana*)[(a)]	MRSA	Appendix I	Critically endangered
Non-human primates/monkeys			
Chimpanzee (*Pan troglodytes*)	CLI, ERY, MRSA, PEN, TET, T/S	Appendix I	Endangered
Gorilla (*Gorilla gorilla gorilla*)[(a)]	PEN	Appendix I	Critically endangered
Rhesus macaque (*Macaca mulatta*)[(a)]	CIP, CLI, ERY, GEN, MRSA, PEN, TET, T/S	Appendix II	
Singaporean long-tailed macaque (*Macaca fascicularis*)	CIP, ERY, GEN, KAN, MRSA, PEN, TET	Appendix II	Vulnerable
Southern pig-tailed macaque (*Macaca nemestrina*)[(a)]	CIP, ERY, GEN, MRSA, PEN, TET	Appendix II	Vulnerable
Marine mammals			
Risso's dolphin (*Grampus griseus*)[(a)]	MRSA, PEN	Appendix II	
Bottlenose dolphin (*Tursiops truncates*)[(a)]	MRSA, PEN	Appendix II	
Birds			
Northern bald ibis	CIP, MRSA, PEN, TET	Appendix I	Regionally extinct
Peregrine (*Falco peregrinus*)[(a)]	CIP	Appendix I	
Cinereous vulture	CLI, ERY, MRSA, PEN, TET	Appendix II	Near threatened
Eurasian griffon vulture (*Gyps fulvus*)	MRSA, TET	Appendix II	

BLA: β-lactams; CIP: ciprofloxacin; CLI: clindamycin; ERY: erythromycin; FUS: fusidic acid; GEN: gentamicin; KAN: kanamycin; MRSA: methicillin-resistant *S. aureus* with the *mecA* gene or phenotypic resistance (oxacillin and/or cefoxitin); PEN: penicillin; TET: tetracycline; T/S: trim-sulfa antimicrobials.
(a): Isolates originated from infections.

Parameter 2 – Mortality in wild species

Mortality of AMR *S. aureus* infections has not been systematically studied in wildlife. Fatal infections have sporadically been reported in several species, e.g. Black bear (McBurney et al., 2000), Black

rhinoceros (Clausen and Ashford, 1980), dolphins (Mazzariol et al., 2018), red squirrels (Simpson et al., 2013), etc.

Environment

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

Fatal infections with (AMR) *S. aureus* in wildlife have sporadically been reported (Clausen and Ashford, 1980; McBurney et al., 2000; Simpson et al., 2013; Mazzariol et al., 2018). Links with environmental persistence have not been studied. It has been shown that *mecC*-MRSA was present in surface waters and wildlife species that came drinking there, but these cases involved no fatal infections (Porrero et al., 2013, 2014).

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

CFSPH: Yes, as MRSA.
OIE: No.

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

No, but *S. aureus* enterotoxins, haemolysin alpha toxin and toxic shock syndrome toxin (formerly known as staphylococcal enterotoxin F) are in the list.

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

S. aureus itself is not listed as a potential bio-agro-terrorism agent. However, the staphylococcal enterotoxin B (SEB) is listed on the Centers for Disease Control and Prevention (CDC) Bioterrorism Agents/Diseases list (https://emergency.cdc.gov/agent/agentlist-category.asp) as a Category B agent. These are the second highest priority agents that:

- are moderately easy to disseminate;
- result in moderate morbidity rates and low mortality rates;
- require specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance.

It is also listed on the Arizona Department of Health Services 'Bioterrorism Agent Profiles for Health Care Workers' (https://azdhs.gov/documents/preparedness/emergency-preparedness/zebra-manual/zm-s5-staphylococcal.pdf).

In general, SEB is considered in literature as a potent biological weapon with incapacitating effects (Ahanotu et al., 2006; Bhaskar and Sant, 2020). It is one out of 25 currently characterised staphylococcal enterotoxins and has its toxic effect from its ability to function as a superantigen, toxins able to evoke an immune response of large proportions, commonly resulting in food poisoning and flu-like symptoms that can lead to multi-organ failure and death (Bhaskar and Sant, 2020). AMR *S. aureus* strains carrying this and related toxins have frequently been described in both horses and cattle (Little et al., 2021; Patel et al., 2021).

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

There are no officially/internationally recognised OIE certified diagnostic tests for (AMR) *S. aureus* in bovines or equines, neither for identification and typing of the bacteria nor for resistance determination.

The EU Reference Laboratory for antimicrobial resistance (DTU Food in Denmark) provides protocols for a number of diagnostic tools for MRSA (https://www.eurl-ar.eu/protocols.aspx):

- PCR amplification of *mecA*, *mecC*, *spa* and *pvl*;
- Determination of MIC by sensititre;
- Reading and interpretation of MIC;

- Isolation of MRSA from food-producing animals and farm environment;
- Protocol for *spa*-typing;
- MLST typing.

In Section 3.1.1.8, a brief overview is given on the broad variety of pheno- and genotypic tools used for identification and typing of *S. aureus* as well as for the antimicrobial susceptibility testing.

Effectiveness

Parameter 2 – Sensitivity and specificity of diagnostic tests

There are no officially/internationally recognised OIE certified diagnostic tests for (AMR) *S. aureus* in bovines or equines, neither for identification and typing of the bacteria nor for resistance determination.

Of many of the tools mentioned in Section 3.1.1.8, sensitivity and specificity data are available yet not always based on animal (bovine/equine) isolates. More data can be found in some of the references mentioned there.

Notably, to identify *S. aureus* IMI through milk, the sensitivity of a single milk sample to allow determination of the infection status of a gland is not perfect, particularly when employing a typical sample volume of 10 μl. A second or third sample for bacterial culture is necessary to reach a high sensitivity of > 95%, owing to the irregular pattern of *S. aureus* shedding in milk (Rainard et al., 2018).

Feasibility

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

To investigate carriage of (AMR) *S. aureus* in cattle and horses requires, as in other animals, samples from the nose, skin, mucous membranes or the rectum. Van den Eede et al. (2013) found the nasal vestibulum to be the optimal testing site to detect LA-MRSA (CC398) in horses.

For IMI, milk samples need to be taken, preferably more than one, as described above (Rainard et al., 2018). The number and location of the quarters to sample might vary depending on the study set-up, as do the choice to pool the samples.

For other infections, samples need to be taken depending on the infection site.

3.1.4.2. Article 7(d)(ii) Vaccination

Availability

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

There is a single vaccine on the European market against *S. aureus* mastitis: STARTVAC (Hipra SA). Other vaccines are not available in Europe, neither for bovines nor horses.

Table 11 summarises the characteristics of STARTVAC (Rainard et al., 2021). Information from the European Medicines Agency (EMA) can be found online (https://www.ema.europa.eu/en/medicines/veterinary/EPAR/startvac).

Table 11: Characteristics of the STARTVAC vaccine

Way of administration	Intramuscular injection
Field protection	Schukken et al. (2014) • 2 large dairy herds; • 21–month observation period; • Moderate reduction in the incidence of new staphylococcal IMIs: reduction of the 'basic reproduction ratio' of 45% for *S. aureus*. Bradley et al. (2015) • 7 farms; • No reduction of the incidence or prevalence of clinical or subclinical mastitis; • Associated with a significant reduction in the severity of clinical cases and milk losses with a return on investment of 2.57 to 1; • Most clinical cases (25%) were due to *E. coli*; clinical cases caused by *S. aureus* accounted for only 2.5%.

	Landin et al. (2015) • Herd with high *S. aureus* mastitis prevalence; • No beneficial effect on udder health, milk production or culling rate. Freick et al. (2016) • Herd in which *S. aureus* was the predominant pathogen; The vaccine was not an appropriate tool to manage the *S. aureus* problem.
Duration of protection	According to the EMA document, the full immunisation scheme induces immunity from approximately day 13 after the first injection until approximately day 78 after the third injection.
Yearly availability/ production capacity	There are no known issues concerning the yearly availability or production capacity.

In Northern America, another vaccine is licensed, the Lysigin vaccine (Boehringer Ingelheim Vetmedica, Inc.). The vaccine is administered by the subcutaneous route (Rainard et al., 2021). Lysigin vaccine efficacy has been evaluated in several studies, as discussed in Rainard et al. (2021). A review by Middleton (2008) showed variable results with a decreased clinical severity of mastitis, lower milk SCC and sometimes a reduction in the incidence of IMI. More unfavourable results were obtained in a study with heifers vaccinated twice in late gestation in which the only positive effect of the vaccine was a reduction in the duration of clinical mastitis after challenge (Middleton et al., 2006). Another field study by the same research group did not show a reduction in the prevalence or incidence of *S. aureus* or coagulase-negative staphylococci IMI by the Lysigin vaccine (Middleton et al., 2009).

Parameter 2 – Availability/production capacity (per year)

See Table 11.

Effectiveness

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

See Table 11.

Parameter 4 – Duration of protection

See Table 11.

Feasibility

Parameter 5 – Way of administration

See Table 11.

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

Availability

Parameter 1 – Types of drugs available on the market

There are various antimicrobial drugs available on the market to treat *S. aureus* infections in cattle and horses. Evidently, treatment options depend on the resistance pattern determined. Since not all RoIs are necessarily present simultaneously, the overview below will not consider any drug unavailable for reasons of resistance.

For antimicrobial therapy of dairy cow *S. aureus* mastitis during lactation or the dry period, various antimicrobial compounds are available, but β-lactam antimicrobials are among the most used and have especially high cure rates when applied as dry cow therapy (Schnitt and Tenhagen, 2020). These include natural penicillins, aminopenicillins, β-lactamase-resistant penicillins and cephalosporins, and can be combined with clavulanic acid. Others include aminoglycosides (neomycin, kanamycin), lincosamides (pirlimycin, lincomycin, etc.), macrolides (spiramycin, tylosin, etc.), ansamycines and still others. Most of the substances are typically used intramammary, some can also be administered systemically. Fluoroquinolones can also be applied systemically for treatment of *S. aureus* mastitis (Alfonseca-Silva et al., 2021).

There are no studies on antibiotic treatment outcomes for mastitis caused by MRSA, but as the β-lactams, the most important class used in an essential aspect of *S. aureus* mastitis control, dry cow therapy, are probably ineffective, culling might be the only chance to remove MRSA from dairy herds (Schnitt and Tenhagen, 2020).

To treat *S. aureus* mastitis, often combinations of drugs are applied, notably penicillin–neomycin and penicillin–novobiocin.

Formulations of the compounds can be varying, with an important effect on efficacy (Barkema et al., 2006; Alfonseca-Silva et al., 2021).

In addition to antimicrobials, various other (non-traditional) compounds are available for mastitis treatment: prednisolone, bovine lactoferrin, nisin (bacteriocins), ginseng, cytokines, essential oils and other herbal and homoeopathic remedies (Barkema et al., 2006; Rainard et al., 2018).

Preventive pre- or post-milking teat dips can contain various compounds, such as lactic acid, chlorhexidine or iodine.

For treatment of other cattle infections caused by *S. aureus*, the standard palette of antimicrobials is available, including amphenicols, trim-sulfo antimicrobials, tetracyclines, aminoglycosides and fluoroquinolones. Several antibacterial and antimicrobial-free disinfecting sprays exist.

SSTI in horses may be treated with a selected number of antimicrobial compounds, including penicillin, ampicillin, oxacillin, ceftiofur, cefquinome, amphenicols, gentamicin, tetracycline, (potentiated) sulfonamides and fluoroquinolones. This is due to the fact that horses are naturally highly sensitive for antimicrobials, with respect to the risk of developing dysbacteriosis (Costa et al., 2015; Arnold et al., 2021). Depending on whether the horses are meant for food production or not, the availability might differ.

There are no specific treatment regimens for horse SSTI caused by MRSA. Except from the fact that no β-lactam antibiotics registered for veterinary purpose can be used, treatment options also depend on additional antimicrobial resistances the MRSA strain carries. For example, the equine clade of MRSA CC398 is typically resistant to gentamicin (Cuny and Witte, 2017). In general, it is therefore of utmost importance that the choice of the antimicrobial agent to treat infections caused by multi-resistant staphylococci is based on the result of an antimicrobial susceptibility test (Boyen et al., 2013). It has been reported that antimicrobial agents that are considered to be critically important for the treatment of multidrug-resistant *Staphylococcus* infections in human medicine, such as mupirocin, fusidic acid, linezolid, daptomycin, teicoplanin, vancomycin, tigecycline and streptogramins, which should principally be avoided at all cost, may be occasionally used topically or for regional perfusion therapy in horses (Boyen et al., 2013). Indeed, in case of superficial or local infections, such as SSTI, local treatment with antiseptic or antimicrobial agents should be considered, as this route of treatment not only results in low levels of systemic antimicrobial selection pressure but also allows reaching (very) high antimicrobial concentrations at the infected site, which may result in successful treatment of 'resistant' strains (Boyen et al., 2013).

In several (European) countries, the use of the critically important antimicrobials in animals has been restricted due to antimicrobial resistance concerns. This might lead to the use of 'older' antimicrobials which can have a longer waiting period for the animal to be available for the food chain.

Parameter 2 – Availability/production capacity (per year)

Production capacity is not known to be a problem relating to products used for treatment of AMR *S. aureus* in cattle or horses.

As for the availability, the new EU legislation should make the market better accessible to increase the availability of antimicrobial products throughout Europe, by harmonising the way of distributing products and easing the rules of cascade.

Effectiveness

Parameter 3 – Therapeutic effects in the field (effectiveness)

Antimicrobial therapy during lactation or the dry period results in real or apparent cure rates that are highly variable (from 4% to 92%), depending on a number of factors including herd transmission rates, cow, pathogen and treatment regimen (Barkema et al., 2006; Rainard et al., 2018). As to host-level factors, lower probability of cure is associated with ageing of the cow (primiparous vs. higher parity), high levels of SCC (> 10^6 cells/mL), duration of the mammary infection (> 2–4 weeks), high bacterial load in milk before treatment and number (> 1) and position (hindquarters) of infected quarters. These factors are helpful for selection of the cows that may benefit from treatment and

guide the decision to treat or not. However, herd-level factors such as transmission rates may influence the economic justification for lactational therapy of subclinical *S. aureus* mastitis and should also be considered when making treatment decisions (Rainard et al., 2018).

Pathogen factors also play a role, but with the exception of antimicrobial resistance, they remain poorly defined. Resistance to β-lactam antibiotics is the most well-known antibiotic resistance of *S. aureus* mastitis isolates and it has been shown that the cure rate is lower for penicillin-resistant isolates regardless of the antimicrobial molecule used for treatment (Barkema et al., 2006). This has led to the suggestion to limit the testing for antimicrobial susceptibility to testing sensitivity to penicillin or β-lactamase production before deciding to treat (Rainard et al., 2018). Yet, the mechanisms underlying this association remain poorly understood. Elsewhere in this fact-sheet, information can be found regarding the resistances found in *S. aureus* in IMI, and the EFSA scientific opinion gives a detailed overview of resistance levels worldwide against various compounds (EFSA AHAW Panel, 2021a).

To improve treatment efficacy, variations in combination of drugs, route of application (mammary vs. systemic) and duration of treatment have been applied. There are no guidelines on specific combinations of antimicrobials to circumvent antimicrobial resistance. Some combinations of drugs seem to have synergistic effects, for others like penicillin–neomycin, efficacy is unclear (Barkema et al., 2006). Also, combined treatment by systemic and intramammary routes is not always more effective. Extended treatment is generally associated with a higher probability of cure (Barkema et al., 2006; Rainard et al., 2018; Sartori et al., 2018). It must be taken in consideration that when the same active compound is used, treatment efficacy can differ considerably between different formulations of that compound. It is not always possible to differentiate between the effect of the active compound and the effect of the commercial product and its route or dose of administration (Barkema et al., 2006).

For the alternative treatments cited under Parameter 1 in this section, adequate data on the efficacy are lacking (Barkema et al., 2006; Rainard et al., 2018).

In horses, local treatment of superficial or local infections with antiseptic or antimicrobial agents should be considered. This route of treatment allows reaching high antimicrobial concentrations at the infected site, resulting in successful treatment even if isolates would show acquired or intrinsic resistance (Boyen et al., 2013). The clinical response, which should be monitored frequently, is the main guideline in evaluating the efficacy of local treatments in practice (Boyen et al., 2013).

The prognosis for MRSA infection in horses depends more on the severity and location of the infection than on the fact that MRSA is involved, as long as MRSA is identified early and appropriate antimicrobial therapy is initiated. With appropriate treatment, it is likely that the prognosis for MRSA infection is no different than that for infections caused by susceptible strains (Weese, 2009).

Feasibility

Parameter 4 – Way of administration

Antimicrobial treatment of subclinical or clinical mastitis can be done by only intramammary administration or the combination of intramammary and systemic treatment. For SSTIs, topical and systemic treatments are available.

Recently, guidelines for a more responsible use of antimicrobials, including guidance for avoiding it, have been provided in some European countries (see for example https://www.amcra.be/nl/adviezen-en-wetgeving/ (in Dutch), https://epruma.eu/home/best-practice-guides/). This encompasses describing approaches to implementing responsible use of antibiotics for further optimisation of animal health. In Belgium, the Belgian centre of expertise in Antimicrobial Consumption and Resistance in Animals (AMCRA) provides a free-of-charge website (https://formularium.amcra.be/) formulating responsible use guidelines for the most common diseases in livestock and companion animals.

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

Availability

Parameter 1 – Available biosecurity measures

Biosecurity is the whole set of measures to avoid the introduction of diseases in a herd (external biosecurity) and the dissemination of the disease within a herd (internal biosecurity) (Dewulf and Van Immerseel, 2018).

To avoid re-introducing bacteria into a *S. aureus*-free herd or introducing new lineages into an infected herd, maintaining a closed herd is desirable. When purchasing cows, if necessary for herd expansion or animal replacement, a number of precautions have to be taken (Rainard et al., 2018).

For veterinary clinics, maintaining a closed system is per definition impossible but testing of horses or applying a risk classification of equine patients at admission might be important (van Balen et al., 2014; Walther et al., 2014) yet impractical and expensive (Steinman et al., 2015). Other general external biosecurity measures, like limiting the sources of new 'material' and maintaining strict visitor protocols (Dewulf and Van Immerseel, 2018), might be applicable for dairy and horse farms and veterinary clinics. This might be particularly important for LA-MRSA, as it is likely that its introduction into dairy and veal calf herds results from contamination events from pigs (on mixed farms) or human sources (veterinarians) (Hansen et al., 2019; Schnitt and Tenhagen, 2020). From an external biosecurity point of view, industrial white veal calf farming is extremely challenging, with animals from numerous different farms and countries being mixed under very stressful conditions. There is, however, no indication that specifically the mixing contributes to the introduction of LA-MRSA in the herds. Besides, *S. aureus* is not a pathogen of importance for veal calves. Suspected introductions of MRSA (CC98) in equine clinics through staff members have been described (Steinman et al., 2015; Brennan et al., 2016). For MRSA with a potential wildlife reservoir, like CC133 and *mecC* strains, restricting contact with wildlife, e.g. on pastures, might be relevant.

Internal biosecurity measures are of particular importance for *S. aureus* IMI, since this is deemed mainly a contagious mastitis pathogen (in contrast to environmental pathogens) although it is not always the case (Klaas and Zadoks, 2017). To contain contagious *S. aureus* mastitis, implementation of standard mastitis prevention measures is usually effective (Rainard et al., 2018). These measures have been drafted in mastitis control plans, variants of which have been based on the original 5-points plan (Neave et al., 1969; Ruegg, 2017), like the 10-point Mastitis Control Program of the National Mastitis Council (https://www.nmconline.org/wp-content/uploads/2016/08/RECOMMENDED-MASTITIS-CONTROL-PROGRAM-International.pdf, with a variant specifically for heifer mastitis: https://www.nmconline.org/wp-content/uploads/2018/04/NMC-Factsheet-Heifer-Mastitis-and-Control.pdf), a 7-point plan (https://m2-magazine.org/7-point-plan-mastitis-control/), national plans in Norway (Osterås and Sølverød, 2009) and Switzerland (Kirchhofer et al., 2011), or still other variants (Lam et al., 2013; Sartori et al., 2018).

In essence, such plans come down to some general principles as described for example by the Food and Agriculture Organization of the United Nations (FAO) (https://www.fao.org/3/t0218e/t0218e04.htm):

- Adopt good cow management practices (e.g. feeding, housing, hygiene, etc.);
- Reduce exposure to pathogens (e.g. through equipment cleaning, post- and pre-milk teat-dipping, etc.);
- Reduce the chances of pathogens penetrating the teat duct (e.g. by maintenance of milk equipment to ensure stable teat end vacuum, etc.);
- Reduce the duration of infections (e.g. by culling of chronically affected cows and treating cows at drying off);
- Reduce mastitis in non-lactating growing cattle or cows in the dry period (e.g. by adopting fly control measures, as horn flies are considered possible vectors for *S. aureus* mastitis in dairy heifers (Owens et al., 1998; Anderson et al., 2012), and by treating cows at drying off and using dry cow teat sealant).

For containing MRSA outbreaks and to avoid spreading (AMR) *S. aureus* in horse clinics, some major internal biosecurity principles, including (personal) hygiene measures, internal screening procedures, cleaning and disinfection practices and isolation of affected animals can be applied (Bergström et al., 2012; Boyen et al., 2013; Steinman et al., 2015; Rocktäschel et al., 2020).

Effectiveness

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

In general, mastitis control plans have been very effective to reduce *S. aureus* contagious mastitis (Sartori et al., 2018). This appears to be similar for MRSA, as also proper milking-time hygiene and techniques are needed to prevent spread of MRSA within dairy herds (Locatelli et al., 2017; Schnitt et al., 2020). In some herds, however, these classical control measures appear to be ineffective because of the occurrence of infections by *S. aureus* strains of type patterns similar to that of environmental pathogens, requiring alternative measures such as managing bacterial load in bedding material or choosing appropriate bedding and housing to avoid injury (Klaas and Zadoks, 2018; Rainard et al., 2018; Leuenberger et al., 2019). Within a farm, multiple epidemiological types of

S. aureus might be present (Rainard et al., 2018; Leuenberger et al., 2019). The roles of extra-mammary colonisation of healthy persistent carriers and of environmental sources as a reservoir for IMI are not well defined, and the drivers of the shift from colonisation to IMI still needs to be investigated using modern molecular epidemiological methods (Rainard et al., 2018).

Considering horses, given that introduction of new animals in a clinic is mostly on an individual basis and that MRSA can be introduced on multiple occasions in a clinic (van Balen et al., 2014; Bortolami et al., 2017), testing (based on a risk classification) can be expected to be effective to identify (AMR) *S. aureus* carriers upon admission (Weese and Lefebvre, 2007). However, this approach might be impractical and expensive (Steinman et al., 2015). Infection control measures such as passive surveillance, where horses in which MRSA infection is suspected are tested and from each case of post-operative wound infection a horse swab is sent for culture and antimicrobial susceptibility testing, are effective to reduce the risk for recurring MRSA infections (Steinman et al., 2015). This can be combined with decolonisation treatment of carrier personnel, isolation of all horses colonised or infected with MRSA and discharge of these horses as soon as medically feasible (Steinman et al., 2015). Internal screening procedures incorporating high-risk areas (such as intensive care units) or equipment (anaesthetic machine y-piece) in routine environmental bacterial monitoring, allow quick intervention and implementation of enhanced cleaning and disinfection, leading to elimination of likely reservoirs for veterinary hospital-acquired infections and the containment of transmission between horses and personnel (van Balen et al., 2014; Steinman et al., 2015; Bortolami et al., 2017).

On two Canadian horse farms, active screening and strict implementation of infection control protocols resulted in a rapid decrease in the number of colonised horses (Weese and Rousseau, 2005). Noteworthy, some major subsets of the equine population, such as breeding farms, are characterised by the frequent contact of horses with veterinary personnel, frequent antimicrobial use (AMU), regular inter-farm movement of horses and care by a constant group of farm personnel that may concurrently be managing sick horses (Weese and Lefebvre, 2007). In general, horses have frequent contact with other horse populations, and considering furthermore the fact that the identification of carrier or colonised horses most likely does not reach 100% sensitivity and the lack of efficient decolonisation protocols for horses (Boyen et al., 2013), preventing MRSA introduction into horse farms is likely challenging.

Feasibility

Parameter 3 – Feasibility of biosecurity measures

The feasibility of the standard mastitis control plans is illustrated by the fact that their broad implementation has been very effective in reducing contagious *S. aureus* mastitis. The elements therein relating to biosecurity mostly concern cleaning, disinfecting and maintenance, and are not difficult or costly, but require a certain dedication and routine. This also accounts for MRSA, as also proper milking-time hygiene and techniques are needed to prevent spread of MRSA within dairy herds (Locatelli et al., 2017; Schnitt et al., 2020). However, a difficulty in applying the standard mastitis control plans for contagious *S. aureus* and for MRSA is the fact that dry-cow therapy cannot be done with β-lactam antimicrobials (Schnitt and Tenhagen, 2020).

Also successfully applying internal biosecurity measures in equine clinics require dedication and routine (Boyen et al., 2013; Steinman et al., 2015). Rigorous application of external biosecurity measures might be more difficult considering that truly closed environments are difficult or impossible to obtain, and humans, including the veterinarian, can be the source of introduction. This accounts for horses as well as cattle. Modern genotyping tools might be a valuable asset to inform biosecurity measures (Sartori et al., 2018).

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

Availability

Parameter 1 – Available movement restriction measures

Except for common external biosecurity measures, restricting the (economic) movements of animals and products is not considered an important prevention and control measure for AMR *S. aureus* in cattle and horses.

Effectiveness

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

No data were found to assess the effectiveness of restricting (economic) animal movements in preventing spread of AMR *S. aureus* between farms or clinics.

Feasibility

Parameter 3 – Feasibility of restriction of animal movement

Restricting animal movement may be feasible but would seriously disrupt the normal production practices in cattle and horse farming, and is per definition impossible for veterinary clinics. Even though carriage of AMR *S. aureus* is a risk factor for both IMI in dairy cows and SSTI in horses, introduction of AMR *S. aureus* into a herd or clinic will not necessarily lead to serious disease outbreaks, questioning the feasibility of restricting the animal movement. Furthermore, AMR *S. aureus* can also have an in-farm environmental or endemic presence, which will not be avoided with restricting animal movements.

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

Availability

Parameter 1 – Available methods for killing animals

As noted in Section 3.1.1.4, culling of chronically affected dairy cows is part of the standard mastitis prevention plans. Chronic infections that have resisted one or two treatments are considered impossible to cure, and culling is the best solution to reduce the risk of infection spread within the herd (Rainard et al., 2018). Resistance to treatment can be related to antimicrobial resistance, but it is unclear whether (LA-) MRSA IMI has a higher risk for culling. Chronic IMI is considered to be rather due to factors like immune-evasion, cell internalisation, biofilm formation and the forming of small colony variants (Grunert et al., 2018; Rainard et al., 2018).

In beef cattle, veal calves and horses, killing is not considered an available method for controlling or preventing (AMR) *S. aureus*.

Effectiveness

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

It is not known to what extent the culling step in the mastitis control programmes has contributed to the overall success of the programmes in reducing (contagious) *S. aureus* IMI, and there are no data available specifically for IMI caused by AMR *S. aureus*. However, culling is considered the best solution to reduce the risk of infection spread within the herd in case of chronic IMI (Rainard et al., 2018).

Feasibility

Parameter 3 – Feasibility of killing animals

Culling is not a purely epidemiological measure, as welfare issues, social and psychological factors and particularly economic considerations play a vital part (Lehenbauer and Oltjen, 1998; Haine et al., 2017). As the probability of cure has a large impact on the economic benefit of treatment, cost-benefit analyses are necessary before application of any treatment, including side effects like the persistence of infected cows in a herd as a source of new contaminations (Rainard et al., 2018). When deciding to apply culling, care must be taken to have used diagnostic tools with sufficient discriminatory power in order to distinguish contagious with sporadic *S. aureus* IMI cases (Rainard et al., 2018).

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

Availability

Parameter 1 – Available disposal option

No specific disposal measures are taken when live animals or carcasses are affected with AMR *S. aureus*. In fact, MRSA is frequently found on carcasses meant for consumption (Sergelidis and Angelidis, 2017), but apart from standard disinfection procedures and personal hygiene protective measures for slaughterhouse workers, no actions are taken.

Discarding milk is not an epidemiological measure for preventing or controlling spread of AMR *S. aureus*.

No information was found on any specific measures for disposal of horse carcasses or by-products affected by AMR *S. aureus*.

Effectiveness

Parameter 2 – Effectiveness of disposal option

Disposal of carcasses and milk is not considered a measure for preventing or controlling spread of AMR *S. aureus*.

Feasibility

Parameter 3 – Feasibility of disposal option

The procedures for disposal of carcasses and milk affected by AMR *S. aureus* do not differ from the standard methods used for carcasses and milk unaffected by AMR *S. aureus*.

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)

There can be a certain additional cost when mastitis is caused by an AMR *S. aureus* compared to a sensitive *S. aureus*. For example, treatment of young animals with moderate SCC elevation and IMI with penicillin-sensitive *S. aureus* strains is economically viable, but treatment of older animals with strongly elevated SCC and IMI with penicillin-resistant *S. aureus* is not (Barkema et al., 2006). Due to the high variation in the probability of cure between animals, the importance of additional factors (e.g. transmission rate, cow age, costs of antibiotics and discarded milk, etc.) and the variation in regulatory and economic conditions between countries (Barkema et al., 2006), the cost of control for AMR *S. aureus* likely plays at 'case level' and is difficult to assess at sector or national level. Even though several countries have their own variants of a mastitis control programme, the cost of this is not clear. It has been reported that applying a Dutch mastitis control programme, farm-specific costs could decrease with €400, leading to a total possible reduction in the sector of €8 million (Lam et al., 2013). The part (AMR) *S. aureus* plays in this is however unclear. In cattle, antimicrobial resistance is only one of a number of factors influencing treatment success for *S. aureus* mastitis and it is reasonable to expect the costs for control measures specifically for AMR *S. aureus* in dairy cattle IMI to be similar to those for control measures due to regular *S. aureus*.

In beef cattle or veal calves, AMR *S. aureus* is considered an occasional opportunistic pathogen, likely acting as regular *S. aureus*. Specific control measures are not in place for (AMR) *S. aureus* in these species.

For horses, specifically in horse clinics additional costs may emerge for adapting health management and biosecurity protocols to avoid entrance and spread of AMR *S. aureus*. However, these measures will have in theory a general positive effect on containment of regular *S. aureus* and other diseases as well, and if the additional costs would be measurable, it might not be clear what part would need to be allocated to AMR *S. aureus* specifically.

No information was found on the additional costs that might be brought by treatment failures due to antimicrobial resistance in horses.

Parameter 2 – Cost of eradication (culling, compensation)

There is no information available on the cost of culling specifically of cows suffering from AMR *S. aureus* IMI. In beef cattle, veal calves or horses, eradication due to (AMR) *S. aureus* infections is not feasible.

Parameter 3 – Cost of surveillance and monitoring

Worldwide, numerous studies have been performed the last two decades into the presence and epidemiology of especially LA-MRSA in animals, including cattle and horses. The cost of these is not clear.

In Europe, Commission Implementing Decision (EU) 2020/1729[2] does not include monitoring and reporting of antimicrobial resistance in *S. aureus*. However, EFSA recommends a periodically, harmonised monitoring and reporting of AMR in MRSA in food producing animals and food in accordance with Directive 2003/99/EC[3] (EFSA, 2012, 2021). Among the recommendations on the food-producing animals for MRSA monitoring, it is recommended to perform consistently on a regular basis (every third year) a monitoring of bulk tank milk samples on dairy farms and of nasal swabs of fattening veal calves (under 1 year of age) at the slaughterhouse (if production exceeds 10 million tonnes slaughtered/year). For beef animals and horses, a voluntary monitoring is recommended, also every third year, of nostril swabs to be collected at the slaughterhouse. Furthermore, it is recommended to collect, on a voluntary base, every third year, samples of fresh meat of bovines and veal at the cutting plant or retail, and of raw milk (products) at the dairy processing plant or retail. Prevalence data, *spa*-typing and MLST data are requested. Furthermore, antimicrobial resistance data to a set of antimicrobials is requested on a voluntary base (EFSA, 2012, 2021). The overall cost this brings to each MS is unclear.

Specific monitoring programmes might exist in individual farms or clinics, but they are not applied at sector or national level, hence no information on the cost of this was found.

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

Bans or sanctions have not been applied due to AMR *S. aureus* in cattle or horses, and hence information on trade losses is unavailable.

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

Mastitis is described as the most costly disease in the dairy sector (Halasa et al., 2007). Although several models have been developed to estimate the costs of mastitis and associated containment measures (Huijps et al., 2008), the costs specifically for *S. aureus* mastitis is not known, hence, neither is the specific impact of antimicrobial resistance. A rough estimation could be done when assuming that the weight *S. aureus* has as a causative agent of clinical mastitis is approximately 10% (Olde Riekerink et al., 2008; Verbeke et al., 2014; Chung et al., 2021), and approximately 20% for subclinical mastitis (Bradley et al., 2007; Chung et al., 2021); relating this to the estimated cost per case of clinical mastitis and subclinical mastitis of €287 and €102, respectively (Halasa et al., 2007). However, in some countries, highly differing weights have been found (e.g. Bradley et al. (2007): 3.3% in clinical mastitis, Keane (2019): 23% in clinical mastitis) and this assumption does not take into account the highly varying resistance rates reported for *S. aureus* (Barkema et al., 2006), specifically for MRSA (Schnitt and Tenhagen, 2020).

The financial importance of AMR *S. aureus* is not known for other cattle and horses.

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

In several countries, in the EU but also worldwide, initiatives have been set up to work towards sustainable and altogether lowered AMU in animals, including horses and cattle. Such initiatives can concern the set-up of dedicated organisations that try to achieve a reduced, responsible AMU in animals (for example the Netherlands Veterinary Medicines Institute, AMCRA, the European Platform for the Responsible Using of Medicines in Animals (EPRUMA) at the European level, etc.). Their work includes publishing guidelines for improved disease prevention and control measures in clinics or farms or AMU best-practice guidelines (see for example https://www.amcra.be/nl/adviezen-en-wetgeving/ (in Dutch), https://epruma.eu/home/best-practice-guides/). This encompasses describing approaches to implementing responsible use of antibiotics for further optimisation of animal health, guidance on housing, biosecurity, nutrition, etc., and presenting a decision tree on the use of veterinary antibiotics in food-producing animals. In Belgium, AMCRA provides a free-of-charge website (https://formularium.amcra.be/) formulating responsible use guidelines for the most common diseases in livestock and companion animals.

[2] Commission Implementing Decision (EU) 2020/1729 of 17 November 2020 on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria and repealing Implementing Decision 2013/652/EU (notified under document C (2020) 7894). OJ L 387, 19.11.2020, p. 8–21.

[3] Directive 2003/99/EC of the European Parliament and of the Council of 17 November 2003 on the monitoring of zoonoses and zoonotic agents, amending Council Decision 90/424/EEC and repealing Council Directive 92/117/EEC. OJ L 325, 12.12.2003, p. 31–40.

In general, the public and political awareness and attention for AMU in animals, and the measures required to achieve a sustainable reduction, have increased over the years (e.g. https://fve.org/fve-congratulates-the-european-parliament-for-taking-a-one-health-approach-and-voting-for-science-based-regulation-in-europe/). Despite this subjective perception of a growing societal awareness on the issues of AMU and antimicrobial resistance in animals, data that objectively measure this, specifically for AMR *S. aureus*, were not found. It is furthermore difficult to know whether society truly accepts the existing or possible measures as that assumes society is fully aware of and understands the implications of these measures. In the UK and the USA, farmers believed that misconceptions existed with consumers about AMU in agriculture and felt that consumers believed raising animals without antibiotics would significantly improve animal welfare. Subsequently, farmers believe consumer misconceptions and marketing strategies are driving regulations, thus endangering agricultural sustainability in the future (McKernan et al., 2021).

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

Animal welfare could, e.g. be impacted by treatment failure hence prolonged disease conditions, by the forceful application due to antimicrobial resistance of antimicrobial therapy that has adverse effects (compared to the product(s) of first choice), by delaying or avoiding antimicrobial therapy due to AMU monitoring regulations (if e.g. applying further therapy would mean trespassing a usage threshold leading to penalties), or by market-driven schemes for animals to be raised without antibiotics (McKernan et al., 2021). Also isolating animals to avoid further spread of AMR *S. aureus*, preventing animals to display their normal social behaviour, might be suspected to impair welfare. There is little data available to quantitatively or qualitatively assess welfare impact of those factors. However, farmers and vets have been found to worry that reduced AMU, for example by legislative restrictions feared to threaten their future ability to treat sick animals effectively, would compromise animal health and welfare (McKernan et al., 2021).

Parameter 2 – Wildlife depopulation as control measure

Wildlife depopulation is not applied as a control measure for AMR *S. aureus* in domestic animals.

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)

No data are available that allow to assess the impact of biocides, antimicrobials or other medical drugs, used for control of AMR *S. aureus* in cattle and horses, on the environment and biodiversity. Clearly, residues in more or less active form, including critically important antimicrobials like fluoroquinolones, are heavily dispersed into the environment through manure application on fields, especially in heavy-using sectors like the veal calf sector (Huygens et al., 2021). In Belgium for example, use of fluoroquinolones is legally prohibited to cases where laboratory testing data proof that no other antimicrobials are effective for the disease, hence indicative for the occurrence of antimicrobial resistance in the involved bacteria. Manure might also contain AMR bacteria itself, for example *E. coli* (Huygens et al., 2021). The role specifically of AMR *S. aureus* in this is unclear.

Biodiversity

Parameter 1 – Mortality in wild species

There are no reports on mortality in wildlife species due to control measures for control and prevention of *S. aureus* infections in cattle or horses.

3.2. Assessment of AMR *Staphylococcus aureus* 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 12 and Figure 1, the results of the expert judgement on the Article 5 criteria of the AHL for AMR *S. aureus* in cattle and horses are presented.

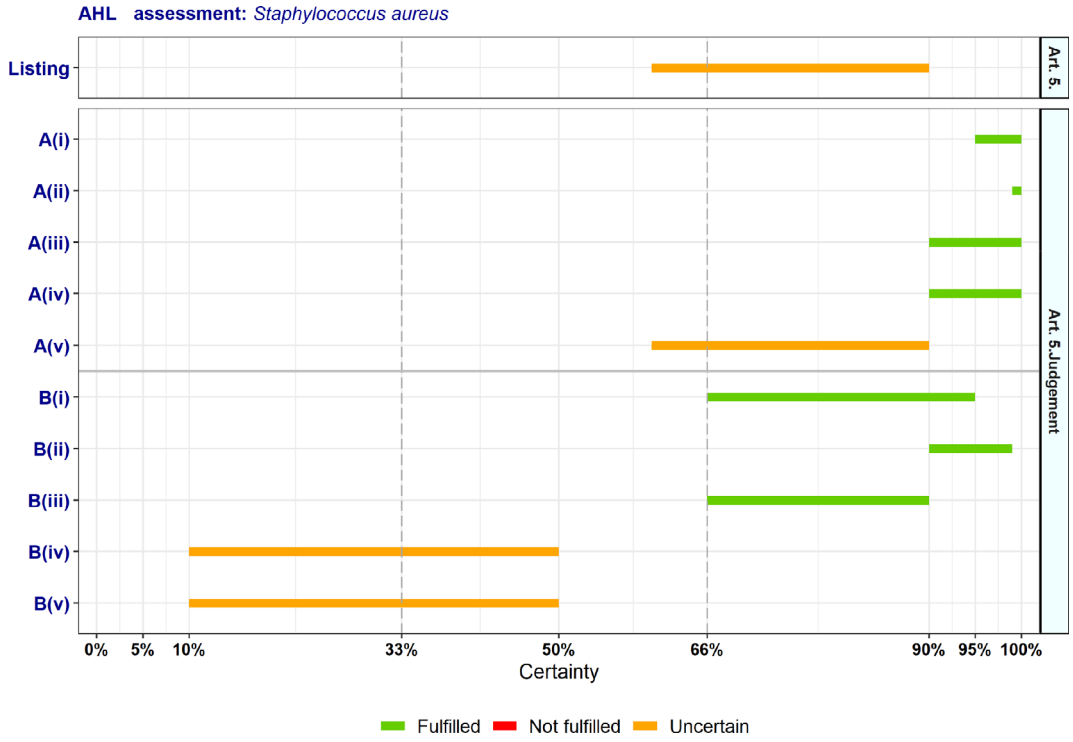
The distribution of the individual answers (probability ranges) provided by each expert for each criterion are reported in Sections A.1 and A.2 of Appendix A.

Table 12: Outcome of the expert judgement on Article 5 criteria

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**
A(i)	The disease is transmissible	95–100	Fulfilled	0	12
A(ii)	Animal species are either susceptible to the disease or vectors and reservoirs thereof exist in the Union	99–100	Fulfilled	0	12
A(iii)	The disease causes negative effects on animal health or poses a risk to public health due to its zoonotic character	90–100	Fulfilled	0	12
A(iv)	Diagnostic tools are available for the disease	90–100	Fulfilled	0	12
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	60–90	Uncertain	0	12
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	66–95	Fulfilled	0	12
B(ii)	The disease agent has developed resistance to treatments which poses a significant danger to public and/or animal health in the Union	90–99	Fulfilled	0	12
B(iii)	The disease causes or could cause a significant negative economic impact affecting agriculture or aquaculture production in the Union	66–90	Fulfilled	0	12
B(iv)	The disease has the potential to generate a crisis or the disease agent could be used for the purpose of bioterrorism	10–50	Uncertain	0	12
B(v)	The disease has or could have a significant negative impact on the environment, including biodiversity, of the Union	10–50	Uncertain	0	12

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 *S. aureus* 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)

- A large array of diagnostic, therapeutic and prophylactic tools exist, but (AMR) *S. aureus* is still a major animal health problem.
- Preventive measures are available and relate mainly to hygienic, biosecurity and health management practices, which are effective if applied appropriately and considered as proportionate.
- Differences in effectiveness and feasibility exist between species and production systems, e.g. for mastitis in dairy cows prevention and control systems exist in several MSs and are considered as effective, whereas in others it may not be the case.
- Vaccines are available, but their efficacy is controversial.

Criterion B(iv) (the disease has the potential to generate a crisis or the disease agent could be used for the purpose of bioterrorism)

- Enterotoxins may be used for bioterrorism, but not the bacterium itself. The presence of the toxin is linked neither to disease prevalence nor to antimicrobial resistance.
- *S. aureus* is already widespread and considered to have a limited potential for causing a crisis due to the low mortality rate. Uncertainty remains if AMR strains have higher potential.

Criterion B(v) (the disease has or could have a significant negative impact on the environment, including biodiversity, of the Union)

- AMR strains have been isolated from several wild species, but it is not clear whether fatal infections in wild animals also include AMR strains.
- There is a large degree of uncertainty as to whether AMR strains can cause a significant negative impact on wildlife, as wild animals are normally not treated (with some exceptions in rehabilitation centres or game animal holdings before releasing them into the wild).

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 12, AMR *S. aureus* complies with four criteria of the first set (A(i)–A(iv)), but there is uncertainty (60–90% probability) on the assessment on compliance with Criterion A(v). Therefore, it is uncertain whether AMR *S. aureus* 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 60–90% (Figure 1).

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

In Tables 13–17 and related graphs (Figures 2–4), the results of the expert judgement on AMR *S. aureus* in cattle and 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 are reported in Sections B.1 and B.2 of Appendix B.

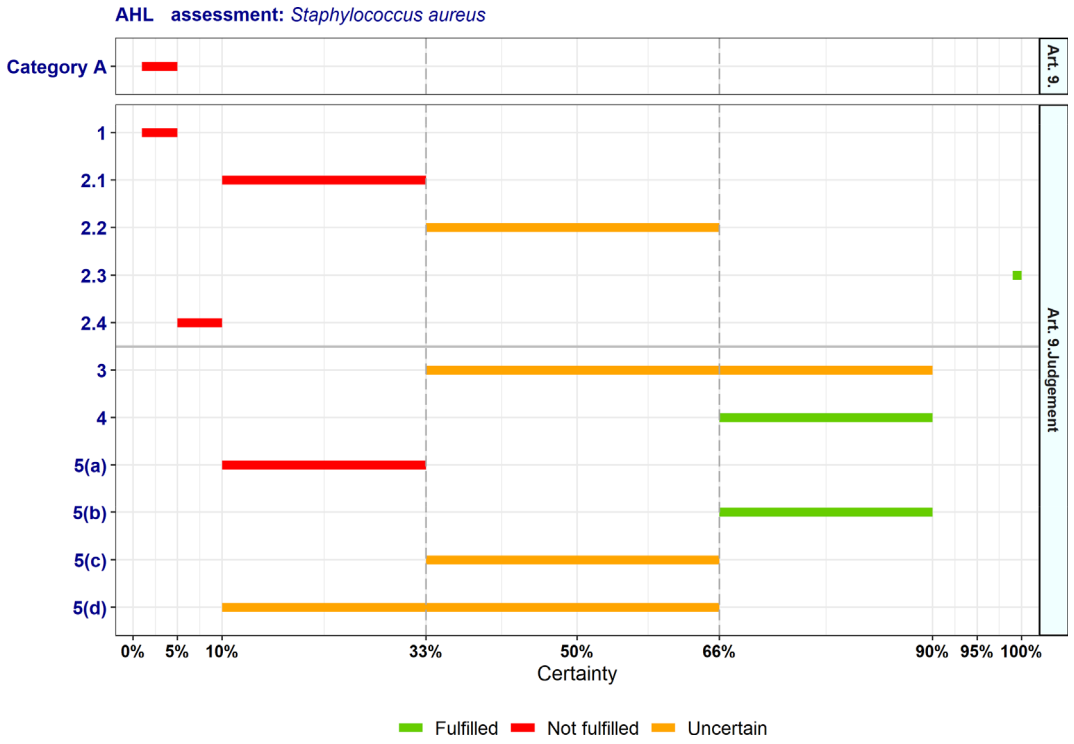
3.3.1. Detailed outcome on Category A criteria

Table 13: 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	1–5	Not fulfilled	0	12
2.1	The disease is highly transmissible	10–33	Not fulfilled	0	12
2.2	There are possibilities of airborne or waterborne or vector-borne spread	33–66	Uncertain	0	12
2.3	The disease affects multiple species of kept and wild animals or single species of kept animals of economic importance	99–100	Fulfilled	0	12
2.4	The disease may result in high morbidity and significant mortality rates	5–10	Not fulfilled	0	12
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	33–90	Uncertain	0	12
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	66–90	Fulfilled	0	12
5(a)	The disease has a significant impact on society, with in particular an impact on labour markets	10–33	Not fulfilled	0	12
5(b)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	66–90	Fulfilled	0	12

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	33–66	Uncertain	0	12
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	10–66	Uncertain	0	12

na: not applicable.



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

- Long-distance airborne spread of *S. aureus* is not common, but local airborne spread via dust may occur.
- Local transmission via vectors (house and stable flies) is reported.
- (AMR) *S. aureus* has been found in water, but long-distance waterborne spread has not been observed.

Criterion 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):

- Animal-to-human transmission of AMR strains is well documented and results in general in asymptomatic infection or intermittent carriage, but also very severe cases including fatalities occur.
- As an opportunistic pathogen that is already endemic worldwide, pandemic potential is considered to be limited.

- There is a potential for significant consequences for public health, as a longer-term risk of zoonotic transfer is the development of host adaptation, with the potential to introduce new clones with the capacity for pandemic spread in humans.
- Contaminated food products are a possible source of human infections but seem to be a minor risk. Food safety could be an issue via the consumption of contaminated raw milk.

Criterion 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)

- AMR strains may contaminate the environment around affected farms, but the impact thereof is still unclear.
- Several wild species show infection with AMR strains potentially transmitted by farms via the environment, but this does not necessarily imply a significant impact. A major change of the proportion of MRSA may, however, have a significant impact on the environment.
- Antimicrobial residues can accumulate in the environment and major use of chemicals as a hygienic measure may affect the environment.

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):

- AMR strains were found in protected species, but their importance in causing also fatal infections is unclear, although the potential seems to be real (fatal infections in wildlife have sporadically been reported including endangered species).
- There is uncertainty as to how significant the impact on biodiversity is. It may be more significant in case of spread of AMR clones or absence of control.
- The sole detection of AMR *S. aureus* in many species does not necessarily imply a significant impact.

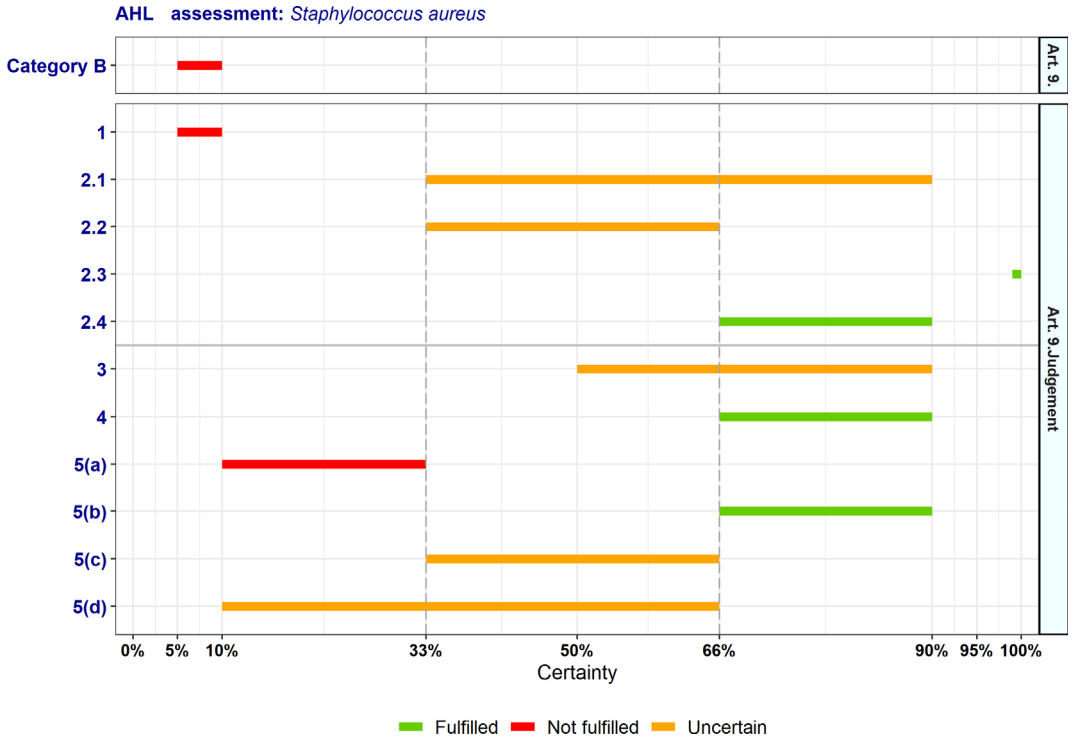
3.3.2. Detailed outcome on Category B criteria

Table 14: 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	5–10	Not fulfilled	0	12
2.1	The disease is moderately to highly transmissible	33–90	Uncertain	0	12
2.2	There are possibilities of airborne or waterborne or vector-borne spread	33–66	Uncertain	0	12
2.3	The disease affects single or multiple species	–	Fulfilled	0	12
2.4	The disease may result in high morbidity with in general low mortality	66–90	Fulfilled	0	12
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	50–90	Uncertain	0	12
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	66–90	Fulfilled	0	12

5(a)	The disease has a significant impact on society, with in particular an impact on labour markets	10–33	Not fulfilled	0	12
5(b)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	66–90	Fulfilled	0	12
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	33–66	Uncertain	0	12
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	10–66	Uncertain	0	12

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):

- Most evidence suggests low to moderate transmissibility, but it is unknown whether MRSA is more transmissible than non-resistant *S. aureus* strains.
- Different transmissibility rates were observed in dairy cows, where low levels of shedding were reported, and in veal calves, where rapid and more extensive spread was observed, suggesting a high transmissibility under certain conditions.

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

Criterion 3 (the disease has a zoonotic potential with significant consequences for public health, including epidemic potential, or possible significant threats to food safety):

- There is clear evidence of zoonotic transmission.

- AMR strains from cattle and horses are currently present with no apparent epidemic and pandemic potential or significant impact on public health.
- Some strains of MRSA may cause local outbreaks with epidemic characteristics.
- Contact with and consumption of contaminated food products (carcasses, meat, milk) have been described as possible sources of MRSA in humans, but this is generally considered only a minor risk.

Criterion 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): See above in Section 3.3.1.1.

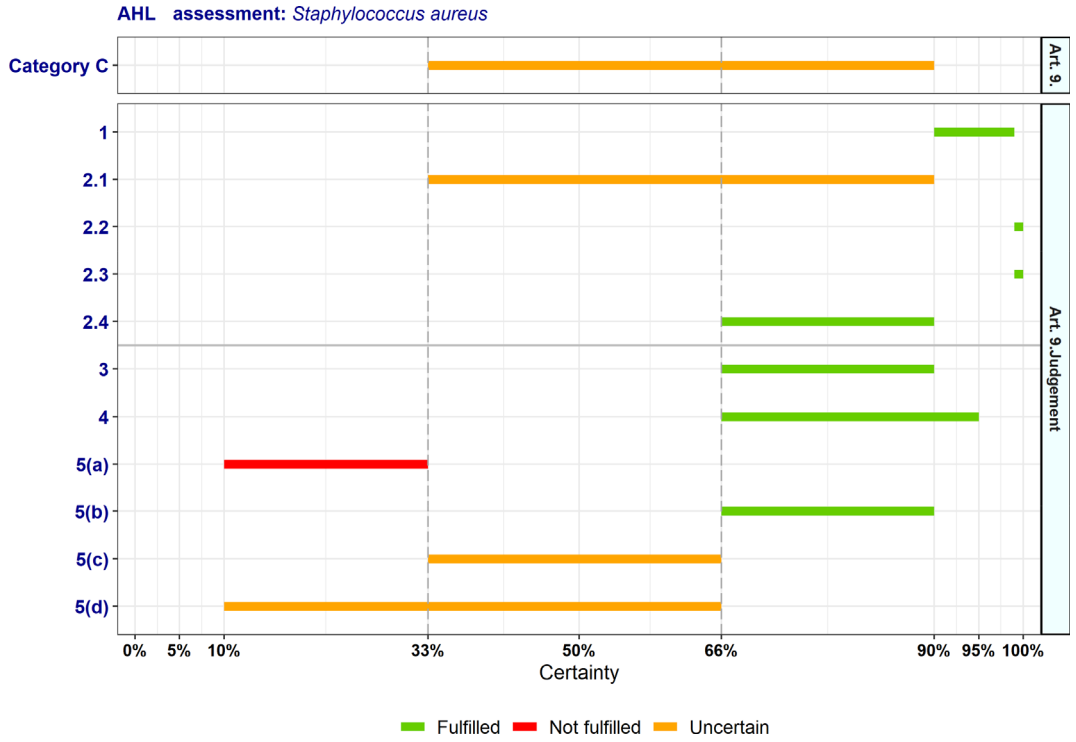
Criterion 5(d) (the disease has a significant impact in the long term on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds): See above in Section 3.3.1.1.

3.3.3. Detailed outcome on Category C criteria

Table 15: 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	90–99	Fulfilled	0	12
2.1	The disease is moderately to highly transmissible	33–90	Uncertain	0	12
2.2	The disease is transmitted mainly by direct or indirect transmission	–	Fulfilled	0	12
2.3	The disease affects single or multiple species	–	Fulfilled	0	12
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	66–90	Fulfilled	0	12
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	66–90	Fulfilled	0	12
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	66–95	Fulfilled	0	12
5(a)	The disease has a significant impact on society, with in particular an impact on labour markets	10–33	Not fulfilled	0	12
5(b)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	66–90	Fulfilled	0	12
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	33–66	Uncertain	0	12
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	10–66	Uncertain	0	12

na: not applicable.



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

Criterion 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): 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 16: 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	10–33	Not fulfilled	0	12

na: not applicable.

3.3.5. Detailed outcome on Category E criteria

Table 17: 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.)	60–90	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 13–17. 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 *S. aureus* as in Article 9, is presented in Table 18 and Figure 5.

Table 18: Outcome of the assessment on criteria in Annex IV of the AHL for the purpose of categorisation as in Article 9

	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)**
Category	**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	1–5	10–33	33–66	99–100	5–10	33–90	66–90	10–33	66–90	33–66	10–66
B	5–10	33–90	33–66	–	66–90	50–90	66–90	10–33	66–90	33–66	10–66
C	90–99	33–90	–	–	66–90	66–90	66–95	10–33	66–90	33–66	10–66
D	10–33										
E	60–90										

Probability ranges (% certainty; –: criterion fulfilled by default) and fulfilment of criteria (green: fulfilled; red: not fulfilled; orange: uncertain) (EFSA AHAW Panel, 2017).

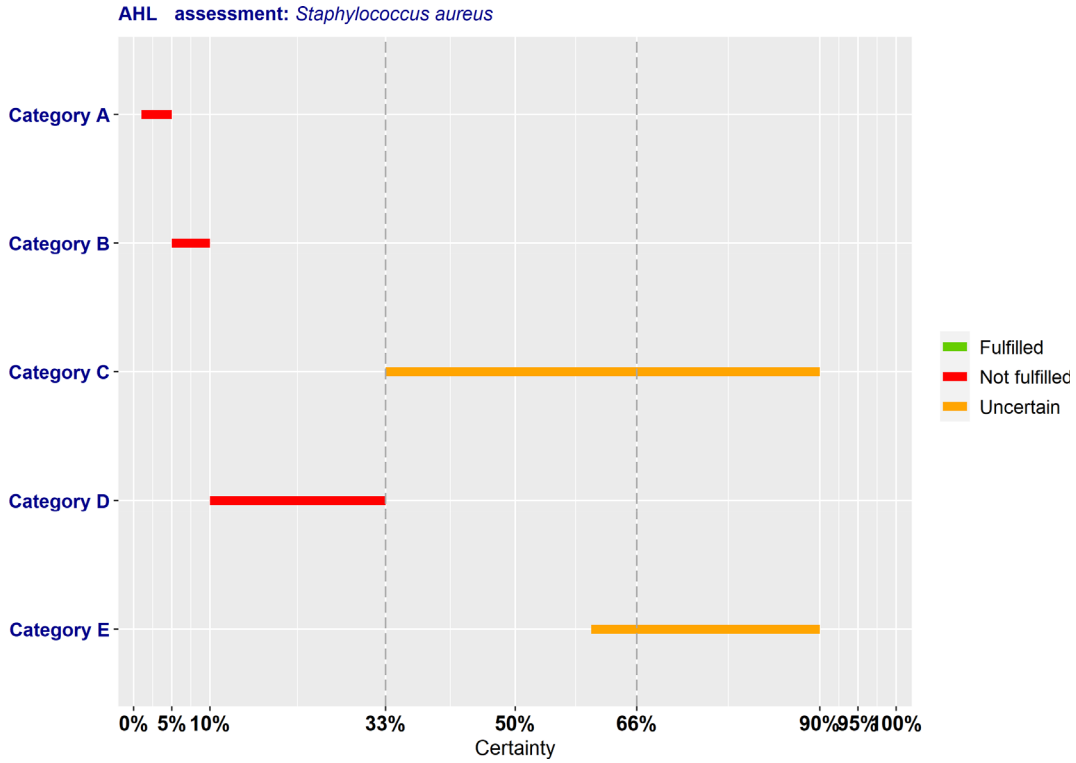


Figure 5: Outcome of the expert judgement on criteria in Annex IV and overall probabilities for categorisation of the AMR bacterium in accordance with Article 9

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

1) To be assigned to Category A, a disease needs to comply with all criteria of the first set (1, 2.1–2.4) and, according to the assessment, AMR *S. aureus* complies only with Criterion 2.3 (99–100% probability). The assessment was inconclusive on compliance with Criterion 2.2 (33–66% 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 *S. aureus* complies with Criteria 4 (66–90% probability) and 5(b) (66–90% probability). The assessment was inconclusive on compliance with Criteria 3 (33–90% probability), 5(c) (33–66% probability) and 5(d) (10–66% probability). Overall, it was assessed with 1–5% probability that AMR *S. aureus* 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 *S. aureus* complies only with Criteria 2.3 (fulfilled by default) and 2.4 (66–90% probability). The assessment was inconclusive on compliance with Criteria 2.1 (33–90% probability) and 2.2 (33–66% 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 *S. aureus* complies with Criteria 4 (66–90% probability) and 5(b) (66–90% probability). The assessment was inconclusive on compliance with Criteria 3 (50–90% probability), 5(c) (33–66% probability) and 5(d) (10–66% probability). Overall, it was assessed with 5–10% probability that AMR *S. aureus* 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 *S. aureus* complies with Criteria 1 (90–99% probability), 2.2 (fulfilled by default), 2.3 (fulfilled by default) and 2.4 (66–90% probability). The assessment was inconclusive on compliance with Criterion 2.1 (33–90% 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 *S. aureus* complies with Criteria 3 (66–90% probability), 4 (66–95% probability) and 5(b) (66–90% probability). The assessment was inconclusive on compliance with Criteria 5(c) (33–66% probability) and 5(d) (10–66% probability). Overall, it was assessed with 33–90% probability that AMR *S. aureus* 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 Section 1, 2, 3 or 5 of Annex IV of the AHL and with the specific Criterion D of Section 4, with which AMR *S. aureus* does not comply (10–33% 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 is inconclusive (60–90% probability of fulfilling the criteria).

3.4. Assessment of AMR *Staphylococcus aureus* 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 *S. aureus* 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.[4]

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 *S. aureus* according to the criteria of Article 8(3) of the AHL include mainly mammals, birds, reptiles and fish.

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 (60–90% probability) whether AMR *S. aureus* can be considered eligible to be listed for Union intervention as laid down in Article 5 of the AHL.

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 1–5% probability ('extremely unlikely') that AMR *S. aureus* 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.

[4] 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.

- The AHAW Panel considered with 5–10% probability ('very unlikely') that AMR *S. aureus* 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 (33–90% probability, from 'as likely as not' to 'likely') whether AMR *S. aureus* 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 considered with 10–33% probability ('unlikely') that AMR *S. aureus* 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 (60–90% probability) whether AMR *S. aureus* 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 *S. aureus* according to Article 8(3) of the AHL include mainly mammals, birds, reptiles and fish.

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 *S. aureus* is inconclusive on its eligibility to be listed for Union intervention, specific initiatives (e.g. monitoring or applied research) into various aspects of AMR *S. aureus* can be useful to better understand its distribution and to assess its impact on animal health and welfare in the EU.

References

Abb-Schwedler K, Maeschli A, Boss R, Graber HU, Steiner A and Klocke P, 2014. Feeding mastitis milk to organic dairy calves: effect on health and performance during suckling and on udder health at first calving. BMC Veterinary Research, 10, 1–11. https://doi.org/10.1186/s12917-014-0267-7

Abdelbary MM, Wittenberg A, Cuny C, Layer F, Kurt K, Wieler LH, Walther B, Skov R, Larsen J, Hasman H, Fitzgerald JR, Smith TC, Wagenaar JA, Pantosti A, Hallin M, Struelens MJ, Edwards G, Böse R, Nübel U and Witte W, 2014. Phylogenetic analysis of *Staphylococcus aureus* CC398 reveals a sub-lineage epidemiologically associated with infections in horses. PLoS One, 9, e88083. https://doi.org/10.1371/journal.pone.0088083

Aires-de-Sousa M, 2017. Methicillin-resistant *Staphylococcus aureus* among animals: current overview. Clinical Microbiology and Infection, 23, 373–380.

Akkou M, Bouchiat C, Antri K, Bes M, Tristan A, Dauwalder O, Martins-Simoes P, Rasigade JP, Etienne J, Vandenesch F, Ramdani-Bouguessa N and Laurent F, 2018. New host shift from human to cows within *Staphylococcus aureus* involved in bovine mastitis and nasal carriage of animal's caretakers. Veterinary Microbiology, 223, 173–180. https://doi.org/10.1016/j.vetmic.2018.08.003

Albert E, Biksi I, Német Z, Csuka E, Kelemen B, Morvay F, Bakos Z, Bodó G, Tóth B, Collaud A, Rossano A and Perreten V, 2019. Outbreaks of a methicillin-resistant *Staphylococcus aureus* Clone ST398-t011 in a hungarian equine clinic: emergence of rifampicin and chloramphenicol resistance after treatment with these antibiotics. Microbiological Drug Resistance, 25, 1219–1226. https://doi.org/10.1089/mdr.2018.0384

Alekish MO, Bani Ismail Z, Gharaibeh M and Abu-Qatoush L, 2020. Genetic relatedness, antibiogram and virulence factors of *Staphylococcus aureus* isolated from bovine mastitis and related human contacts. Polish Journal of Veterinary Sciences, 23, 133–141. https://doi.org/10.24425/pjvs.2020.132757

Antoci E, Pinzone MR, Nunnari G, Stefani S and Cacopardo B, 2013. Prevalence and molecular characteristics of methicillin-resistant *Staphylococcus aureus* (MRSA) among subjects working on bovine dairy farms. Infez Medicine, 21, 125–129.

van Alen S, Ballhausen B, Peters G, Friedrich AW, Mellmann A, Köck R and Becker K, 2017. In the centre of an epidemic: Fifteen years of LA-MRSA CC398 at the University Hospital Munster. Veterinary Microbiology, 200, 19–24. https://doi.org/10.1016/j.vetmic.2016.01.021

Ahanotu E, Alvelo-Ceron D, Ravita T and Gaunt E, 2006. Applied Biosafety, 11, 120–126. https://doi.org/10.1177/153567600601100303 Published in Volume: 11 Issue 3: September 1, 2006.

Alfonseca-Silva E, Cruz-Villa JC, Gutiérrez L and Sumano H, 2021. Successful treatment of recurrent subclinical mastitis in cows caused by enrofloxacin resistant bacteria by means of the sequential intramammary infusion of enrofloxacin HCl-2H2O and ceftiofur HCl: a clinical trial. Journal of Veterinary Science, 22, e78. https://doi.org/10.4142/jvs.2021.22.e78

Anderson KL, Lyman R, Moury K, Ray D, Watson DW and Correa MT, 2012. Molecular epidemiology of *Staphylococcus aureus* mastitis in dairy heifers. Journal of Dairy Science, 95, 4921–4930. https://doi.org/10.3168/jds.2011-4913

Anjum MF, Marco-Jimenez F, Duncan D, Marín C, Smith RP and Evans SJ, 2019. Livestock-associated methicillin-resistant *Staphylococcus aureus* from animals and animal products in the UK. Frontiers in Microbiology, 10, 2136. https://doi.org/10.3389/fmicb.2019.02136

Antimicrobial Resistance Collaborators, 2022. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet. https://doi.org/10.1016/S0140-6736(21)02724-0

Argudín MA, Tenhagen BA, Fetsch A, Sachsenröder J, Käsbohrer A, Schroeter A, Hammerl JA, Hertwig S, Helmuth R, Bräunig J, Mendoza MC, Appel B, Rodicio MR and Guerra B, 2011. Virulence and resistance determinants of German *Staphylococcus aureus* ST398 isolates from nonhuman sources. Applied Environmental Microbiology, 77, 3052–3060. https://doi.org/10.1128/AEM.02260-10. Epub 2011 Mar 4. PMID: 21378035; PMCID: PMC3126402.

Arnold C, Pilla R, Chaffin K, Lidbury J, Steiner J and Suchodolski J, 2021. Alterations in the fecal microbiome and metabolome of horses with antimicrobial-associated diarrhea compared to antibiotic-treated and non-treated healthy case controls. Animals, 11, 1807.

Åvall-Jääskeläinen S, Koort J, Simojoki H and Taponen S, 2021. Genomic analysis of *Staphylococcus aureus* Isolates associated with peracute non-gangrenous or gangrenous mastitis and comparison with other mastitis-associated *Staphylococcus aureus* Isolates. Frontiers in Microbiology, 12. https://doi.org/10.3389/fmicb.2021.688819

Baldoni D, Haschke M, Rajacic Z, Zimmerli W and Trampuz A, 2009. Linezolid alone or combined with rifampin against methicillin-resistant *Staphylococcus aureus* in experimental foreign-body infection. Antimicrobial Agents and Chemotherapy, 53, 1142–1148. https://doi.org/10.1128/AAC.00775-08

van Balen J, Mowery J, Piraino-Sandoval M, Nava-Hoet RC, Kohn C and Hoet AE, 2014. Molecular epidemiology of environmental MRSA at an equine teaching hospital: introduction, circulation and maintenance. Veterinary Research, 45, 1–12. https://doi.org/10.1186/1297-9716-45-31

Baptiste KE, Williams K, Willams NJ, Wattret A, Clegg PD, Dawson S, Corkill JE, O'Neill T and Hart CA, 2005. Methicillin-resistant staphylococci in companion animals. Emerging Infectious Diseases, 11, 1942–1944. https://doi.org/10.3201/eid1112.050241

Barkema HW, Schukken YH and Zadoks RN, 2006. Invited review: Tte role of cow, pathogen, and treatment regimen in the therapeutic success of bovine *Staphylococcus aureus* mastitis. Journal of Dairy Science, 89, 1877–1895. https://doi.org/10.3168/jds.S0022-0302(06)72256-1

Barlow JW, Zadoks RN and Schukken YH, 2013. Effect of lactation therapy on *Staphylococcus aureus* transmission dynamics in two commercial dairy herds. BMC Veterinary Research, 9, 1–12. https://doi.org/10.1186/1746-6148-9-28

Barraud O, Laurent F, François B, Bes M, Vignon P and Ploy MC, 2013. Severe human bone infection due to methicillin-resistant *Staphylococcus aureus* carrying the novel mecC variant. Journal of Antimicrobial Chemotherapy, 68, 2949–2950. https://doi.org/10.1093/jac/dkt274

Becker K, Ballhausen B, Köck R and Kriegeskorte A, 2014. Methicillin resistance in Staphylococcus isolates: the "mec alphabet" with specific consideration of mecC, a mec homolog associated with zoonotic S. aureus lineages. International Journal of Medical Microbiology, 304, 794–804. https://doi.org/10.1016/j.ijmm.2014.06.007

Becker K, Ballhausen B, Kahl BC and Köck R, 2017. The clinical impact of livestock-associated methicillin-resistant *Staphylococcus aureus* of the clonal complex 398 for humans. Veterinary Microbiology, 200, 33–38. https://doi.org/10.1016/j.vetmic.2015.11.013

Bengtsson B, Unnerstad HE, Ekman T, Artursson K, Nilsson-Ost M and Waller KP, 2009. Antimicrobial susceptibility of udder pathogens from cases of acute clinical mastitis in dairy cows. Veterinary Microbiology, 136, 142–149. https://doi.org/10.1016/j.vetmic.2008.10.024

Bergström K, Nyman G, Widgren S, Johnston C, Grönlund-Andersson U and Ransjö U, 2012. Infection prevention and control interventions in the first outbreak of methicillin-resistant *Staphylococcus aureus* infections in an equine hospital in Sweden. Acta Veterinaria Scandinavica, 54, 1–14. https://doi.org/10.1186/1751-0147-54-14

Bergström K, Bengtsson B, Nyman A and Grönlund Andersson U, 2013. Longitudinal study of horses for carriage of methicillin-resistant *Staphylococcus aureus* following wound infections. Veterinary Microbiology, 163, 388–391. https://doi.org/10.1016/j.vetmic.2013.01.004

Bhaskar ASB and Sant B, 2020. In: Handbook on Biological Warfare Preparedness.

Bisdorff B, Scholhölter JL, Claußen K, Pulz M, Nowak D and Radon K, 2012. MRSA-ST398 in livestock farmers and neighbouring residents in a rural area in Germany. Epidemiology & Infection, 140, 1800–1808. https://doi.org/10.1017/S0950268811002378

van den Borne BHP, Graber HU, Voelk V, Sartori C, Steiner A, Haerdi-Landerer MC and Bodmer M, 2017. A longitudinal study on transmission of *Staphylococcus aureus* genotype B in Swiss communal dairy herds. Preventive Veterinary Medicine, 136, 65–68. https://doi.org/10.1016/j.prevetmed.2016.11.008

Bortolami A, Williams NJ, McGowan CM, Kelly PG, Archer DC, Corrò M, Pinchbeck G, Saunders CJ and Timofte D, 2017. Environmental surveillance identifies multiple introductions of MRSA CC398 in an Equine Veterinary Hospital in the UK, 2011–2016. Scientific Reports, 7, 1–9. https://doi.org/10.1038/s41598-017-05559-8

Bos ME, Verstappen KM, van Cleef BA, Dohmen W, Dorado-García A, Graveland H, Duim B, Wagenaar JA, Kluytmans JA and Heederik DJ, 2016. Transmission through air as a possible route of exposure for MRSA. Journal of Exposure Science & Environmental Epidemiology, 26, 263–269. https://doi.org/10.1038/jes.2014.85

Bosch T, Verkade E, van Luit M, Landman F, Kluytmans J and Schouls LM, 2015. Transmission and persistence of livestock-associated methicillin-resistant *Staphylococcus aureus* among veterinarians and their household members. Applied and Environmental Microbiology, 81, 124–129. https://doi.org/10.1128/AEM.02803-14

Boss R, Cosandey A, Luini M, Artursson K, Bardiau M, Breitenwieser F, Hehenberger E, Lam T, Mansfeld M, Michel A, Mösslacher G, Naskova J, Nelson S, Podpečan O, Raemy A, Ryan E, Salat O, Zangerl P, Steiner A and Graber HU, 2016. Bovine *Staphylococcus aureus*: Subtyping, evolution, and zoonotic transfer. Journal of Dairy Science, 99, 515–528. https://doi.org/10.3168/jds.2015-9589

Boyen F, Smet A, Hermans K, Butaye P, Martens A, Martel A and Haesebrouck F, 2013. Methicillin resistant staphylococci and broad-spectrum beta-lactamase producing Enterobacteriaceae in horses. Veterinary Microbiology, 167, 67–77. https://doi.org/10.1016/j.vetmic.2013.05.001

Boyle AG, Rankin SC, Duffee LA and Morris D, 2017. Prevalence of methicillin-resistant *Staphylococcus aureus* from equine nasopharyngeal and guttural pouch wash samples. Journal of Veterinary Internal Medicine, 31, 1551–1555. https://doi.org/10.1111/jvim.14783

Bradley AJ, Breen JE, Payne B, White V and Green MJ, 2015. An investigation of the efficacy of a polyvalent mastitis vaccine using different vaccination regimens under field conditions in the United Kingdom. Journal of Dairy Science, 98, 1706–1720. https://doi.org/10.3168/jds.2014-8332

Bradley AJ, Leach KA, Breen JE, Green LE and Green MJ, 2007. Survey of the incidence and aetiology of mastitis on dairy farms in England and Wales. Veterinary Record, 160, 253–258. https://doi.org/10.1136/vr.160.8.253

Brennan GI, Abbott Y, Burns A, Leonard F, McManus BA, O'Connell B, Coleman DC and Shore AC, 2016. The emergence and spread of multiple livestock-associated clonal complex 398 methicillin-resistant and Methicillin-Susceptible *Staphylococcus aureus* Strains among Animals and Humans in the Republic of Ireland, 2010–2014. PLoS One, 11, e0149396. https://doi.org/10.1371/journal.pone.0149396

Broens EM, Graat EA, van de Giessen AW, Broekhuizen-Stins MJ and de Jong MC, 2012. Quantification of transmission of livestock-associated methicillin resistant *Staphylococcus aureus* in pigs. Veterinary Microbiology, 155, 381–388.

Brouillette E and Malouin F, 2005. The pathogenesis and control of Staphylococcus aureus-induced mastitis: study models in the mouse. Microbes and Infection, 7, 560–568. https://doi.org/10.1016/j.micinf.2004.11.008

Burton S, Reid-Smith R, McClure JT and Weese JS, 2008. Staphylococcus aureus colonization in healthy horses in Atlantic Canada. The Canadian Veterinary Journal, 49, 797.

Busscher JF, van Duijkeren E and Sloet van Oldruitenborgh-Oosterbaan MM, 2006. The prevalence of methicillin-resistant staphylococci in healthy horses in the Netherlands. Veterinary Microbiology, 113, 131–136. https://doi.org/10.1016/j.vetmic.2005.10.028

Capoferri R, Cremonesi P, Castiglioni B, Pisoni G, Roccabianca P, Riva F, Filipe J, Del Corvo M, Stella A, Williams JL, Rupp R and Moroni P, 2021. Comparison of the response of mammary gland tissue from two divergent lines of goat with high and low milk somatic cell scores to an experimental *Staphylococcus aureus* infection. Veterinary Immunology and Immunopathology, 234. https://doi.org/10.1016/j.vetimm.2021.110208

Carfora V, Giacinti G, Sagrafoli D, Marri N, Giangolini G, Alba P, Feltrin F, Sorbara L, Amoruso R, Caprioli A, Amatiste S and Battisti A, 2016a. Methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* in dairy sheep and in-contact humans: an intra-farm study. Journal of Dairy Science, 99, 4251–4258. https://doi.org/10.3168/jds.2016-10912

Carfora V, Caprioli A, Grossi I, Pepe M, Alba P, Lorenzetti S, Amoruso R, Sorbara L, Franco A and Battisti A, 2016b. A methicillin-resistant *Staphylococcus aureus* (MRSA) sequence type 8, spa type t11469 causing infection and colonizing horses in Italy. Pathogens and Disease, 74, ftw025. https://doi.org/10.1093/femspd/ftw025

Castañeda X, García-De-la-Mària C, Gasch O, Pericàs JM, Soy D, Cañas-Pacheco MA, Falces C, García-González J, Hernández-Meneses M, Vidal B, Almela M, Quintana E, Tolosana JM, Fuster D, Llopis J, Dahl A, Moreno A, Marco F, Miró JM and Hospital Clínic Endocarditis Study Group, 2021. Effectiveness of vancomycin plus cloxacillin compared with vancomycin, cloxacillin and daptomycin single therapies in the treatment of methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* in a rabbit model of experimental endocarditis. Journal of Antimicrobial Chemotherapy, 766 pp. 1539–1546. https://doi.org/10.1093/jac/dkab069.

Chrobak-Chmiel D, Kwiecień E, Golke A, Dolka B, Adamczyk K, Biegańska MJ, Spinu M, Binek M and Rzewuska M, 2021. Pigeons as carriers of clinically relevant multidrug-resistant pathogens-a clinical case report and literature review. Frontiers in Veterinary Science, 24. 664226. https://doi.org/10.3389/fvets.2021.664226. PMID: 34109235; PMCID: PMC8180574.

Chambers HF, 1997. Methicillin resistance in staphylococci: molecular and biochemical basis and clinical implications. Clinical Microbiology Reviews, 10, 781–791. https://doi.org/10.1128/CMR.10.4.781

Chen C and Wu F, 2021. Livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) colonisation and infection among livestock workers and veterinarians: a systematic review and meta-analysis. Occupational and Environmental Medicine, 78, 530–540. https://doi.org/10.1136/oemed-2020-106418

Chueahiran S, Yindee J, Boonkham P, Suanpairintr N and Chanchaithong P, 2021. Methicillin-resistant *Staphylococcus aureus* clonal complex 398 as a major MRSA lineage in dogs and cats in Thailand. Antibiotics (Basel), 10, 243. https://doi.org/10.3390/antibiotics10030243

Chung LK, Sahibzada S, Annandale HC, Robertson ID, Waichigo FW, Tufail MS and Aleri JA, 2021. Bacterial pathogens associated with clinical and subclinical mastitis in a Mediterranean pasture-based dairy production system of Australia. Research in Veterinary Science, 141, 103–109. https://doi.org/10.1016/j.rvsc.2021.10.005

Clausen B and Ashford WA, 1980. Bacteriologic survey of black rhinoceros (Diceros bicornis). Journal of Wildlife Diseases, 16, 475–480. https://doi.org/10.7589/0090-3558-16.4.475

van Cleef BA, Graveland H, Haenen AP, van de Giessen AW, Heederik D, Wagenaar JA and Kluytmans JA, 2011. Persistence of livestock-associated methicillin-resistant *Staphylococcus aureus* in field workers after short-term occupational exposure to pigs and veal calves. Journal of Clinical Microbiology, 49, 1030–1033. https://doi.org/10.1128/JCM.00493-10

Cortimiglia C, Luini M, Bianchini V, Marzagalli L, Vezzoli F, Avisani D, Bertoletti M, Ianzano A, Franco A and Battisti A, 2016. Prevalence of *Staphylococcus aureus* and of methicillin-resistant S. aureus clonal complexes in bulk tank milk from dairy cattle herds in Lombardy Region (Northern Italy). Epidemiology & Infection, 144, 3046–3051. https://doi.org/10.1017/S0950268816001576

Costa MC, Stämpfli HR, Arroyo LG, Allen-Vercoe E, Gomes RG and Weese JS, 2015. Changes in the equine fecal microbiota associated with the use of systemic antimicrobial drugs. BMC Veterinary Research, 11, 1–12.

Couto N, Belas A, Kadlec K, Schwarz S and Pomba C, 2015. Clonal diversity, virulence patterns and antimicrobial and biocide susceptibility among human, animal and environmental MRSA in Portugal. Journal of Antimicrobial Chemotherapy, 70, 2483–2487. https://doi.org/10.1093/jac/dkv141

Crombé F, Argudín MA, Vanderhaeghen W, Hermans K, Haesebrouck F and Butaye P, 2013. Transmission dynamics of methicillin-resistant *Staphylococcus aureus* in pigs. Frontiers in Microbiology, 4, 57. https://doi.org/10.3389/fmicb.2013.00057

Cuny C, Strommenger B, Witte W and Stanek C, 2008. Clusters of infections in horses with MRSA ST1, ST254, and ST398 in a veterinary hospital. Microbial Drug Resistance, 14, 307–310. https://doi.org/10.1089/mdr.2008.0845

Cuny C, Abdelbary MMH, Köck R, Layer F, Scheidemann W, Werner G and Witte W, 2016. Methicillin-resistant *Staphylococcus aureus* from infections in horses in Germany are frequent colonizers of veterinarians but rare among MRSA from infections in humans. One Health, 2, 11–17. https://doi.org/10.1016/j.onehlt.2015.11.004

Cuny C, Layer F, Hansen S, Werner G and Witte W, 2019. Nasal colonization of humans with occupational exposure to raw meat and to raw meat products with methicillin-susceptible and methicillin-resistant *Staphylococcus aureus*. Toxins (Basel), 11, 190. https://doi.org/10.3390/toxins11040190

Cuny C and Witte W, 2017. MRSA in equine hospitals and its significance for infections in humans. Veterinary Microbiology, 200, 59–64. https://doi.org/10.1016/j.vetmic.2016.01.013

Cvetnić L, Samardžija M, Duvnjak S, Habrun B, Cvetnić M, Jaki Tkalec V, Đuričić D and Benić M, 2021. Multi locus sequence typing and spa typing of *Staphylococcus aureus* Isolated from the milk of cows with subclinical mastitis in croatia. Microorganisms, 9, 725. https://doi.org/10.3390/microorganisms9040725

Dahms C, Hübner NO, Cuny C and Kramer A, 2014. Occurrence of methicillin-resistant *Staphylococcus aureus* in farm workers and the livestock environment in Mecklenburg-Western Pomerania. Germany. Acta Veterinaria Scandinavica, 56, 53. https://doi.org/10.1186/s13028-014-0053-3

Dalen G, Rachah A, Nørstebø H, Schukken YH and Reksen O, 2019. Dynamics of somatic cell count patterns as a proxy for transmission of mastitis pathogens. Journal of Dairy Science, 102, 11349–11358. https://doi.org/10.3168/jds.2019-16847

de Jong A, Garch FE, Simjee S, Moyaert H, Rose M, Youala M, Siegwart ED and VetPath Study Group, 2018. Monitoring of antimicrobial susceptibility of udder pathogens recovered from cases of clinical mastitis in dairy cows across Europe: VetPath results. Veterinary Microbiology, 213, 73–81. https://doi.org/10.1016/j.vetmic.2017.11.021

De Vliegher S, Fox LK, Piepers S, McDougall S and Barkema HW, 2012. Invited review: mastitis in dairy heifers: nature of the disease, potential impact, prevention, and control. Journal of Dairy Science, 95, 1025–1040. https://doi.org/10.3168/jds.2010-4074

Deiters C, Günnewig V, Friedrich AW, Mellmann A and Köck R, 2015. Are cases of methicillin-resistant *Staphylococcus aureus* clonal complex (CC) 398 among humans still livestock-associated? International Journal of Medical Microbiology, 305, 110–113. https://doi.org/10.1016/j.ijmm.2014.11.007

Deng Z, Koop G, Hogeveen H, Fischer EAJ, van den Borne BHP, van der Tol R and Lam TJGM, 2021. Transmission dynamics of *Staphylococcus aureus* and Streptococcus agalactiae in a Dutch dairy herd using an automatic milking system. Preventive Veterinary Medicine, 192. https://doi.org/10.1016/j.prevetmed.2021.105384

Devriese LA, Nzuambe D and Godard C, 1985. Identification and characteristics of Staphylococci isolated from lesions and normal skin of horses. Veterinary Microbiology, 10, 269–277. https://doi.org/10.1016/0378-1135(85)90052-5

Dewulf J and Van Immerseel F, 2018. General Principles of Biosecurity in Animal Production and Veterinary Medicine in Biosecurity in Animal Production and Veterinary Medicine: From Principles To Practice, 1st Edition. Acco, Leuven, Belgium.

Dohoo I, Smith J, Andersen S, Kelton D, Godden S and Mastitis Research Workers' Conference, 2011. Diagnosing intramammary infections: evaluation of definitions based on a single milk sample. Journal of Dairy Science, 94, 250–261. https://doi.org/10.3168/jds.2010-3559

Dong Q, Liu Y, Li W, Liu Y and Ye X, 2021. Cross-species transmission risk of livestock-associated MRSA: a systematic review and Bayesian meta-analysis of global data. Preventive Veterinary Medicine, 194. https://doi.org/10.1016/j.prevetmed.2021.105429

Dorado-García A, Bos ME, Graveland H, Van Cleef BA, Verstappen KM, Kluytmans JA, Wagenaar JA and Heederik DJ, 2013. Risk factors for persistence of livestock-associated MRSA and environmental exposure in veal calf farmers and their family members: an observational longitudinal study. British Medical Journal Open, 3, e003272. https://doi.org/10.1136/bmjopen-2013-003272

Dube F, Söderlund R, Lampinen Salomonsson M, Troell K and Börjesson S, 2021. Benzylpenicillin-producing Trichophyton erinacei and methicillin resistant *Staphylococcus aureus* carrying the mecC gene on European hedgehogs - a pilot-study. BMC Microbiology, 21, 1–11. https://doi.org/10.1186/s12866-021-02260-9

van Duijkeren E, Moleman M, Sloet van Oldruitenborgh-Oosterbaan MM, Multem J, Troelstra A, Fluit AC, van Wamel WJ, Houwers DJ, de Neeling AJ and Wagenaar JA, 2010. Methicillin-resistant *Staphylococcus aureus* in horses and horse personnel: an investigation of several outbreaks. Veterinary Microbiology, 141, 96–102. https://doi.org/10.1016/j.vetmic.2009.08.009

van Duijkeren E, Ten Horn L, Wagenaar JA, de Bruijn M, Laarhoven L, Verstappen K, de Weerd W, Meessen N and Duim B, 2011. Suspected horse-to-human transmission of MRSA ST398. Emerging Infectious Diseases, 17, 1137–1139. https://doi.org/10.3201/eid/1706.101330

van Duijkeren E, Hengeveld PD, Albers M, Pluister G, Jacobs P, Heres L and van de Giessen AW, 2014. Prevalence of methicillin-resistant *Staphylococcus aureus* carrying mecA or mecC in dairy cattle. Veterinary Microbiology, 171, 364–367.

ECDC, EFSA and EMEA, 2009. Joint scientific report on meticillin resistant *Staphylococcus aureus* (MRSA) in livestock, companion animals and foods. EFSA-Q-2009-00612 (EFSA Scientific Report (2009) 301, 1-10) and EMEA/CVMP/SAGAM/62464/2009.

van den Eede A, Martens A, Lipinska U, Struelens M, Deplano A, Denis O, Haesebrouck F, Gasthuys F and Hermans K, 2009. High occurrence of methicillin-resistant *Staphylococcus aureus* ST398 in equine nasal samples. Veterinary Microbiology, 133,138–144. https://doi.org/10.1016/j.vetmic.2008.06.021

van den Eede A, Martens A, Feryn I, Vanderhaeghen W, Lipinska U, Gasthuys F, Butaye P, Haesebrouck F and Hermans K, 2012. Low MRSA prevalence in horses at farm level. BMC Veterinary Research, 8, 1–4. https://doi.org/10.1186/1746-6148-8-213

van den Eede A, Martens A, Floré K, Denis O, Gasthuys F, Haesebrouck F, Van den Abeele A and Hermans K, 2013. MRSA carriage in the equine community: an investigation of horse-caretaker couples. Veterinary Microbiology, 163, 313–318. https://doi.org/10.1016/j.vetmic.2012.12.038

EFSA (European Food Safety Authority), 2012. Technical specifications on the harmonised monitoring and reporting of antimicrobial resistance in methicillin-resistant *Staphylococcus aureus* in food-producing animals and food. EFSA Journal 2012;10(10):2897, 56 pp. https://doi.org/10.2903/j.efsa.2012.2897

EFSA (European Food Safety Authority), Amore G, Beloeil P-A, Fierro RG, Guerra B, Alexandra P, Rizzi V and Stoicescu A-V, 2021. Manual for reporting 2021 antimicrobial resistance data within the framework of Directive 2003/99/EC and Decision 2020/1729/EU. EFSA Supporting Publication 2021;18(5):EN-6652, 31 pp. https://doi.org/10.2903/sp.efsa.2021.EN-6652

EFSA AHAW Panel (EFSA Panel on Animal Health and Welfare), More S, Bøtner A, Butterworth A, Calistri P, Depner K, Edwards S, Garin-Bastuji B, Good M, Gortázar Schmidt C, Michel V, Miranda MA, Nielsen SS, Raj M, Sihvonen L, Spoolder H, Stegeman JA, Thulke H-H, Velarde A, Willeberg P, Winckler C, Baldinelli F, Broglia A, Candiani D, Gervelmeyer A, Zancanaro G, Kohnle L, Morgado J and Bicout D, 2017. Scientific opinion on an ad hoc method for the assessment on listing and categorisation of animal diseases within the framework of the Animal Health Law. EFSA Journal 2017;15(7):4783, 42 pp. https://doi.org/10.2903/j.efsa.2017.4783

EFSA AHAW Panel (EFSA Panel on Animal Health and Welfare), Nielsen SS, Bicout DJ, Calistri P, Canali E, Drewe JA, Garin-Bastuji B, Gonzales Rojas JL, Gortázar Schmidt C, Herskin M, Michel V, Miranda Chueca MA, Padalino B, Pasquali P, Roberts HC, Spoolder H, Ståhl K, Velarde A, Viltrop A, Winckler C, Dewulf J, Guardabassi L, Hilbert F, Mader R, Baldinelli F and Alvarez J, 2021a. Scientific Opinion on the assessment of animal diseases caused by bacteria resistant to antimicrobials: cattle. EFSA Journal 2021;19(12):6955, 89 pp. https://doi.org/10.2903/j.efsa.2021.6955

EFSA AHAW Panel (EFSA Panel on Animal Health and Welfare), Nielsen SS, Bicout DJ, Calistri P, Canali E, Drewe JA, Garin-Bastuji B, Gonzales Rojas JL, Gortázar Schmidt C, Herskin M, Michel V, Miranda Chueca MA, Padalino B, Pasquali P, Roberts HC, Sihvonen LH, Spoolder H, Ståhl K, Velarde A, Viltrop A, Winckler C, Dewulf J, Guardabassi L, Hilbert F, Mader R, Baldinelli F and Alvarez J, 2021b. Scientific Opinion on the assessment of animal diseases caused by bacteria resistant to antimicrobials: horses. EFSA Journal 2021;19(12):7112, 43 pp. https://doi.org/10.2903/j.efsa.2021.7112

EFSA AHAW Panel (EFSA Panel on Animal Health and Welfare), Nielsen SS, Bicout DJ, Calistri P, Canali E, Drewe JA, Garin-Bastuji B, Gonzales Rojas JL, Gortázar Schmidt C, Herskin M, Michel V, Miranda Chueca MA, Padalino B, Pasquali P, Roberts HC, Sihvonen LH, Spoolder H, Ståhl K, Velarde A, Viltrop A, Winckler C, Guardabassi L, Hilbert F, Mader R, Smith P, Aznar I, Muñoz Guajardo I, Baldinelli F and Alvarez J, 2021c. Scientific Opinion on the ad hoc method for the assessment of animal diseases caused by bacteria resistant to antimicrobials. EFSA Journal 2021;19(6):6645, 29 pp. https://doi.org/10.2903/j.efsa.2021.6645

EFSA Scientific Committee, Benford D, Halldorsson T, Jeger MJ, Knutsen HK, More S, Naegeli H, Noteborn H, Ockleford C, Ricci A, Rychen G, Schlatter JR, Silano V, Solecki R, Turck D, Younes M, Craig P, Hart A, Von Goetz N, Koutsoumanis K, Mortensen A, Ossendorp B, Martino L, Merten C, Mosbach-Schulz O and Hardy A, 2018. Guidance on Uncertainty Analysis in Scientific Assessments. EFSA Journal 2018;16(1):5123, 39 pp. https://doi.org/10.2903/j.efsa.2018.5123

El-Adawy H, Ahmed M, Hotzel H, Monecke S, Schulz J, Hartung J, Ehricht R, Neubauer H and Hafez HM, 2016. Characterization of Methicillin-Resistant *Staphylococcus aureus* Isolated from Healthy Turkeys and Broilers Using DNA Microarrays. Frontiers in Microbiology, 7. https://doi.org/10.3389/fmicb.2016.02019

El-Ashker M, Gwida M, Monecke S, El-Gohary F, Ehricht R, Elsayed M, Akinduti P, El-Fateh M and Maurischat S, 2020. Antimicrobial resistance pattern and virulence profile of S. aureus isolated from household cattle and buffalo with mastitis in Egypt. Veterinary Microbiology, 240. https://doi.org/10.1016/j.vetmic.2019.108535

van Elk CE, Boelens HA, van Belkum A, Foster G and Kuiken T, 2012. Indications for both host-specific and introduced genotypes of *Staphylococcus aureus* in marine mammals. Veterinary Microbiology, 156, 343–346. https://doi.org/10.1016/j.vetmic.2011.10.034

Felten A, Grandry B, Lagrange PH and Casin I, 2002. Evaluation of three techniques for detection of low-level methicillin-resistant *Staphylococcus aureus* (MRSA): a disk diffusion method with cefoxitin and moxalactam, the Vitek 2 system, and the MRSA-screen latex agglutination test. Journal of Clinical Microbiology, 40, 2766–2771. https://doi.org/10.1128/JCM.40.8.2766-2771.2002

Feltrin F, Alba P, Kraushaar B, Ianzano A, Argudín MA, Di Matteo P, Porrero MC, Aarestrup FM, Butaye P, Franco A and Battisti A, 2016. A livestock-associated, multidrug-resistant, methicillin-resistant *Staphylococcus aureus* clonal complex 97 lineage spreading in dairy cattle and pigs in Italy. Applied and Environmental Microbiology, 82, 816–821. https://doi.org/10.1128/AEM.02854-15

Fertner M, Pedersen K and Chriél M, 2019. Experimental exposure of farmed mink (Neovison vison) to livestock-associated methicillin-resistant *Staphylococcus aureus* contaminated feed. Veterinary Microbiology, 231, 45–47. https://doi.org/10.1016/j.vetmic.2019.02.033

Fessler AT, Olde Riekerink RG, Rothkamp A, Kadlec K, Sampimon OC, Lam TJ and Schwarz S, 2012. Characterization of methicillin-resistant *Staphylococcus aureus* CC398 obtained from humans and animals on dairy farms. Veterinary Microbiology, 160, 77–84. https://doi.org/10.1016/j.vetmic.2012.05.005

Firth CL, Käsbohrer A, Pless P, Koeberl-Jelovcan S and Obritzhauser W, 2022. Analysis of antimicrobial use and the presence of antimicrobial-resistant bacteria on austrian dairy farms—a pilot study. Antibiotics, 11, 124. https://doi.org/10.3390/antibiotics11020124

Fitzgerald JR, 2012. Livestock-associated Staphylococcus aureus: origin, evolution and public health threat. Trends in Microbiology, 20, 192–198. https://doi.org/10.1016/j.tim.2012.01.006

Freick M, Frank Y, Steinert K, Hamedy A, Passarge O and Sobiraj A, 2016. Mastitis vaccination using a commercial polyvalent vaccine or a herd-specific *Staphylococcus aureus* vaccine. Results of a controlled field trial on a dairy farm. Tierarztl Prax Ausg G Grosstiere Nutztiere, 44, 219–229. https://doi.org/10.15653/TPG-150912

Frosini SM, Bond R, Rantala M, Grönthal T, Rankin SC, O'Shea K, Timofte D, Schmidt V, Lindsay J and Loeffler A, 2019. Genetic resistance determinants to fusidic acid and chlorhexidine in variably susceptible staphylococci from dogs. BMC Microbiology, 19, 1–10. https://doi.org/10.1186/s12866-019-1449-z

Garcia BLN, Fidelis CE, Freu G, Granja BM and Dos Santos MV, 2021. Evaluation of chromogenic culture media for rapid identification of gram-positive bacteria causing mastitis. Frontiers in Veterinary Science, 8. https://doi.org/10.3389/fvets.2021.662201

García-Álvarez L, Holden MTG, Lindsay H, Webb CR, Brown DFJ, Curran MD, Walpole E, Brooks K, Pickard DJ, Teale C, Parkhill J, Bentley SD, Edwards GF, Girvan EK, Kearns AM, Pichon B, Hill RLR, Larsen AR, Skov RL, Peacock SJ, Maskell DJ and Holmes MA, 2011. Meticillin-resistant *Staphylococcus aureus* with a novel mecA homologue in human and bovine populations in the UK and Denmark: a descriptive study. The Lancet Infectious Diseases, 11, 595–603. https://doi.org/10.1016/S1473-3099(11)70126-8

Haine D, Delgado H, Cue R, Sewalem A, Wade K, Lacroix R, Lefebvre D, Arsenault J, Bouchard É and Dubuc J, 2017. Culling from the herd's perspective-Exploring herd-level management factors and culling rates in Québec dairy herds. Preventive Veterinary Medicine, 1, 132–141. https://doi.org/10.1016/j.prevetmed.2017.08.020

Gharsa H, Ben Sallem R, Ben Slama K, Gómez-Sanz E, Lozano C, Jouini A, Klibi N, Zarazaga M, Boudabous A and Torres C, 2012. High diversity of genetic lineages and virulence genes in nasal *Staphylococcus aureus* isolates from donkeys destined to food consumption in Tunisia with predominance of the ruminant associated CC133 lineage. BMC Veterinary Research, 8, 1–8. https://doi.org/10.1186/1746-6148-8-203

Gindonis V, Taponen S, Myllyniemi AL, Pyörälä S, Nykäsenoja S, Salmenlinna S, Lindholm L and Rantala M, 2013. Occurrence and characterization of methicillin-resistant staphylococci from bovine mastitis milk samples in Finland. Acta Veterinaria Scandinavica, 55, 61. https://doi.org/10.1186/1751-0147-55-61

Glasner C, Sabat AJ, Chlebowicz MA, Vanderhaeghen W, Fetsch A, Guerra B, Huber H, Stephan R, Torres C, Butaye P, Voss A, Wulf M and van Dijl JM, 2013. High-resolution typing by MLVF unveils extensive heterogeneity of European livestock-associated methicillin-resistant *Staphylococcus aureus* isolates with the sequence type 398. International Journal of Medical Microbiology, 303, 124–127. https://doi.org/10.1016/j.ijmm.2013.02.015

Goerge T, Lorenz MB, van Alen S, Hübner NO, Becker K and Köck R, 2017. MRSA colonization and infection among persons with occupational livestock exposure in Europe: prevalence, preventive options and evidence. Veterinary Microbiology, 200, 6–12. https://doi.org/10.1016/j.vetmic.2015.10.027

Gómez-Sanz E, Simón C, Ortega C, Gómez P, Lozano C, Zarazaga M and Torres C, 2014. First detection of methicillin-resistant *Staphylococcus aureus* ST398 and Staphylococcus pseudintermedius ST68 from hospitalized equines in Spain. Zoonoses and Public Health, 61., 192–201. https://doi.org/10.1111/zph.12059

Granja BM, Fidelis CE, Garcia BLN and Dos Santos MV, 2021. Evaluation of chromogenic culture media for rapid identification of microorganisms isolated from cows with clinical and subclinical mastitis. Journal of Dairy Science, 104, 9115–9129. https://doi.org/10.3168/jds.2020-19513

Graveland H, Wagenaar JA, Heesterbeek H, Mevius D, van Duijkeren E and Heederik D, 2010. Methicillin resistant *Staphylococcus aureus* ST398 in veal calf farming: human MRSA carriage related with animal antimicrobial usage and farm hygiene. PLoS One, 5, e10990. https://doi.org/10.1371/journal.pone.0010990

Graveland H, Wagenaar JA, Verstappen KM, Oosting-van Schothorst I, Heederik DJ and Bos ME, 2012. Dynamics of MRSA carriage in veal calves: a longitudinal field study. Preventive Veterinary Medicine, 107, 180–186. https://doi.org/10.1016/j.prevetmed.2012.06.006

Gröhn YT, Wilson DJ, González RN, Hertl JA, Schulte H, Bennett G and Schukken YH, 2004. Effect of pathogen-specific clinical mastitis on milk yield in dairy cows. Journal of Dairy Science, 87, 3358–3374. https://doi.org/10.3168/jds.S0022-0302(04)73472-4

Grunert T, Stessl B, Wolf F, Sordelli DO, Buzzola FR and Ehling-Schulz M, 2018. Distinct phenotypic traits of *Staphylococcus aureus* are associated with persistent, contagious bovine intramammary infections. Scientific Reports, 8, 1–10. https://doi.org/10.1038/s41598-018-34371-1

Guérin F, Fines-Guyon M, Meignen P, Delente G, Fondrinier C, Bourdon N, Cattoir V and Léon A, 2017. Nationwide molecular epidemiology of methicillin-resistant *Staphylococcus aureus* responsible for horse infections in France. BMC Microbiology, 17, 104. https://doi.org/10.1186/s12866-016-0924-z

Gurjar A, Gioia G, Schukken Y, Welcome F, Zadoks R and Moroni P, 2012. Molecular diagnostics applied to mastitis problems on dairy farms. Veterinary Clinics: Food Animal Practice, 28, 565–576. https://doi.org/10.1016/j.cvfa.2012.07.011

Haag AF, Fitzgerald JR and Penadés JR, 2019. Staphylococcus aureus in Animals. Microbiology. Spectrum, 7. https://doi.org/10.1128/microbiolspec.GPP3-0060-2019

Haenni M, Châtre P, Tasse J, Nowak N, Bes M, Madec JY and Laurent F, 2014. Geographical clustering of mecC-positive *Staphylococcus aureus* from bovine mastitis in France. Journal of Antimicrobial Chemotherapy, 69, 2292–2293. https://doi.org/10.1093/jac/dku130

Haenni M, Châtre P, Dupieux C, Métayer V, Maillard K, Bes M, Madec JY and Laurent F, 2015. mecC-positive MRSA in horses. Journal of Antimicrobial Chemotherapy, 70, 3401–3402. https://doi.org/10.1093/jac/dkv278

Halasa T, Huijps K, Osteras O and Hogeveen H, 2007. Economic effects of bovine mastitis and mastitis management: a review. Veterinary Quarterly, 29, 18–31.

Hansen JE, Larsen AR, Skov RL, Chriél M, Larsen G, Angen Ø, Larsen J, Lassen DCK and Pedersen K, 2017. Livestock-associated methicillin-resistant *Staphylococcus aureus* is widespread in farmed mink (Neovison vison). Veterinary Microbiology, 207, 44–49. https://doi.org/10.1016/j.vetmic.2017.05.027

Hansen JE, Ronco T, Stegger M, Sieber RN, Fertner ME, Martin HL, Farre M, Toft N, Larsen AR and Pedersen K, 2019. LA-MRSA CC398 in dairy cattle and veal calf farms indicates spillover from pig production. Frontiers in Microbiology, 10, 2733. https://doi.org/10.3389/fmicb.2019.02733

Hansen JE, Stegger M, Pedersen K, Sieber RN, Larsen J, Larsen G, Lilje B, Chriél M, Andersen PS and Larsen AR, 2020. Spread of LA-MRSA CC398 in Danish mink (Neovison vison) and mink farm workers. Veterinary Microbiology, 245. https://doi.org/10.1016/j.vetmic.2020.108705

Harrison EM, Paterson GK, Holden MT, Larsen J, Stegger M, Larsen AR, Petersen A, Skov RL, Christensen JM, Bak Zeuthen A, Heltberg O, Harris SR, Zadoks RN, Parkhill J, Peacock SJ and Holmes MA, 2013. Whole genome sequencing identifies zoonotic transmission of MRSA isolates with the novel mecA homologue mecC. EMBO Molecular Medicine, 5, 509–515. https://doi.org/10.1002/emmm.201202413

Heaton CJ, Gerbig GR, Sensius LD, Patel V and Smith TC, 2020. Staphylococcus aureus epidemiology in wildlife: a systematic review. Antibiotics (Basel), 9, 89. https://doi.org/10.3390/antibiotics9020089

Heidemann Olsen R, Christensen H, Kabell S and Bisgaard M, 2018. Characterization of prevalent bacterial pathogens associated with pododermatitis in table egg layers. Avian Pathology, 47, 281–285. https://doi.org/10.1080/03079457.2018.1440066

Hower S, Phillips MC, Brodsky M, Dameron A, Tamargo MA, Salazar NC, Jackson CR, Barrett JB, Davidson M, Davis J, Mukherjee S, Ewing RY, Gidley ML, Sinigalliano CD, Johns L, Johnson FE, Adebanjo O and Plano LR, 2013. Clonally related methicillin-resistant *Staphylococcus aureus* isolated from short-finned pilot whales (Globicephala macrorhynchus), human volunteers, and a bayfront cetacean rehabilitation facility. Microbial Ecology, 65, 1024–1038. https://doi.org/10.1007/s00248-013-0178-3

Huijps K, Lam TJ and Hogeveen H, 2008. Costs of mastitis: facts and perception. Journal of Dairy Research, 75, 113–120. https://doi.org/10.1017/S0022029907002932

Huygens J, Daeseleire E, Mahillon J, Van Elst D, Decrop J, Meirlaen J, Dewulf J, Heyndrickx M and Rasschaert G, 2021. Presence of antibiotic residues and antibiotic resistant bacteria in cattle manure intended for fertilization of agricultural fields: a one health perspective. Antibiotics (Basel), 10, 410. https://doi.org/10.3390/antibiotics10040410

Islam MZ, Espinosa-Gongora C, Damborg P, Sieber RN, Munk R, Husted L, Moodley A, Skov R, Larsen J and Guardabassi L, 2017. Horses in Denmark are a reservoir of diverse clones of methicillin-resistant and -susceptible Staphylococcus aureus. Frontiers in Microbiology, 8, 543. https://doi.org/10.3389/fmicb.2017.00543

Juhász-Kaszanyitzky E, Jánosi S, Somogyi P, Dán A, van der Graaf-van BL, van Duijkeren E and Wagenaar JA, 2007. MRSA transmission between cows and humans. Emerging Infectious Diseases, 13, 630–632. https://doi.org/10.3201/eid1304.060833

Kadlec K, Fessler AT, Hauschild T and Schwarz S, 2012. Novel and uncommon antimicrobial resistance genes in livestock-associated methicillin-resistant Staphylococcus aureus. Clinical Microbiology & Infection, 18, 745–755. https://doi.org/10.1111/j.1469-0691.2012.03842.x

Kaspar U, von Lützau K, Schlattmann A, Rösler U, Köck R and Becker K, 2019. Zoonotic multidrug-resistant microorganisms among non-hospitalized horses from Germany. One Health, 7. https://doi.org/10.1016/j.onehlt.2019.100091

Keane OM, 2019. Symposium review: intramammary infections-major pathogens and strain-associated complexity. Journal of Dairy Science, 102, 4713–4726. https://doi.org/10.3168/jds.2018-15326

Kerro Dego O, Pacha PA, Gillespie BE and Pighetti GM, 2020. Experimental *Staphylococcus aureus* mastitis infection model by teat dipping in bacterial culture suspension in dairy cows. Animals (Basel), 10, 751. https://doi.org/10.3390/ani10050751

Kerro-Dego O, Prysliak T, Perez-Casal J and Potter AA, 2012. Role of GapC in the pathogenesis of Staphylococcus aureus. Veterinary Microbiology, 156, 443–447.

Khemiri M, Abbassi MS, Couto N, Mansouri R, Hammami S and Pomba C, 2018. Genetic characterisation of *Staphylococcus aureus* isolated from milk and nasal samples of healthy cows in Tunisia: first report of ST97-t267-agrI-SCCmecV MRSA of bovine origin in Tunisia. Journal of Global Antimicrobial Resistance, 14, 161–165. https://doi.org/10.1016/j.jgar.2018.03.013

Kim HK, Missiakas D and Schneewind O, 2014. Mouse models for infectious diseases caused by Staphylococcus aureus. Journal of Immunological Methods, 410, 88–99. https://doi.org/10.1016/j.jim.2014.04.007

Kirchhofer M, Kaufmann T, Guélat-Brechbühl M, Michel A, Syring C and Bodmer M, 2011. Systematic sanitation of dairy herds with mastitis caused by Staphylococcus aureus. [In German]. Schweizer Archiv Fur Tierheilkunde, 153, 361–368. https://doi.org/10.1024/0036-7281/a000222

Kirkeby C, Zervens L, Toft N, Schwarz D, Farre M, Hechinger S and Halasa T, 2019. Transmission dynamics of *Staphylococcus aureus* within two Danish dairy cattle herds. Journal of Dairy Science, 102, 1428–1442. https://doi.org/10.3168/jds.2018-15106

Klaas IC and Zadoks RN, 2018. An update on environmental mastitis: challenging perceptions. Transbound Emerging Disease, 65,166–185. https://doi.org/10.1111/tbed.12704

Kluytmans J, van Belkum A and Verbrugh H, 1997. Nasal carriage of Staphylococcus aureus: epidemiology, underlying mechanisms, and associated risks. Clinical Microbiology Reviews, 10, 505–520. https://doi.org/10.1128/CMR.10.3.505

Kreausukon K, Fetsch A, Kraushaar B, Alt K, Müller K, Krömker V, Zessin KH, Käsbohrer A and Tenhagen BA, 2012. Prevalence, antimicrobial resistance, and molecular characterization of methicillin-resistant *Staphylococcus aureus* from bulk tank milk of dairy herds. Journal of Dairy Science, 95, 4382–4388. https://doi.org/10.3168/jds.2011-5198

Krukowski H, Bakuła Z, Iskra M, Olender A, Bis-Wencel H and Jagielski T, 2020. The first outbreak of methicillin-resistant *Staphylococcus aureus* in dairy cattle in Poland with evidence of on-farm and intrahousehold transmission. Journal of Dairy Science, 103, 10577–10584. https://doi.org/10.3168/jds.2020-18291

Lam TJ, DeJong MC, Schukken YH and Brand A, 1996. Mathematical modeling to estimate efficacy of postmilking teat disinfection in split-udder trials of dairy cows. Journal of Dairy Science, 79, 62–70.

Lam TJ, van den Borne BH, Jansen J, Huijps K, van Veersen JC, van Schaik G and Hogeveen H, 2013. Improving bovine udder health: a national mastitis control program in the Netherlands. Journal of Dairy Science, 96, 1301–1311.

Larsen J, Petersen A, Sørum M, Stegger M, van Alphen L, Valentiner-Branth P, Knudsen LK, Larsen LS, Feingold B, Price LB, Andersen PS, Larsen AR and Skov RL, 2015. Meticillin-resistant *Staphylococcus aureus* CC398 is an increasing cause of disease in people with no livestock contact in Denmark, 1999 to 2011. Eurosurveillance, 20. https://doi.org/10.2807/1560-7917.ES.2015.20.37.30021

Larsen J, Stegger M, Andersen PS, Petersen A, Larsen AR, Westh H, Agersø Y, Fetsch A, Kraushaar B, Käsbohrer A, Feβler AT, Schwarz S, Cuny C, Witte W, Butaye P, Denis O, Haenni M, Madec JY, Jouy E, Laurent F, Battisti A, Franco A, Alba P, Mammina C, Pantosti A, Monaco M, Wagenaar JA, de Boer E, van Duijkeren E, Heck M, Domínguez L, Torres C, Zarazaga M, Price LB and Skov RL, 2016. Evidence for human adaptation and foodborne transmission of livestock-associated methicillin-resistant Staphylococcus aureus. Clinical Infectious Diseases, 63, 1349–1352. https://doi.org/10.1093/cid/ciw532

Larsen J, Raisen CL, Ba X, Sadgrove NJ, Padilla-González GF, Simmonds MSJ, Loncaric I, Kerschner H, Apfalter P, Hartl R, Deplano A, Vandendriessche S, Černá Bolfíková B, Hulva P, Arendrup MC, Hare RK, Barnadas C, Stegger M, Sieber RN, Skov RL, Petersen A, Angen Ø, Rasmussen SL, Espinosa-Gongora C, Aarestrup FM, Lindholm LJ, Nykäsenoja SM, Laurent F, Becker K, Walther B, Kehrenberg C, Cuny C, Layer F, Werner G, Witte W, Stamm I, Moroni P, Jørgensen HJ, de Lencastre H, Cercenado E, García-Garrote F, Börjesson S, Hæggman S, Perreten V, Teale CJ, Waller AS, Pichon B, Curran MD, Ellington MJ, Welch JJ, Peacock SJ, Seilly DJ, Morgan FJE, Parkhill J, Hadjirin NF, Lindsay JA, Holden MTG, Edwards GF, Foster G, Paterson GK, Didelot X, Holmes MA, Harrison EM and Larsen AR, 2022. Emergence of methicillin resistance predates the clinical use of antibiotics. Nature, 1–7. https://doi.org/10.1038/s41586-021-04265-w

Le Maréchal C, Jan G, Even S, McCulloch JA, Azevedo V, Thiéry R, Vautor E and Le Loir Y, 2009. Development of serological proteome analysis of mastitis by *Staphylococcus aureus* in ewes. Journal of Microbiological Methods, 79, 131–136. https://doi.org/10.1016/j.mimet.2009.08.017

Lee AS, de Lencastre H, Garau J, Kluytmans J, Malhotra-Kumar S, Peschel A and Harbarth S, 2018. Methicillin-resistant Staphylococcus aureus. Nature Reviews Disease Primers, 4, 1–23. https://doi.org/10.1038/nrdp.2018.33

Lehenbauer TW and Oltjen JW, 1998. Dairy cow culling strategies: making economical culling decisions. Journal of Dairy Science, 81, 264–271. https://doi.org/10.3168/jds.S0022-0302(98)75575-4

Leijon M, Atkins E, Persson Waller K and Artursson K, 2021. Longitudinal study of *Staphylococcus aureus* genotypes isolated from bovine clinical mastitis. Journal of Dairy Science, 104, 11945–11954. https://doi.org/10.3168/jds.2021-20562

Leuenberger A, Sartori C, Boss R, Resch G, Oechslin F, Steiner A, Moreillon P and Graber HU, 2019. Genotypes of Staphylococcus aureus: on-farm epidemiology and the consequences for prevention of intramammary infections. Journal of Dairy Science, 102, 3295–3309. https://doi.org/10.3168/jds.2018-15181

Lienen T, Schnitt A, Hammerl JA, Maurischat S and Tenhagen BA, 2021. Genomic distinctions of LA-MRSA ST398 on dairy farms from different german federal states with a low risk of severe human infections. Frontiers in Microbiology, 3390. https://doi.org/10.3389/fmicb.2020.575321

Lima MC, de Barros M, Scatamburlo TM, Polveiro RC, de Castro LK, Guimarães SHS, da Costa SL, da Costa MM and Moreira MAS, 2020. Profiles of Staphyloccocus aureus isolated from goat persistent mastitis before and after treatment with enrofloxacin. BMC Microbiology, 20, 1–11. https://doi.org/10.1186/s12866-020-01793-9

Little SV, Hillhouse AE, Lawhon SD and Bryan LK, 2021. Analysis of virulence and antimicrobial resistance gene carriage in *Staphylococcus aureus* infections in equids using whole-genome sequencing. mSphere, 6, e0019620. https://doi.org/10.1128/mSphere.00196-20. Epub 2021 Aug 4. PMID: 34346711; PMCID: PMC8386420.

Liu Y, Han C, Chen Z, Guo D and Ye X, 2020. Relationship between livestock exposure and methicillin-resistant *Staphylococcus aureus* carriage in humans: a systematic review and dose-response meta-analysis. International Journal of Antimicrobial Agents, 55. https://doi.org/10.1016/j.ijantimicag.2019.09.014

Locatelli C, Cremonesi P, Bertocchi L, Zanoni MG, Barberio A, Drigo I, Varisco G, Castiglioni B, Bronzo V and Moroni P, 2016. Short communication: methicillin-resistant *Staphylococcus aureus* in bulk tank milk of dairy cows and effect of swine population density. Journal of Dairy Science, 99, 2151–2156. https://doi.org/10.3168/jds.2015-9940

Locatelli C, Cremonesi P, Caprioli A, Carfora V, Ianzano A, Barberio A, Morandi S, Casula A, Castiglioni B, Bronzo V and Moroni P, 2017. Occurrence of methicillin-resistant *Staphylococcus aureus* in dairy cattle herds, related swine farms, and humans in contact with herds. Journal of Dairy Science, 100, 608–619. https://doi.org/10.3168/jds.2016-11797

Loncaric I, Lepuschitz S, Ruppitsch W, Trstan A, Andreadis T, Bouchlis N, Marbach H, Schauer B, Szostak MP, Feßler AT, Künzel F, Licka T, Springer B, Allerberger F, Monecke S, Ehricht R, Schwarz S and Spergser J, 2019. Increased genetic diversity of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from companion animals. Veterinary Microbiology, 235, 118–126. https://doi.org/10.1016/j.vetmic.2019.06.013

Long Y, Li L, Xu T, Wu X, Gao Y, Huang J, He C, Ma T, Ma L, Cheng C and Zhao C, 2021. Hedgehog artificial macrophage with atomic-catalytic centers to combat Drug-resistant bacteria. Nature Communications, 12, 1–11. https://doi.org/10.1038/s41467-021-26456-9

Lowder BV, Guinane CM, Ben Zakour NL, Weinert LA, Conway-Morris A, Cartwright RA, Simpson AJ, Rambaut A, Nübel U and Fitzgerald JR, 2009. Recent human-to-poultry host jump, adaptation, and pandemic spread of Staphylococcus aureus. Proceedings of the National Academy of Sciences, 106, 19545–19550. https://doi.org/10.1073/pnas.0909285106

Lozano C, Fernández-Fernández R, Ruiz-Ripa L, Gómez P, Zarazaga M and Torres C, 2020. Human mecC-carrying MRSA: clinical implications and risk factors. Microorganisms, 8, 1615. https://doi.org/10.3390/microorganisms8101615

Luini M, Cremonesi P, Magro G, Bianchini V, Minozzi G, Castiglioni B and Piccinini R, 2015. Methicillin-resistant *Staphylococcus aureus* (MRSA) is associated with low within-herd prevalence of intra-mammary infections in dairy cows: genotyping of isolates. Veterinary Microbiology, 178, 270–274. https://doi.org/10.1016/j.vetmic.2015.05.010

Maes N, Magdalena J, Rottiers S, De Gheldre Y and Struelens MJ, 2002. Evaluation of a triplex PCR assay to discriminate *Staphylococcus aureus* from coagulase-negative Staphylococci and determine methicillin resistance from blood cultures. Journal of Clinical Microbiology, 40, 1514–1517. https://doi.org/10.1128/JCM.40.4.1514-1517.2002

Magro G, Rebolini M, Beretta D and Piccinini R, 2018. Methicillin-resistant *Staphylococcus aureus* CC22-MRSA-IV as an agent of dairy cow intramammary infections. Veterinary Microbiology, 227, 29–33. https://doi.org/10.1016/j.vetmic.2018.10.021

Mama OM, Gómez P, Ruiz-Ripa L, Gómez-Sanz E, Zarazaga M and Torres C, 2019. Antimicrobial resistance, virulence, and genetic lineages of Staphylococci from horses destined for human consumption: high detection of S. aureus Isolates of lineage ST1640 and those carrying the lukPQ Gene. Animals (Basel), 9, 900. https://doi.org/10.3390/ani9110900

Marra A, 2020. Animal Models for Drug Development for MRSA. Methicillin-Resistant Staphylococcus Aureus (MRSA) Protocols, 2069, 253–266. https://doi.org/10.1007/978-1-4939-9849-4_17
Mazzariol S, Corrò M, Tonon E, Biancani B, Centelleghe C and Gili C, 2018. Death associated to methicillin resistant *Staphylococcus aureus* ST8 infection in two dolphins maintained under human care, Italy. Frontiers in Immunology, 9, 2726. https://doi.org/10.3389/fimmu.2018.02726
McBurney S, Veitch AM and Daoust PY, 2000. Bacterial valvular endocarditis in a black bear from Labrador. Journal of Wildlife Diseases, 36, 788–791. https://doi.org/10.7589/0090-3558-36.4.788
McKernan C, Benson T, Farrell S and Dean M, 2021. Antimicrobial use in agriculture: critical review of the factors influencing behaviour. JAC-antimicrobial Resistance, 3, dlab178. https://doi.org/10.1093/jacamr/dlab178
Middleton JR, 2008. Staphylococcus aureus antigens and challenges in vaccine development. Expert Review of Vaccines, 7, 805–815. https://doi.org/10.1586/14760584.7.6.805
Middleton JR, Ma J, Rinehart CL, Taylor VN, Luby CD and Steevens BJ, 2006. Efficacy of different Lysigin formulations in the prevention of *Staphylococcus aureus* intramammary infection in dairy heifers. Journal of Dairy Research, 73, 10–19. https://doi.org/10.1017/S0022029905001354
Middleton JR, Luby CD and Adams DS, 2009. Efficacy of vaccination against staphylococcal mastitis: a review and new data. Veterinary Microbiology, 134, 192–198. https://doi.org/10.1016/j.vetmic.2008.09.053
Monecke S, Kuhnert P, Hotzel H, Slickers P and Ehricht R, 2007. Microarray based study on virulence-associated genes and resistance determinants of *Staphylococcus aureus* isolates from cattle. Veterinary Microbiology, 125, 128–140. https://doi.org/10.1016/j.vetmic.2007.05.016
Monecke S, Gavier-Widén D, Hotzel H, Peters M, Guenther S, Lazaris A, Loncaric I, Müller E, Reissig A, Ruppelt-Lorz A, Shore AC, Walter B, Coleman DC and Ehricht R, 2016. Diversity of *Staphylococcus aureus* Isolates in European Wildlife. PLoS One, 11, e0168433.
Montgomery JM, Gillespie D, Sastrawan P, Fredeking TM and Stewart GL, 2002. Aerobic salivary bacteria in wild and captive Komodo dragons. Journal of Wildlife Diseases, 38, 545–551. https://doi.org/10.7589/0090-3558-38.3.545
Monistero V, Barberio A, Biscarini F, Cremonesi P, Castiglioni B, Graber HU, Bottini E, Ceballos-Marquez A, Kroemker V, Petzer IM, Pollera C, Santisteban C, Veiga Dos Santos M, Bronzo V, Piccinini R, Re G, Cocchi M and Moroni P, 2020. Different distribution of antimicrobial resistance genes and virulence profiles of *Staphylococcus aureus* strains isolated from clinical mastitis in six countries. Journal of Dairy Science, 103, 3431–3446. https://doi.org/10.3168/jds.2019-17141
Murphy RJT, Ramsay JP, Lee YT, Pang S, O'Dea MA, Pearson JC, Axon JE, Raby E, Abdulgader SM, Whitelaw A and Coombs GW, 2019. Multiple introductions of methicillin-resistant *Staphylococcus aureus* ST612 into Western Australia associated both with human and equine reservoirs. International Journal of Antimicrobial Agents, 54, 681–685. https://doi.org/10.1016/j.ijantimicag.2019.08.022
Neave FK, Dodd FH, Kingwill RG and Westgarth DR, 1969. Control of mastitis in the dairy herd by hygiene and management. Journal of Dairy Science, 52, 696–707.
Nemeghaire S, Argudín MA, Haesebrouck F and Butaye P, 2014. Epidemiology and molecular characterization of methicillin-resistant *Staphylococcus aureus* nasal carriage isolates from bovines. BMC Veterinary Research, 10, 1–9. https://doi.org/10.1186/1746-6148-10-153
Nikolaisen NK, Lassen DCK, Chriél M, Larsen G, Jensen VF and Pedersen K, 2017. Antimicrobial resistance among pathogenic bacteria from mink (Neovison vison) in Denmark. Acta Veterinaria Scandinavica, 59, 1–10. https://doi.org/10.1186/s13028-017-0328-6
Nowakiewicz A, Ziółkowska G, Zięba P, Gnat S, Wojtanowicz-Markiewicz K and Trościańczyk A, 2016. Coagulase-positive Staphylococcus isolated from wildlife: identification, molecular characterization and evaluation of resistance profiles with focus on a methicillin-resistant strain. Comparative Immunology, Microbiology and Infectious Diseases, 44, 21–28. https://doi.org/10.1016/j.cimid.2015.11.003
Olde Riekerink RG, Barkema HW, Kelton DF and Scholl DT, 2008. Incidence rate of clinical mastitis on Canadian dairy farms. Journal of Dairy Science, 91, 1366–1377. https://doi.org/10.3168/jds.2007-0757
Olofsson TC, Butler É, Lindholm C, Nilson B, Michanek P and Vásquez A, 2016. Fighting off wound pathogens in horses with honeybee lactic acid bacteria. Current Microbiology, 73, 463–473. https://doi.org/10.1007/s00284-016-1080-2
Osterås O and Sølverød L, 2009. Norwegian mastitis control programme. Irish Veterinary Journal, 62, 1–8. https://doi.org/10.1186/2046-0481-62-S4-S26
Overbeek BP, Maathuis-de Haan WEA and Stoffer G, 2017. MRSA infection via a staff member with eczema. [Article in Dutch]. Nederlands tijdschrift voor geneeskunde, 161, D904.
Owens WE, Oliver SP, Gillespie BE, Ray CH and Nickerson SC, 1998. Role of horn flies (Haematobia irritans) in Staphylococcus aureus-induced mastitis in dairy heifers. American Journal of Veterinary Research, 59, 1122–1124.
Papadopoulos P, Papadopoulos T, Angelidis AS, Kotzamanidis C, Zdragas A, Papa A, Filioussis G and Sergelidis D, 2019. Prevalence, antimicrobial susceptibility and characterization of *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* isolated from dairy industries in north-central and north-eastern Greece. International Journal of Food Microbiology, 16, 35–41. https://doi.org/10.1016/j.ijfoodmicro.2018.11.007

Papadopoulos P, Papadopoulos T, Angelidis AS, Boukouvala E, Zdragas A, Papa A, Hadjichristodoulou C and Sergelidis D, 2018. Prevalence of *Staphylococcus aureus* and of methicillin-resistant S. aureus (MRSA) along the production chain of dairy products in north-western Greece. Food Microbiology, 69, 43–50. https://doi.org/10.1016/j.fm.2017.07.016. Epub 2017 Jul 28. PMID: 28941908.

Pascu C, Herman V, Iancu I and Costinar L, 2022. Etiology of Mastitis and Antimicrobial Resistance in Dairy Cattle Farms in the Western Part of Romania. Antibiotics (Basel), 11, 57. https://doi.org/10.3390/antibiotics11010057

Paterson GK, Larsen AR, Robb A, Edwards GE, Pennycott TW, Foster G, Mot D, Hermans K, Baert K, Peacock SJ, Parkhill J, Zadoks RN and Holmes MA, 2012. The newly described mecA homologue, mecALGA251, is present in methicillin-resistant *Staphylococcus aureus* isolates from a diverse range of host species. Journal of Antimicrobial Chemotherapy, 67, 2809–2813. https://doi.org/10.1093/jac/dks329

Paterson GK, Harrison EM and Holmes MA, 2014a. The emergence of mecC methicillin-resistant Staphylococcus aureus. Trends in Microbiology, 22, 42–47. https://doi.org/10.1016/j.tim.2013.11.003

Paterson GK, Morgan FJ, Harrison EM, Peacock SJ, Parkhill J, Zadoks RN and Holmes MA, 2014b. Prevalence and properties of mecC methicillin-resistant *Staphylococcus aureus* (MRSA) in bovine bulk tank milk in Great Britain. Journal of Antimicrobial Chemotherapy, 69, 598–602. https://doi.org/10.1093/jac/dkt417

Penadés M, Viana D, García-Quirós A, Muñoz-Silvestre A, Moreno-Grua E, Pérez-Fuentes S, Pascual JJ, Corpa JM and Selva L, 2020. Differences in virulence between the two more prevalent *Staphylococcus aureus* clonal complexes in rabbitries (CC121 and CC96) using an experimental model of mammary gland infection. Veterinary Research, 51, 1–15. https://doi.org/10.1186/s13567-020-0740-1

Pitkälä A, Haveri M, Pyörälä S, Myllys V and Honkanen-Buzalski T, 2004. Bovine mastitis in Finland 2001–prevalence, distribution of bacteria, and antimicrobial resistance. Journal of Dairy Science, 87, 2433–2441. https://doi.org/10.3168/jds.S0022-0302(04)73366-4

Plaza-Rodríguez C, Alt K, Grobbel M, Hammerl JA, Irrgang A, Szabo I, Stingl K, Schuh E, Wiehle L, Pfefferkorn B, Naumann S, Kaesbohrer A and Tenhagen BA, 2021. Wildlife as sentinels of antimicrobial resistance in Germany? Frontiers in Veterinary Science, 7, 1251. https://doi.org/10.3389/fvets.2020.627821

Pletinckx LJ, Dewulf J, De Bleecker Y, Rasschaert G, Goddeeris BM and De Man I, 2013. Evaluation of different chromogenic media for the detection of methicillin-resistant *Staphylococcus aureus* CC398 in broilers. European Journal of Clinical Microbiology & Infectious Diseases, 32, 1023–1026. https://doi.org/10.1007/s10096-013-1844-6

Plommet MG and Wilson JB, 1969. Serological typing of *Staphylococcus aureus* from wild animals. Journal of Comparative Pathology, 79, 425–433. https://doi.org/10.1016/0021-9975(69)90062-0

Porrero MC, Mentaberre G, Sánchez S, Fernández-Llario P, Gómez-Barrero S, Navarro-Gonzalez N, Serrano E, Casas-Díaz E, Marco I, Fernández-Garayzabal JF, Mateos A, Vidal D, Lavín S and Domínguez L, 2013. Methicillin resistant *Staphylococcus aureus* (MRSA) carriage in different free-living wild animal species in Spain. The Veterinary Journal, 198, 127–130. https://doi.org/10.1016/j.tvjl.2013.06.004

Porrero MC, Valverde A, Fernández-Llario P, Díez-Guerrier A, Mateos A, Lavín S, Cantón R, Fernández-Garayzabal JF and Domínguez L, 2014. Staphylococcus aureus carrying mecC gene in animals and urban wastewater. Spain. Emerging Infectious Diseases, 20, 899–901.

Power E and Murphy S, 2002. Staphylococcus aureus septicaemia in a killer whale. The Veterinary Record, 150, 819.

Price LB, Stegger M, Hasman H, Aziz M, Larsen J, Andersen PS, Pearson T, Waters AE, Foster JT, Schupp J, Gillece J, Driebe E, Liu CM, Springer B, Zdovc I, Battisti A, Franco A, Zmudzki J, Schwarz S, Butaye P, Jouy E, Pomba C, Porrero MC, Ruimy R, Smith TC, Robinson DA, Weese JS, Arriola CS, Yu F, Laurent F, Keim P, Skov R and Aarestrup FM, 2012. Staphylococcus aureus CC398: host adaptation and emergence of methicillin resistance in livestock. MBio, 3, e00305–e311. https://doi.org/10.1128/mBio.00305-11

Quraishi A, Kaur P, Singh Sharma N and Arora AK, 2021. Antibiotic sensitivity patterns in Staphylococcus spp. isolated from goat milk in association with molecular detection of antibiotic resistance genes. Iranian Journal of Veterinary Research, 22, 239–243. https://doi.org/10.22099/ijvr.2021.38465.5599

Rainard P, Foucras G, Fitzgerald JR, Watts JL, Koop G and Middleton JR, 2018. Knowledge gaps and research priorities in *Staphylococcus aureus* mastitis control. Transboundary and Emerging Diseases, 65, 149–165. https://doi.org/10.1111/tbed.12698

Rainard P, Gilbert FB, Germon P and Foucras G, 2021. Invited review: a critical appraisal of mastitis vaccines for dairy cows. Journal of Dairy Science, 104, 10427–10448. https://doi.org/10.3168/jds.2021-20434

Rankin S, Roberts S, O'Shea K, Maloney D, Lorenzo M and Benson CE, 2005. Panton-valentine leukocidin (PVL) toxin positive MRSA strains isolated from companion animals. Veterinary Microbiology, 108, 145–148.

Rasschaert G, Vanderhaeghen W, Dewaele I, Janez N, Huijsdens X, Butaye P and Heyndrickx M, 2009. Comparison of fingerprinting methods for typing methicillin-resistant *Staphylococcus aureus* sequence type 398. Journal of Clinical Microbiology, 47, 3313–3322. https://doi.org/10.1128/JCM.00910-09

Reizner W, Hunter JG, O'Malley NT, Southgate RD, Schwarz EM and Kates SL, 2014. A systematic review of animal models for *Staphylococcus aureus* osteomyelitis. European Cells & Materials, 27, 196–212. https://doi.org/10.22203/ecm.v027a15

Reyher KK, Haine D, Dohoo IR and Revie CW, 2012. Examining the effect of intramammary infections with minor mastitis pathogens on the acquisition of new intramammary infections with major mastitis pathogens–a systematic review and meta-analysis. Journal of Dairy Science, 95, 6483–6502. https://doi.org/10.3168/jds.2012-5594

Rocktäschel T, Renner-Martin K, Cuny C, Brehm W, Truyen U and Speck S, 2020. Surgical hand preparation in an equine hospital: comparison of general practice with a standardised protocol and characterisation of the methicillin-resistant *Staphylococcus aureus* recovered. PLoS One, 15, e0242961. https://doi.org/10.1371/journal.pone.0242961

Ronco T, Klaas IC, Stegger M, Svennesen L, Astrup LB, Farre M and Pedersen K, 2018. Genomic investigation of *Staphylococcus aureus* isolates from bulk tank milk and dairy cows with clinical mastitis. Veterinary Microbiology, 215, 35–42. https://doi.org/10.1016/j.vetmic.2018.01.003

Rosen K, Roesler U, Merle R and Friese A, 2018. Persistent and transient airborne MRSA colonization of piglets in a newly established animal model. Frontiers in Microbiology, 9, 1542. https://doi.org/10.3389/fmicb.2018.01542

Rossi BF, Bonsaglia ECR, Castilho IG, Dantas STA, Salina A, Langoni H, Pantoja JCF, Budri PE, Fitzgerald-Hughes D, Júnior AF and Rall VLM, 2019. Genotyping of long term persistent *Staphylococcus aureus* in bovine subclinical mastitis. Microbial Pathogenesis, 132, 45–50. https://doi.org/10.1016/j.micpath.2019.04.031

Ruegg PL, 2017. A 100-year review: Mastitis detection, management, and prevention. Journal of Dairy Science, 100, 10381–10397. https://doi.org/10.3168/jds.2017-13023

Rüegsegger F, Corti S, Sihto H-M and Johler S, 2014. Toxic bovine mastitis caused by *Staphylococcus aureus* in twin cows. Schweizer Archiv Für Tierheilkunde, 156, 539–542.

Sakwinska O, Giddey M, Moreillon M, Morisset D, Waldvogel A and Moreillon P, 2011. Staphylococcus aureus host range and human-bovine host shift. Applied and Environmental Microbiology, 77, 5908–5915. https://doi.org/10.1128/AEM.00238-11

Sartori C, Boss R, Bodmer M, Leuenberger A, Ivanovic I and Graber HU, 2018. Sanitation of *Staphylococcus aureus* genotype B-positive dairy herds: a field study. Journal of Dairy Science, 101, 6897–6914. https://doi.org/10.3168/jds.2017-13937

Savin M, Bierbaum G, Hammerl JA, Heinemann C, Parcina M, Sib E, Voigt A and Kreyenschmidt J, 2020a. ESKAPE bacteria and extended-spectrum-β-lactamase-producing Escherichia coli isolated from wastewater and process water from German Poultry Slaughterhouses. Applied and Environmental Microbiology, 86, e02748–e2819. https://doi.org/10.1128/AEM.02748-19

Savin M, Bierbaum G, Hammerl JA, Heinemann C, Parcina M, Sib E, Voigt A and Kreyenschmidt J, 2020b. Antibiotic-resistant bacteria and antimicrobial residues in wastewater and process water from German pig slaughterhouses and their receiving municipal wastewater treatment plants. Science of the Total Environment, 727. https://doi.org/10.1016/j.scitotenv.2020.138788

Schlotter K, Huber-Schlenstedt R, Gangl A, Hotzel H, Monecke S, Müller E, Reißig A, Proft S and Ehricht R, 2014. Multiple cases of methicillin-resistant CC130 *Staphylococcus aureus* harboring mecC in milk and swab samples from a Bavarian dairy herd. Journal of Dairy Science, 97, 2782–2788. https://doi.org/10.3168/jds.2013-7378

Schmitt S, Stephan R, Huebschke E, Schaefle D, Merz A and Johler S, 2020. DNA microarray-based characterization and antimicrobial resistance phenotypes of clinical MRSA strains from animal hosts. Journal of Veterinary Science, 21, e54. https://doi.org/10.4142/jvs.2020.21.e54

Schnitt A, Lienen T, Wichmann-Schauer H, Cuny C and Tenhagen BA, 2020. The occurrence and distribution of livestock-associated methicillin-resistant *Staphylococcus aureus* ST398 on German dairy farms. Journal of Dairy Science, 103, 11806–11819. https://doi.org/10.3168/jds.2020-18958

Schnitt A and Tenhagen BA, 2020. Risk factors for the occurrence of methicillin-resistant *Staphylococcus aureus* in dairy herds: an update. Foodborne Pathogens and Disease, 17, 585–596. https://doi.org/10.1089/fpd.2019.2638

Schukken YH, Bronzo V, Locatelli C, Pollera C, Rota N, Casula A, Testa F, Scaccabarozzi L, March R, Zalduendo D, Guix R and Moroni P, 2014. Efficacy of vaccination on *Staphylococcus aureus* and coagulase-negative staphylococci intramammary infection dynamics in 2 dairy herds. Journal of Dairy Science, 97, 5250–5264. https://doi.org/10.3168/jds.2014-8008

Schukken YH, Günther J, Fitzpatrick J, Fontaine MC, Goetze L, Holst O, Leigh J, Petzl W, Schuberth H-J, Sipka A, Smith D, Quesnell R, Watts J, Yancey R, Zerbe H, Gurjar A, Zadoks R and Seyfert H-M; members of the Pfizer mastitis research consortium, 2011. Host-response patterns of intramammary infections in dairy cows. Veterinary Immunology and Immunopathology, 144, 270–289. https://doi.org/10.1016/j.vetimm.2011.08.022

Schwarz S, Feßler AT, Loncaric I, Wu C, Kadlec K, Wang Y and Shen J, 2018. Antimicrobial Resistance among Staphylococci of Animal Origin. Microbiology Spectrum, 6. https://doi.org/10.1128/microbiolspec.ARBA-0010-2017

Sears PM, Smith BS, English PB, Herer PS and Gonzalez RN, 1990. Shedding pattern of *Staphylococcus aureus* from bovine intramammary infections. Journal of Dairy Science, 73, 2785–2789. https://doi.org/10.3168/jds.S0022-0302(90)78964-3

Sekizuka T, Niwa H, Kinoshita Y, Uchida-Fujii E, Inamine Y, Hashino M and Kuroda M, 2020. Identification of a mecA/mecC-positive MRSA ST1-t127 isolate from a racehorse in Japan. Journal of Antimicrobial Chemotherapy, 75, 292–295. https://doi.org/10.1093/jac/dkz459

Sergelidis D and Angelidis AS, 2017. Methicillin-resistant Staphylococcus aureus: a controversial food-borne pathogen. Letters in Applied Microbiology, 64, 409–418. https://doi.org/10.1111/lam.12735

Sieber S, Gerber V, Jandova V, Rossano A, Evison JM and Perreten V, 2011. Evolution of multidrug-resistant *Staphylococcus aureus* infections in horses and colonized personnel in an equine clinic between 2005 and 2010. Microbial Drug Resistance, 17, 471–478. https://doi.org/10.1089/mdr.2010.0188

Silva V, Capelo JL, Igrejas G and Poeta P, 2020. Molecular Epidemiology of *Staphylococcus aureus* Lineages in Wild Animals in Europe: a review. Antibiotics (Basel), 9, 122. https://doi.org/10.3390/antibiotics9030122

Silva V, Ferreira E, Manageiro V, Reis L, Tejedor-Junco MT, Sampaio A, Capelo JL, Caniça M, Igrejas G and Poeta P, 2021. Distribution and clonal diversity of *Staphylococcus aureus* and other Staphylococci in Surface Waters: detection of ST425-t742 and ST130-t843 mecC-Positive MRSA Strains. Antibiotics (Basel), 10, 1416. https://doi.org/10.3390/antibiotics10111416

Simpson VR, Hargreaves J, Butler HM, Davison NJ and Everest DJ, 2013. Causes of mortality and pathological lesions observed post-mortem in red squirrels (Sciurus vulgaris) in Great Britain. BMC Veterinary Research, 9, 1–14. https://doi.org/10.1186/1746-6148-9-229

Siqueira DB, Aéssio FM, Mota RA, Marvulo MF, Mauffrey JF, Monteiro SR, Farias RC, Cunha RC, Oliveira RL, Souza TC, Medeiros ES and Silva JC, 2010. Staphylococcus aureus mastitis in a white-eared opossum (Didelphis albiventris) in the Atlantic Forest of northeast Brazil. Journal of Zoo and Wildlife Medicine, 41, 526–529. https://doi.org/10.1638/2009-0079.1

Smith TC, 2015. Livestock-associated Staphylococcus aureus: the United States experience. PLoS Path, 11, e1004564. https://doi.org/10.1371/journal.ppat.1004564

Smith TC and Wardyn SE, 2015. Human Infections with *Staphylococcus aureus* CC398. Current Environmental Health Reports, 2, 41–51. https://doi.org/10.1007/s40572-014-0034-8

Smyth DS, Feil EJ, Meaney WJ, Hartigan PJ, Tollersrud T, Fitzgerald JR, Enright MC and Smyth CJ, 2009. Molecular genetic typing reveals further insights into the diversity of animal-associated Staphylococcus aureus. Journal of Medical Microbiology, 58, 1343–1353.

Soavi L, Stellini R, Signorini L, Antonini B, Pedroni P, Zanetti L, Milanesi B, Pantosti A, Matteelli A, Pan A and Carosi G, 2010. Methicillin-resistant *Staphylococcus aureus* ST398. Italy. Emerging Infectious Diseases, 16, 346–348. https://doi.org/10.3201/eid1602.091478

Soimala T, Lübke-Becker A, Schwarz S, Feßler AT, Huber C, Semmler T, Merle R, Gehlen H, Eule JC and Walther B, 2018. Occurrence and molecular composition of methicillin-resistant *Staphylococcus aureus* isolated from ocular surfaces of horses presented with ophthalmologic disease. Veterinary Microbiology, 222, 1–6. https://doi.org/10.1016/j.vetmic.2018.06.009

Sørensen AIV, Rosendal T, Widgren S and Halasa T, 2018. Mechanistic modelling of interventions against spread of livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) within a Danish farrow-to-finish pig herd. PLoS One, 13, e0200563. https://doi.org/10.1371/journal.pone.0200563

Spanu T, De Carolis E, Fiori B, Sanguinetti M, D'Inzeo T, Fadda G and Posteraro B, 2011. Evaluation of matrix-assisted laser desorption ionization-time-of-flight mass spectrometry in comparison to rpoB gene sequencing for species identification of bloodstream infection staphylococcal isolates. Clinical Microbiology and Infection, 17, 44–49. https://doi.org/10.1111/j.1469-0691.2010.03181.x

Spohr M, Rau J, Friedrich A, Klittich G, Fetsch A, Guerra B, Hammerl JA and Tenhagen BA, 2011. Methicillin-resistant *Staphylococcus aureus* (MRSA) in three dairy herds in southwest Germany. Zoonoses and Public Health, 58, 252–261. https://doi.org/10.1111/j.1863-2378.2010.01344.x

Spoor LE, McAdam PR, Weinert LA, Rambaut A, Hasman H, Aarestrup FM, Kearns AM, Larsen AR, Skov RL and Fitzgerald JR, 2013. Livestock origin for a human pandemic clone of community-associated methicillin-resistant Staphylococcus aureus. MBio, 4, e00356–e413. https://doi.org/10.1128/mBio.00356-13

Steinman A, Masarwa S, Tirosh-Levy S, Gleser D, Kelmer G, Adler A, Carmeli Y and Schwaber MJ, 2015. Methicillin-resistant *Staphylococcus aureus* spa Type t002 outbreak in horses and staff at a veterinary teaching hospital after its presumed introduction by a veterinarian. Journal of Clinical Microbiology, 53, 2827–2831. https://doi.org/10.1128/JCM.00090-15

Stelder JJ, Kjær LJ, Jensen LB, Boklund AE, Denwood M, Carlsen M and Bødker R, 2021. Livestock-associated MRSA survival on house flies (Musca domestica) and stable flies (Stomoxys calcitrans) after removal from a Danish pig farm. Scientific Reports, 11, 1–10. https://doi.org/10.1038/s41598-021-83228-7

Swinkels JM, Hogeveen H and Zadoks RN, 2005. A partial budget model to estimate economic benefits of lactational treatment of subclinical *Staphylococcus aureus* mastitis. Journal of Dairy Science, 88, 4273–4287. https://doi.org/10.3168/jds.S0022-0302(05)73113-1

Szafraniec GM, Szeleszczuk P and Dolka B, 2022. Review on skeletal disorders caused by Staphylococcus spp. in poultry. Veterinary Quarterly, 25, 1–33. https://doi.org/10.1080/01652176.2022.2033880

Tatar A, Korkmaz M, Yayla M, Polat E, Uslu H, Halici Z and Parlak SN, 2017. The potential role of amlodipine on experimentally induced bacterial rhinosinusitis. Brazilian Journal of Otorhinolaryngology, 83, 619–626. https://doi.org/10.1016/j.bjorl.2016.08.006

Tegegne HA, Florianová M, Gelbíčová T, Karpíšková R and Koláčková I, 2019. Detection and molecular characterization of methicillin-resistant *Staphylococcus aureus* Isolated from bulk tank milk of cows, sheep, and goats. Foodborne Pathogenic Disease, 16, 68–73. https://doi.org/10.1089/fpd.2018.2511

Tenhagen BA, Vossenkuhl B, Käsbohrer A, Alt K, Kraushaar B, Guerra B, Schroeter A and Fetsch A, 2014. Methicillin-resistant *Staphylococcus aureus* in cattle food chains - prevalence, diversity, and antimicrobial resistance in Germany. Journal of Animal Science, 92, 2741–2751. https://doi.org/10.2527/jas.2014-7665

Thomsen TT, Mojsoska B, Cruz JC, Donadio S, Jenssen H, Løbner-Olesen A and Rewitz K, 2016. The Lantibiotic NAI-107 Efficiently Rescues Drosophila melanogaster from Infection with Methicillin-Resistant *Staphylococcus aureus* USA300. Antimicrobial Agents and Chemotherapy, 60, 5427–5436. https://doi.org/10.1128/AAC.02965-15

Tirosh-Levy S, Steinman A, Carmeli Y, Klement E and Navon-Venezia S, 2015. Prevalence and risk factors for colonization with methicillin resistant *Staphylococcus aureus* and other Staphylococci species in hospitalized and farm horses in Israel. Preventive Veterinary Medicine, 122, 135–144. https://doi.org/10.1016/j.prevetmed.2015.09.007

Tomao P, Pirolo M, Agnoletti F, Pantosti A, Battisti A, Di Martino G, Visaggio D, Monaco M, Franco A, Pimentel de Araujo F, Palei M, Benini N, Motta C, Bovo C, Di Renzi S, Vonesch N and Visca P, 2020. Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* from dairy farms in North-eastern Italy. International Journal of Food Microbiology, 332. https://doi.org/10.1016/j.ijfoodmicro.2020.108817

Unnerstad HE, Bengtsson B, af Rantzien MH and Börjesson S, 2013. Methicillin-resistant *Staphylococcus aureus* containing mecC in Swedish dairy cows. Acta Veterinaria Scandinavica, 55, 1–3. https://doi.org/10.1186/1751-0147-55-6

Valente LG, Federer L, Iten M, Grandgirard D, Leib SL, Jakob SM, Haenggi M, Cameron DR, Que YA and Prazak J, 2021. Searching for synergy: combining systemic daptomycin treatment with localised phage therapy for the treatment of experimental pneumonia due to MRSA. BMC Research Notes, 14, 1–4. https://doi.org/10.1186/s13104-021-05796-1

van Rijen MML, Bosch T, Verkade EJM, Schouls L and Kluytmans JA; CAM Study Group, 2014. Livestock-associated MRSA carriage in patients without direct contact with livestock. PLoS One, 9, e100294. https://doi.org/10.1371/journal.pone.0100294

Vancraeynest D, Hermans K, Martel A, Vaneechoutte M, Devriese LA and Haesebrouck F, 2004. Antimicrobial resistance and resistance genes in *Staphylococcus aureus* strains from rabbits. Veterinary Microbiology, 101, 245–251. https://doi.org/10.1016/j.vetmic.2004.03.021

Vandendriessche S, Vanderhaeghen W, Soares FV, Hallin M, Catry B, Hermans K, Butaye P, Haesebrouck F, Struelens MJ and Denis O, 2013. Prevalence, risk factors and genetic diversity of methicillin-resistant *Staphylococcus aureus* carried by humans and animals across livestock production sectors. Journal of Antimicrobial Chemotherapy, 68, 1510–1516. https://doi.org/10.1093/jac/dkt047

Vanderhaeghen W, Cerpentier T, Adriaensen C, Vicca J, Hermans K and Butaye P, 2010a. Methicillin-resistant *Staphylococcus aureus* (MRSA) ST398 associated with clinical and subclinical mastitis in Belgian cows. Veterinary Microbiology, 144, 166–171. https://doi.org/10.1016/j.vetmic.2009.12.044

Vanderhaeghen W, Hermans K, Haesebrouck F and Butaye P, 2010b. Methicillin-resistant *Staphylococcus aureus* (MRSA) in food production animals. Epidemiology & Infection, 138, 606–625. https://doi.org/10.1017/S0950268809991567

Vanderhaeghen W, Piepers S, Leroy F, Van Coillie E, Haesebrouck F and De Vliegher S, 2015. Identification, typing, ecology and epidemiology of coagulase negative staphylococci associated with ruminants. The Veterinary Journal, 203, 44–51. https://doi.org/10.1016/j.tvjl.2014.11.001

Verbeke J, Piepers S, Supré K and De Vliegher S, 2014. Pathogen-specific incidence rate of clinical mastitis in Flemish dairy herds, severity, and association with herd hygiene. Journal of Dairy Science, 97, 6926–6934. https://doi.org/10.3168/jds.2014-8173

Vengust M, Anderson ME, Rousseau J and Weese JS, 2006. Methicillin-resistant staphylococcal colonization in clinically normal dogs and horses in the community. Letters in Applied Microbiology, 43, 602–606. https://doi.org/10.1111/j.1472-765X.2006.02018.x

Vidal A, Baldomà L, Molina-López RA, Martin M and Darwich L, 2017. Microbiological diagnosis and antimicrobial sensitivity profiles in diseased free-living raptors. Avian Pathology, 46, 442–450. https://doi.org/10.1080/03079457.2017.1304529

Voss A, Loeffen F, Bakker J, Klaassen C and Wulf M, 2005. Methicillin-resistant *Staphylococcus aureus* in pig farming. Emerging Infectious Diseases, 11, 1965–1966. https://doi.org/10.3201/eid1112.050428

Waage S, Mørk T, Røros A, Aasland D, Hunshamar A and Odegaard SA, 1999. Bacteria associated with clinical mastitis in dairy heifers. Journal of Dairy Science, 82, 712–719. https://doi.org/10.3168/jds.S0022-0302(99)75288-4

Walter J, Espelage W, Adlhoch C, Cuny C, Schink S, Jansen A, Witte W, Eckmanns T and Hermes J, 2017. Persistence of nasal colonisation with methicillin resistant *Staphylococcus aureus* CC398 among participants of veterinary conferences and occurrence among their household members: a prospective cohort study, Germany 2008–2014. Veterinary Microbiology, 200, 13–18. https://doi.org/10.1016/j.vetmic.2016.03.015

Walther B, Wieler LH, Friedrich AW, Hanssen AM, Kohn B, Brunnberg L and Lübke-Becker A, 2008. Methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from small and exotic animals at a university hospital during routine microbiological examinations. Veterinary Microbiology, 127, 171–178. https://doi.org/10.1016/j.vetmic.2007.07.018

Walther B, Monecke S, Ruscher C, Friedrich AW, Ehricht R, Slickers P, Soba A, Wleklinski CG, Wieler LH and Lübke-Becker A, 2009. Comparative molecular analysis substantiates zoonotic potential of equine methicillin-resistant Staphylococcus aureus. Journal of Clinical Microbiology, 47, 704–710. https://doi.org/10.1128/JCM.01626-08

Walther B, Janssen T, Gehlen H, Vincze S, Borchers K, Wieler LH, Barton AK and Lübke-Becker A, 2014. Infection control and hygiene management in equine hospitals. [In German]. Berliner Und Munchener Tierarztliche Wochenschrift, 127, 486–497.
Wang Y, Liu Q, Liu Q, Gao Q, Lu H, Meng H, Xie Y, Huang Q, Ma X, Wang H, Qin J, Li Q, Li T, Xia Q and Li M, 2018. Phylogenetic analysis and virulence determinant of the host-adapted *Staphylococcus aureus* lineage ST188 in China. Emerging Microbes & Infections, 7, 1–11. https://doi.org/10.1038/s41426-018-0048-7
Waqar N, Amin Q, Munir T, Ikram MS, Shahzad N, Mirza A, Ali A and Arshad MI, 2019. A cross-sectional study of methicillin-resistant *Staphylococcus aureus* at the equine-human interface. Tropical Animal Health and Production, 51, 1927–1933. https://doi.org/10.1007/s11250-019-01888-0
Weese JS, 2009. Treating Methicillin-Resistant *Staphylococcus aureus* Infection. Compendium Equine, 4, 274–277.
Weese JS and Lefebvre SL, 2007. Risk factors for methicillin-resistant *Staphylococcus aureus* colonization in horses admitted to a veterinary teaching hospital. The Canadian Veterinary Journal, 48, 921–926.
Weese JS and Rousseau J, 2005. Attempted eradication of methicillin-resistant *Staphylococcus aureus* colonisation in horses on two farms. Equine Veterinary Journal, 37, 510–514.
Weese JS, Archambault M, Willey BM, Hearn P, Kreiswirth BN, Said-Salim B, McGeer A, Likhoshvay Y, Prescott JF and Low DE, 2005a. Methicillin-resistant *Staphylococcus aureus* in horses and horse personnel, 2000–2002. Emerging Infectious Diseases, 11, 430–435. https://doi.org/10.3201/eid1103.040481
Weese JS, Rousseau J, Traub-Dargatz JL, Willey BM, McGeer AJ and Low DE, 2005b. Community-associated methicillin-resistant *Staphylococcus aureus* in horses and humans who work with horses. Journal of the American Veterinary Medical Association, 226, 580–583. https://doi.org/10.2460/javma.2005.226.580
Weese JS, Rousseau J, Willey BM, Archambault M, McGeer A and Low DE, 2006. Methicillin-resistant *Staphylococcus aureus* in horses at a veterinary teaching hospital: frequency, characterization, and association with clinical disease. Journal of Veterinary Internal Medicine, 20, 182–186.
Wendlandt S, Schwarz S and Silley P, 2013. Methicillin-resistant Staphylococcus aureus: a food-borne pathogen? Annual Review of Food Science and Technology, 4, 117–139.
Wu K, Conly J, Surette M, Sibley C, Elsayed S and Zhang K, 2012. Assessment of virulence diversity of methicillin-resistant *Staphylococcus aureus* strains with a Drosophila melanogaster infection model. BMC Microbiology, 12, 1–10. https://doi.org/10.1186/1471-2180-12-274
Wulf MW, Markestein A, van der Linden FT, Voss A, Klaassen C and Verduin CM, 2008. First outbreak of methicillin-resistant *Staphylococcus aureus* ST398 in a Dutch hospital, June 2007. Eurosurveillance, 13, 3–4.
Yasuda R, Kawano J, Matsuo E, Masuda T, Shimizu A, Anzai T and Hashikura S, 2002. Distribution of mecA-harboring staphylococci in healthy mares. Journal of Veterinary Medical Science, 64, 821–827. https://doi.org/10.1292/jvms.64.821
Zaatout N and Hezil D, 2021. A meta-analysis of the global prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from clinical and subclinical bovine mastitis. Journal of Applied Microbiology. https://doi.org/10.1111/jam.15192. Online ahead of print.
Zadoks RN, Allore HG, Hagenaars TJ, Barkema HW and Schukken YH, 2002. A mathematical model of *Staphylococcus aureus* control in dairy herds. Epidemiology and Infection, 129, 397–416.
Zadoks RN, Middleton JR, McDougall S, Katholm J and Schukken YH, 2011. Molecular epidemiology of mastitis pathogens of dairy cattle and comparative relevance to humans. Journal of Mammary Gland Biology and Neoplasia, 16, 357–372. https://doi.org/10.1007/s10911-011-9236-y
Zambrano-Mila M, Rodriguez AS, Rivera-Olivero IA, Salas-Rueda M, Caceres-Orellana MV, de Waard JH and Garcia-Bereguiain MA, 2020. Methicillin resistant *Staphylococcus aureus* carriage among guinea pigs raised as livestock in Ecuador. One Health, 9. https://doi.org/10.1016/j.onehlt.2019.100118
Zhou W, Li X, Osmundson T, Shi L, Ren J and Yan H, 2018. WGS analysis of ST9-MRSA-XII isolates from live pigs in China provides insights into transmission among porcine, human and bovine hosts. Journal of Antimicrobial Chemotherapy, 73, 2652–2661. https://doi.org/10.1093/jac/dky245

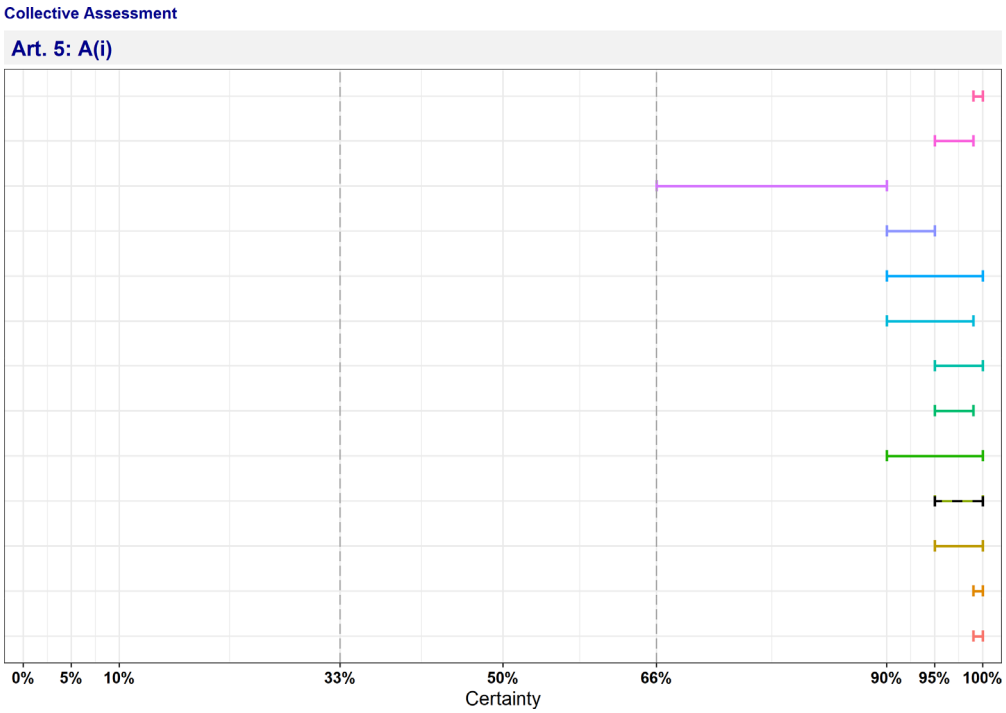
Abbreviations

AG	Aminoglycosides
AHAW	Animal Health and Welfare
AHL	Animal Health Law
AL	Animal level
AMCRA	Antimicrobial Consumption and Resistance in Animals
AMR	Antimicrobial-resistant
AMU	Antimicrobial use
BLA	β-lactams
BTM	Bulk tank milk
CA	Community-associated
CC	Clonal complex
CDC	Centers for Disease Control and Prevention

CFSPH	Center for Food Security and Public Health
CI	Current impact
CIP	Ciprofloxacin
CITES	Convention on International Trade in Endangered Species
CLI	Clindamycin
CM	Clinical mastitis
DALY	Disability-adjusted life year
DIVA	Differentiation of infected from vaccinated animals
EPRUMA	European Platform for the Responsible Using of Medicines in Animals
ENR	Enrofloxacin
ERY	Erythromycin
FAO	Food and Agriculture Organization of the United Nations
FL	Farm level
FQ	Fluoroquinolones
FUS	Fusidic acid
GEN	Gentamicin
HA	Hospital-associated
IRCM	Incidence rate of clinical mastitis
IDR	Incidence density rate
IMI	Intramammary infection
IUCN	International Union for Conservation of Nature
IR	Incidence rate
KAN	Kanamycin
LA	Livestock-associated
LIN	Lincomycin
LS	Lincosamides
MALDI-TOF MS	Matrix-assisted laser desorption ionisation–time-of-flight mass spectrometry
MIC	Minimum inhibitory concentration
ML	Macrolides
MLST	Multi-locus sequence typing
MRSA	Methicillin-resistant *S. aureus*
MS	Member State
MSSA	Methicillin-susceptible *S. aureus*
NA	Not applicable
NEO	Neomycin
NOR	Norfloxacin
OIE	Office International des Épizooties (World Organisation for Animal Health)
QL	Quarter level
PEN	Penicillin
PI	Potential impact
RoI	Resistance of Interest
SCC	Somatic cell count
SCM	Subclinical mastitis
SEB	Staphylococcal enterotoxin B
SSTI	Skin and soft tissue infection
ST	Sequence type
TET	Tetracycline
TMP	Trimethoprim
ToR	Term of Reference
T/S	Trim-sulfa antimicrobials
WGS	Whole genome sequencing

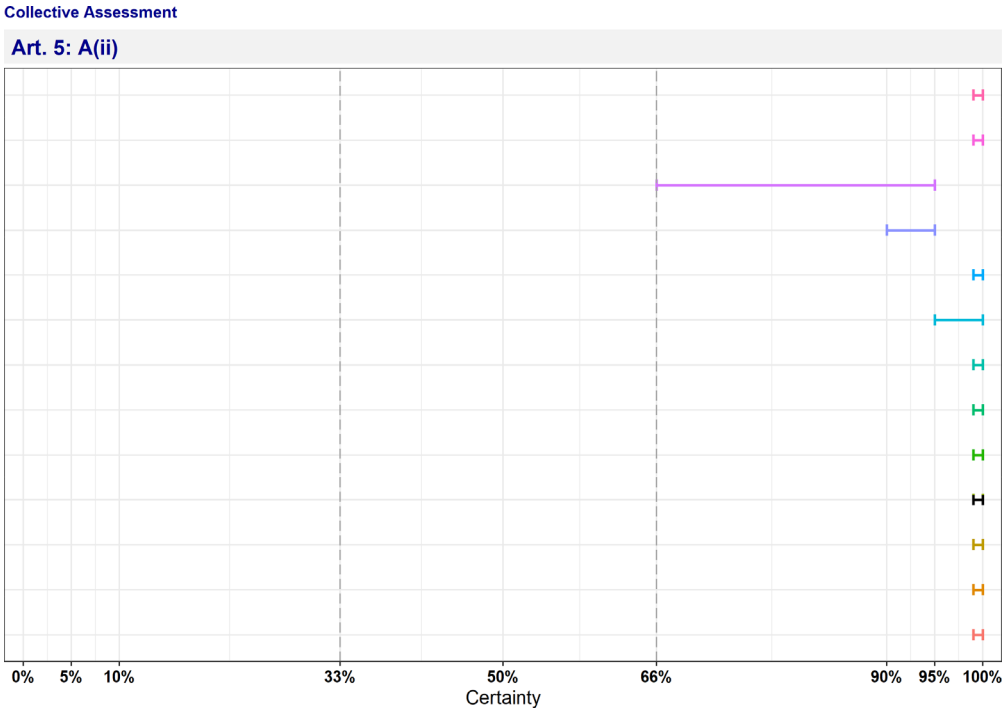
Appendix A – Criteria with certain outcome

A.1. Article 5 criteria



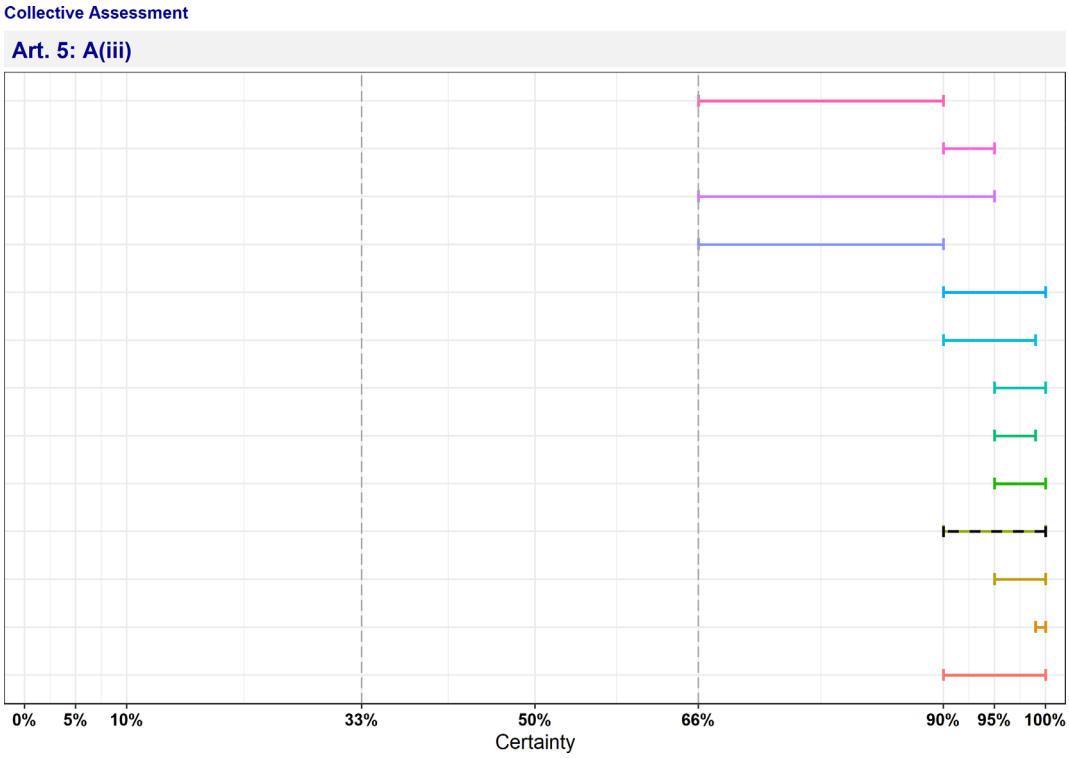
The median range is displayed as a dashed line.

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



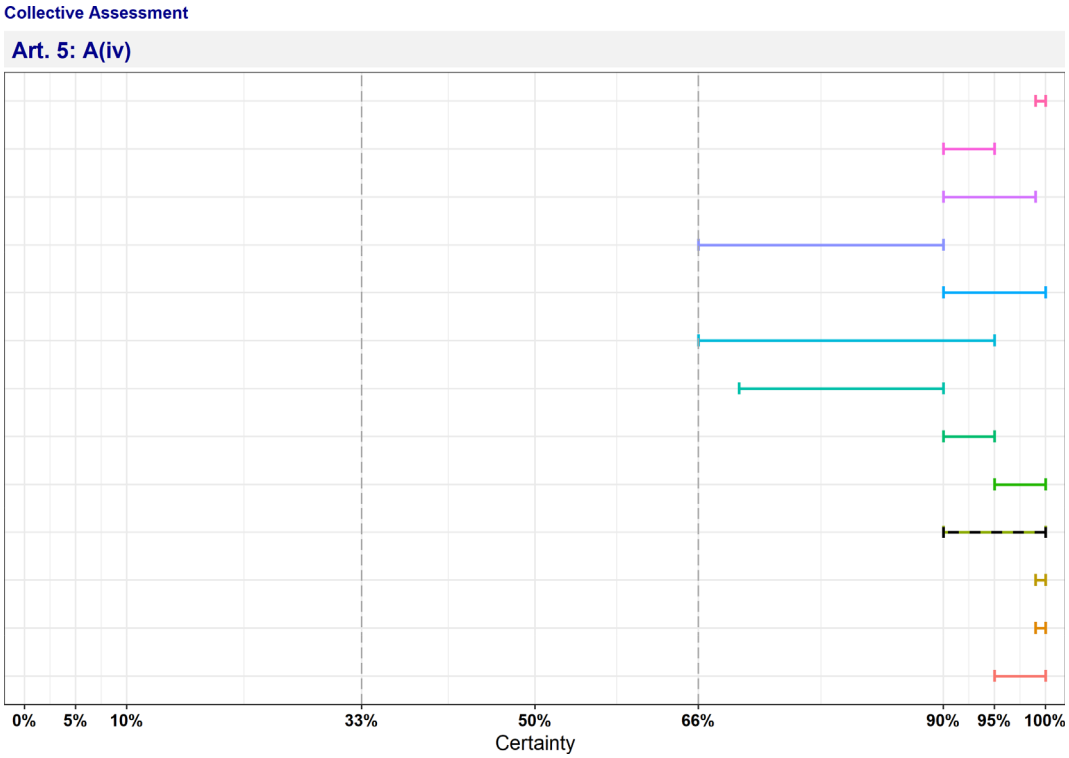
The median range is displayed as a dashed line.

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



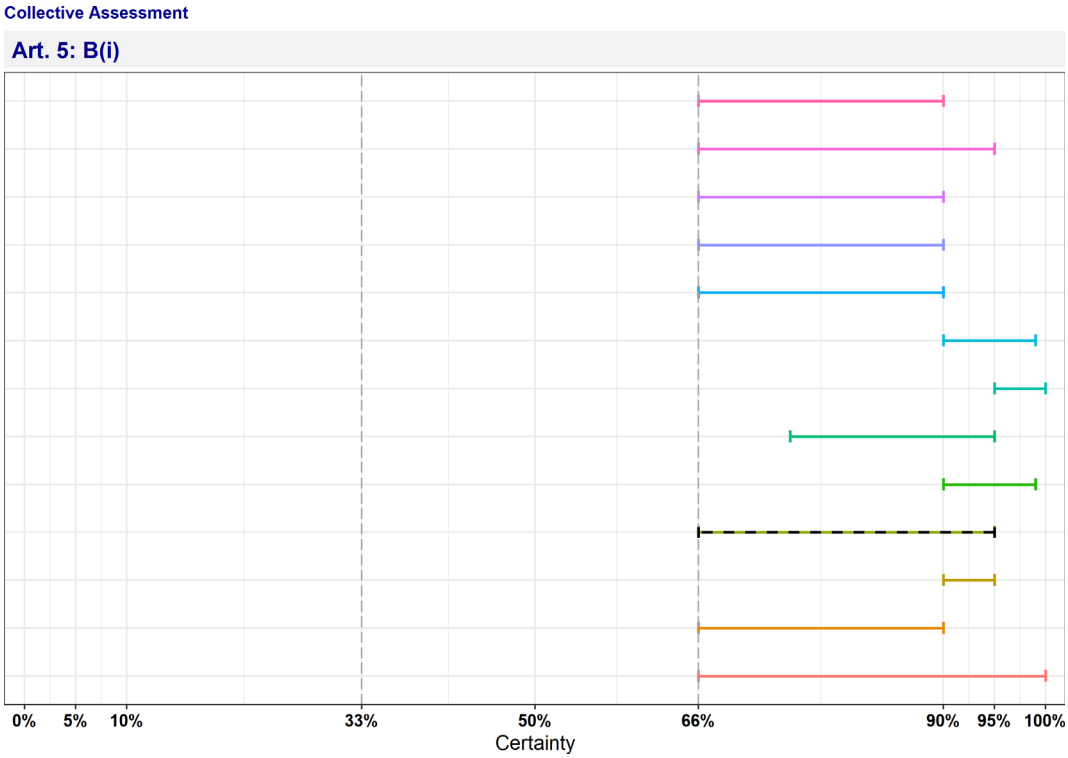
The median range is displayed as a dashed line.

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



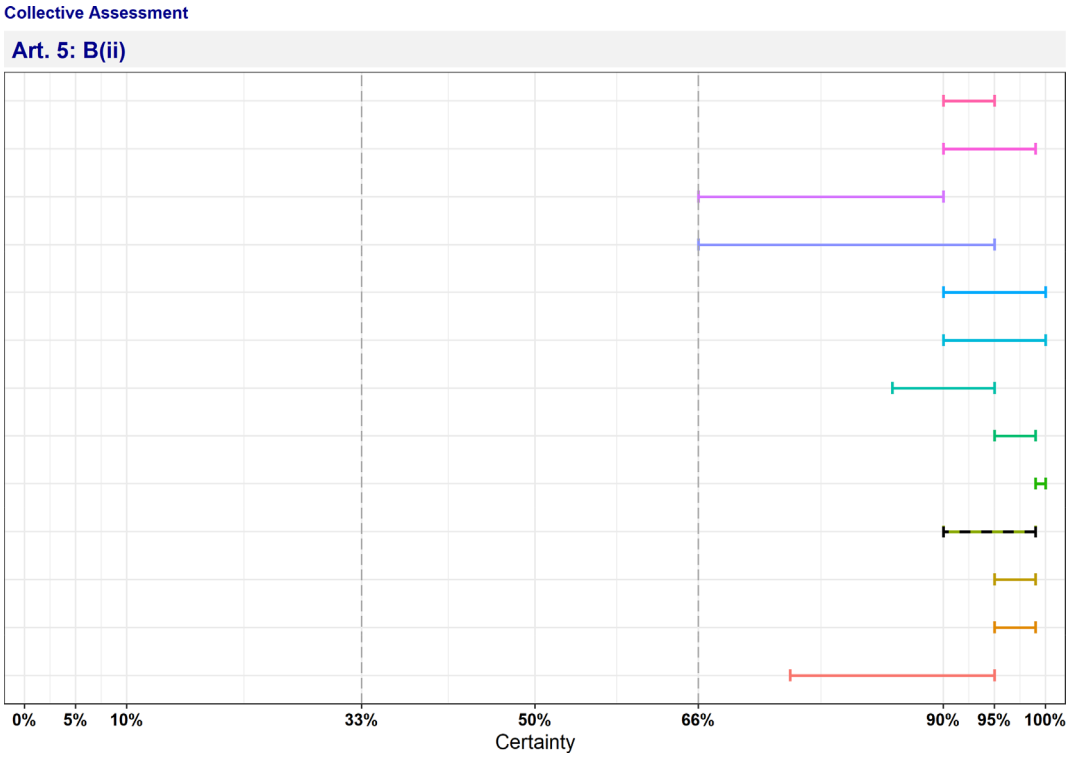
The median range is displayed as a dashed line.

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



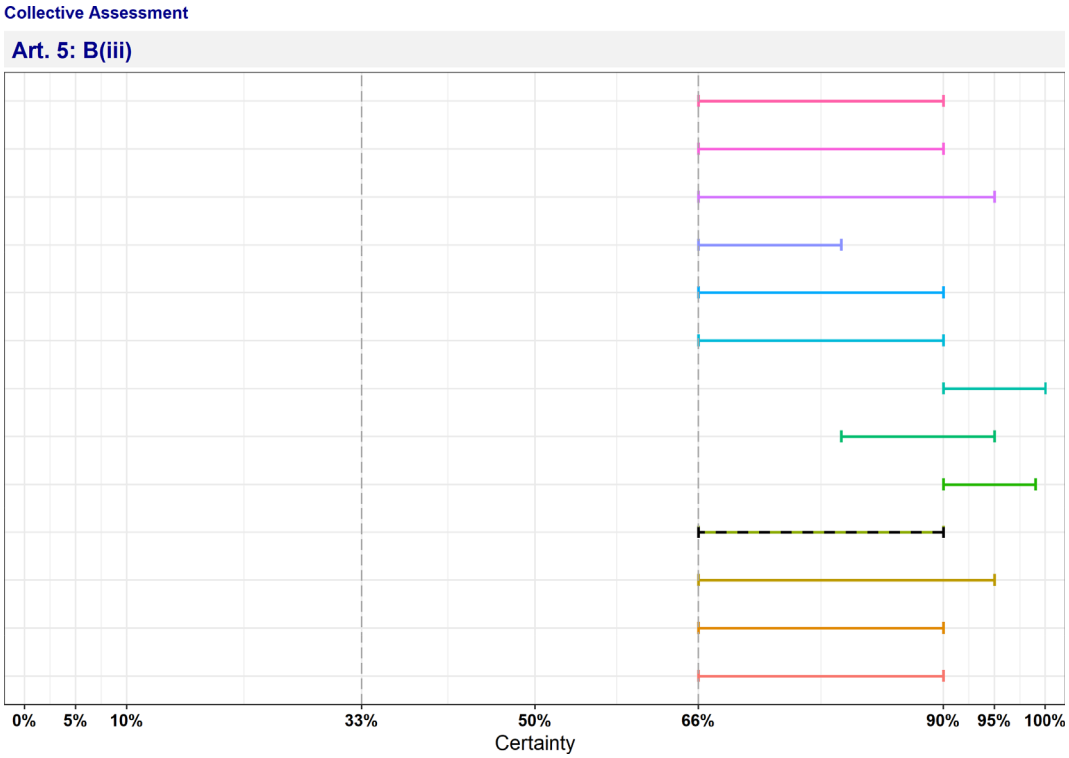
The median range is displayed as a dashed line.

Figure A.5: Individual probability ranges reflecting fulfilment of 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



The median range is displayed as a dashed line.

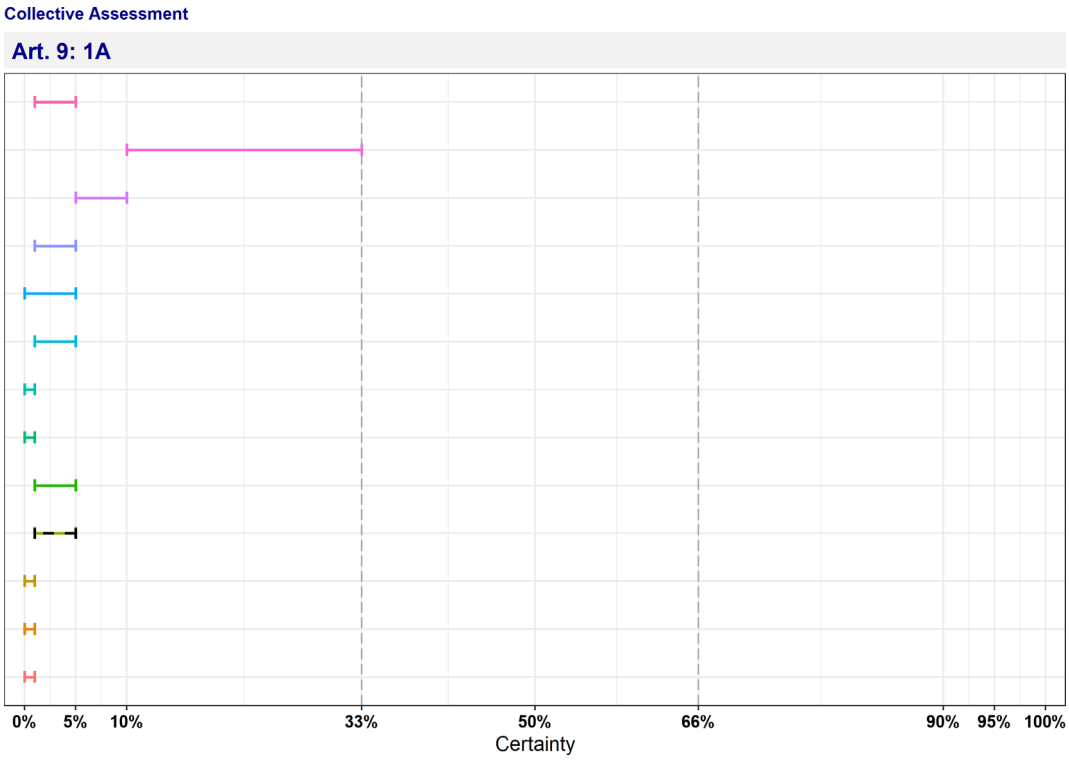
Figure A.6: Individual probability ranges reflecting fulfilment of Criterion B(ii) (the disease agent has developed resistance to treatments which poses a significant danger to public and/or animal health in the Union) after the collective judgement



The median range is displayed as a dashed line.

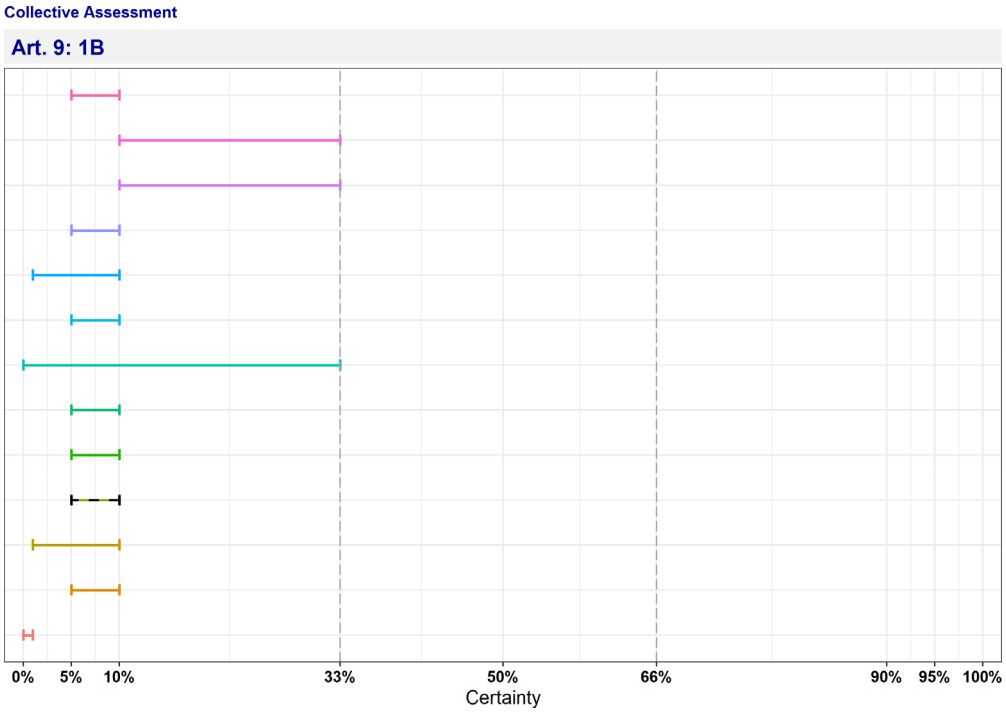
Figure A.7: Individual probability ranges reflecting fulfilment of Criterion B(iii) (the disease causes or could cause a significant negative economic impact affecting agriculture or aquaculture production in the Union) after the collective judgement

A.2. Article 9 criteria



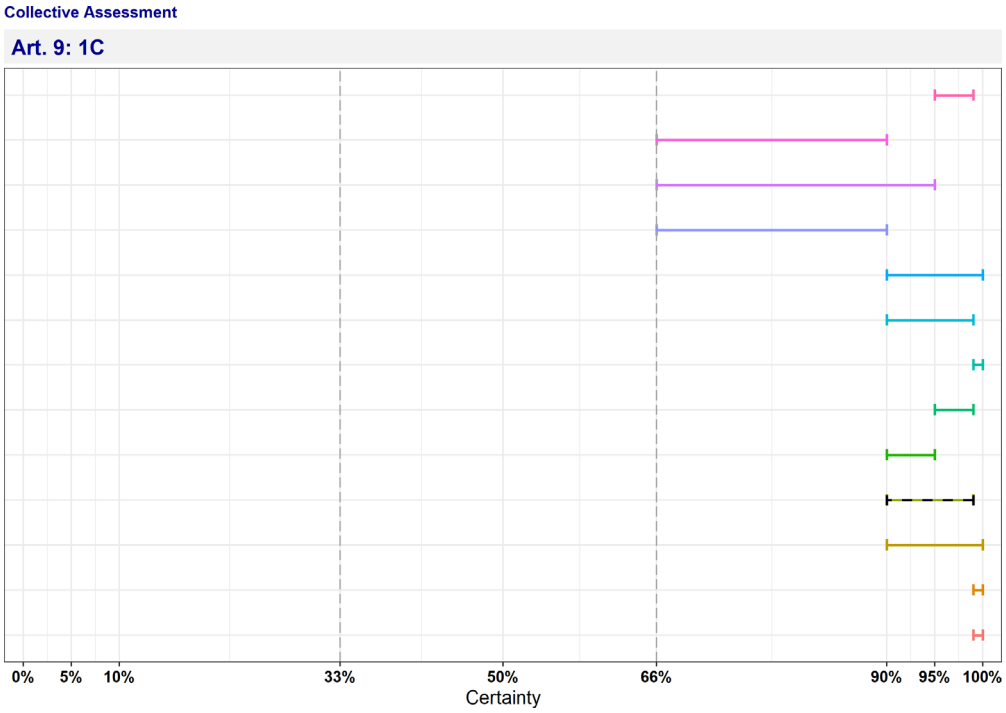
The median range is displayed as a dashed line.

Figure A.8: Individual probability ranges reflecting non-fulfilment of Criterion 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



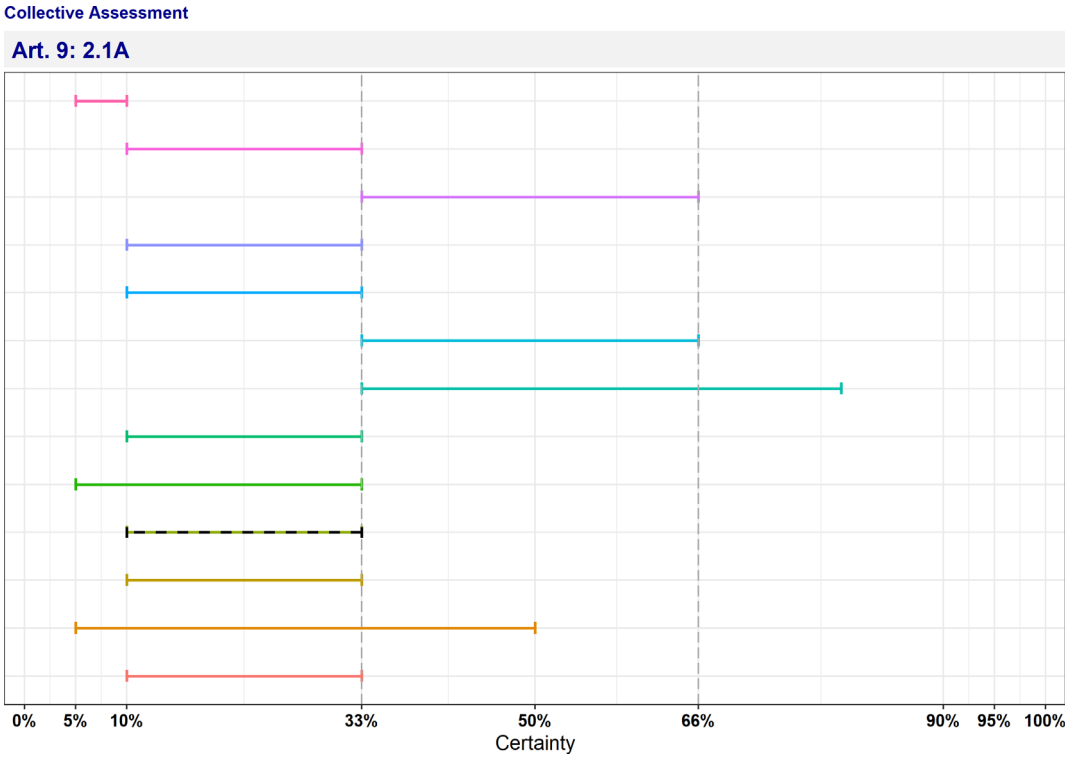
The median range is displayed as a dashed line.

Figure A.9: 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



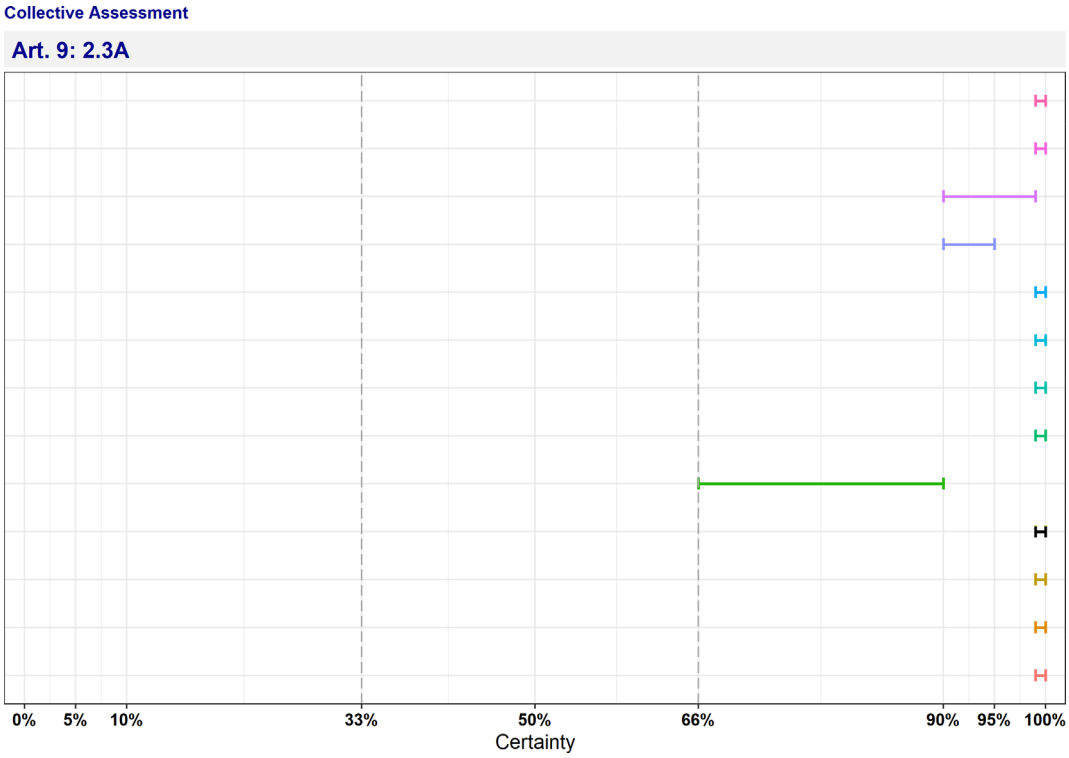
The median range is displayed as a dashed line.

Figure A.10: Individual probability ranges reflecting fulfilment of Criterion 1C (the disease is present in the whole or part of the Union territory with an endemic character) after the collective judgement



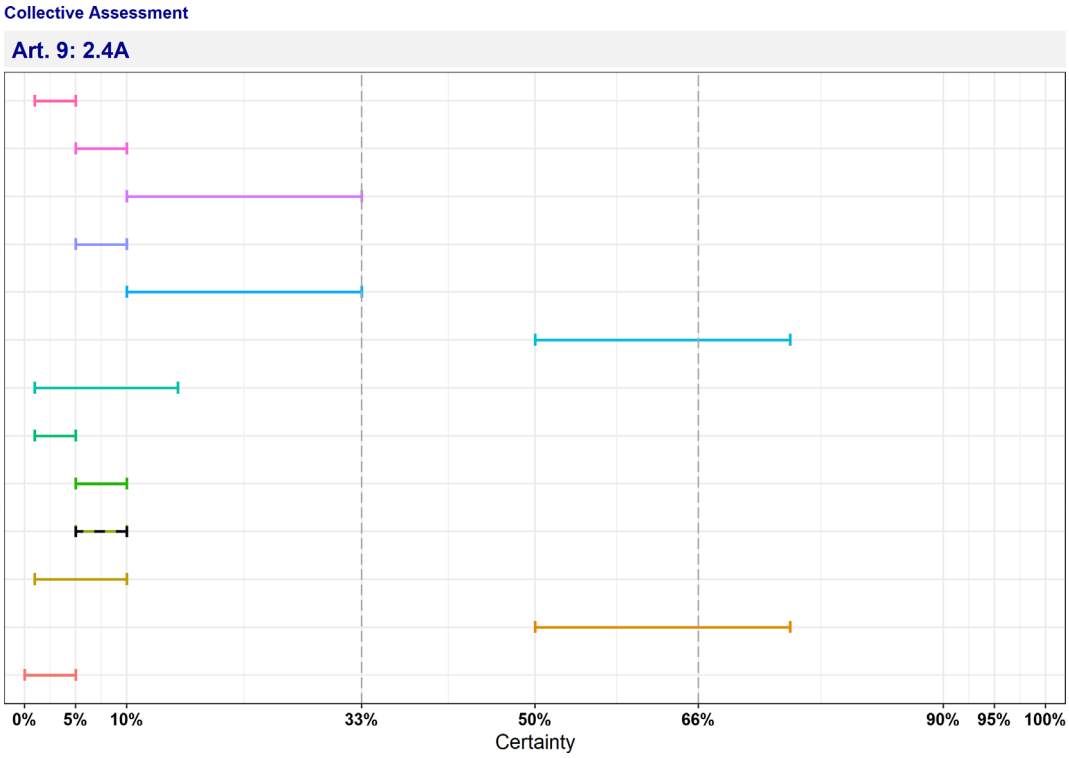
The median range is displayed as a dashed line.

Figure A.11: Individual probability ranges reflecting non-fulfilment of Criterion 2.1A (the disease is highly transmissible) after the collective judgement



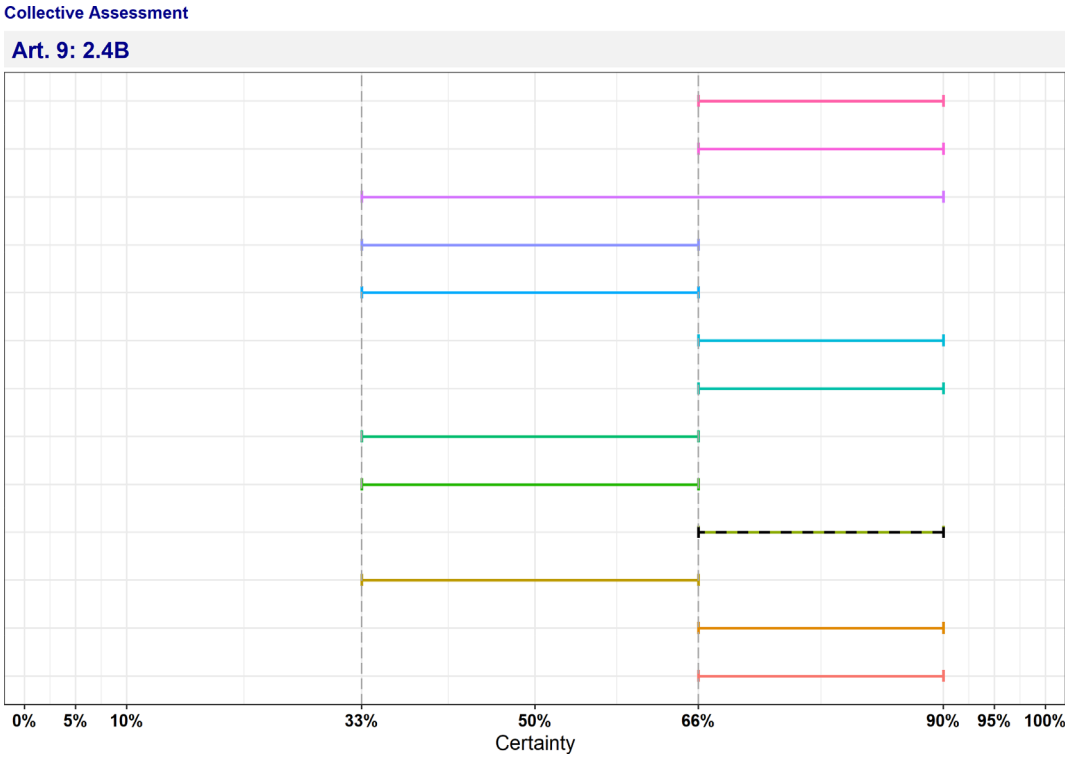
The median range is displayed as a dashed line.

Figure A.12: 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



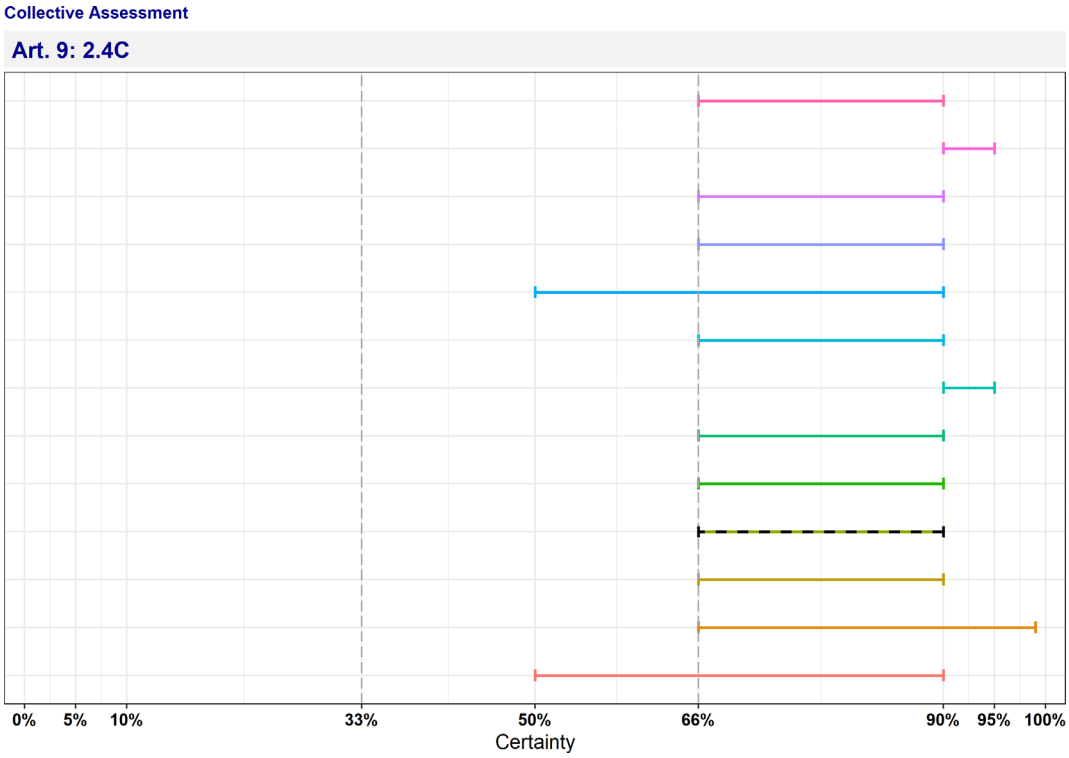
The median range is displayed as a dashed line.

Figure A.13: 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



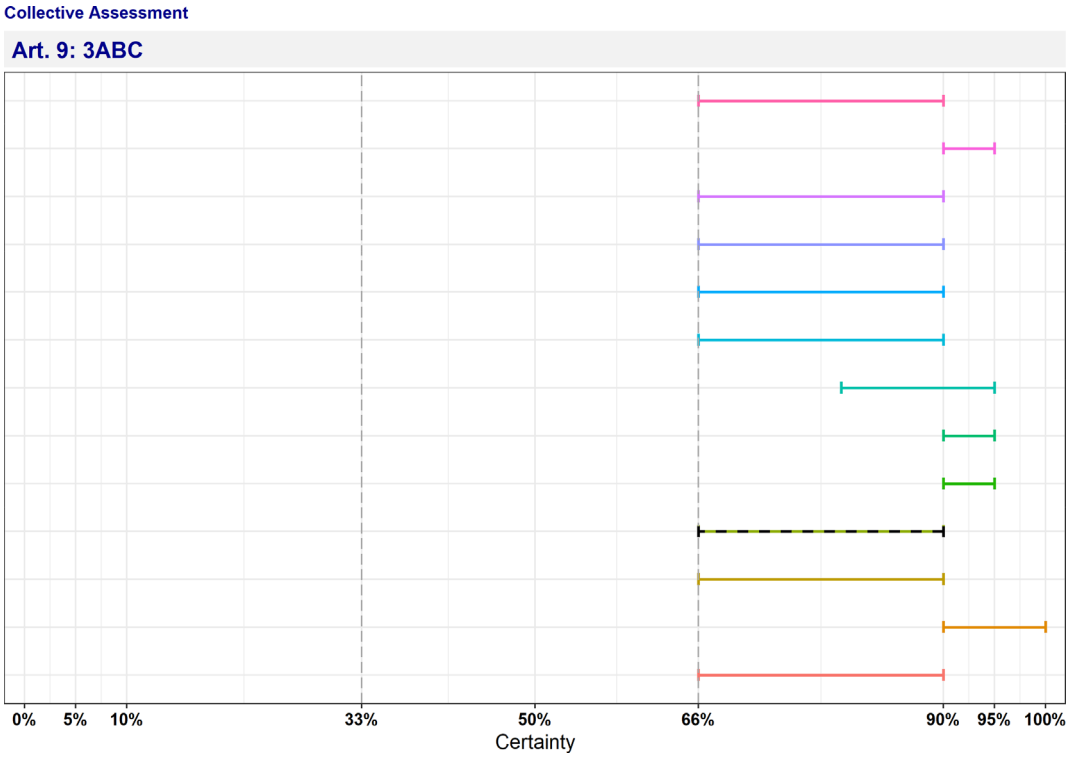
The median range is displayed as a dashed line.

Figure A.14: Individual probability ranges reflecting fulfilment of Criterion 2.4B (the disease may result in high morbidity with in general low mortality) after the collective judgement



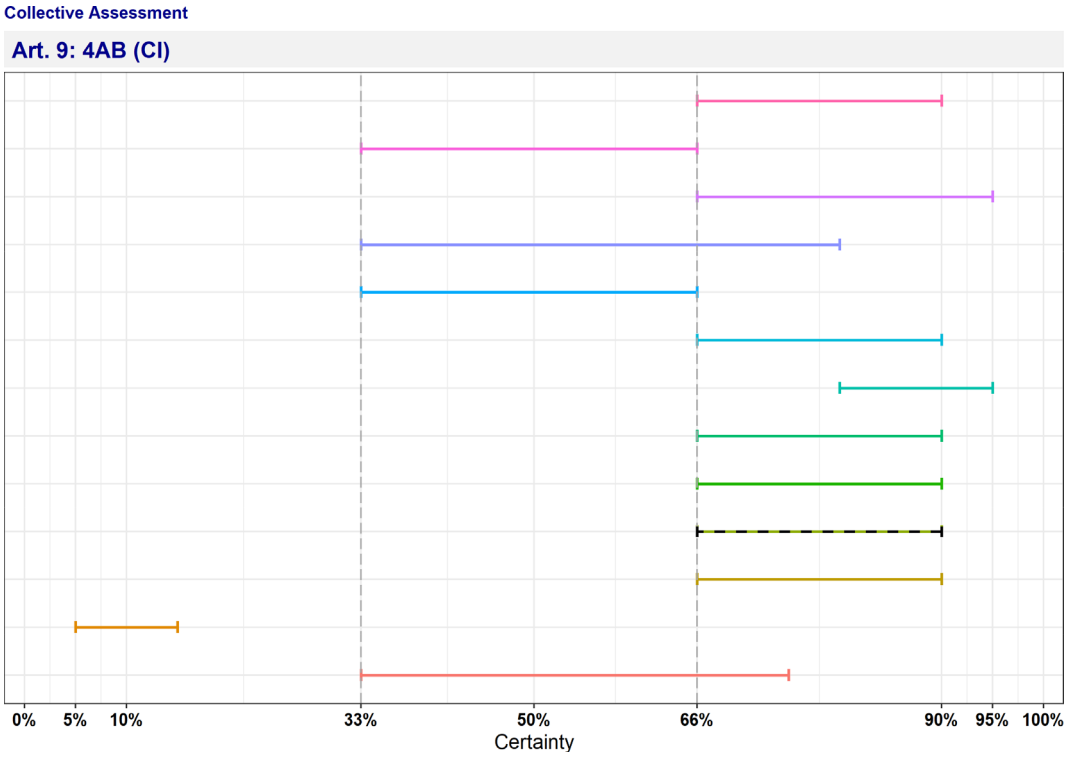
The median range is displayed as a dashed line.

Figure A.15: Individual probability ranges reflecting fulfilment of 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



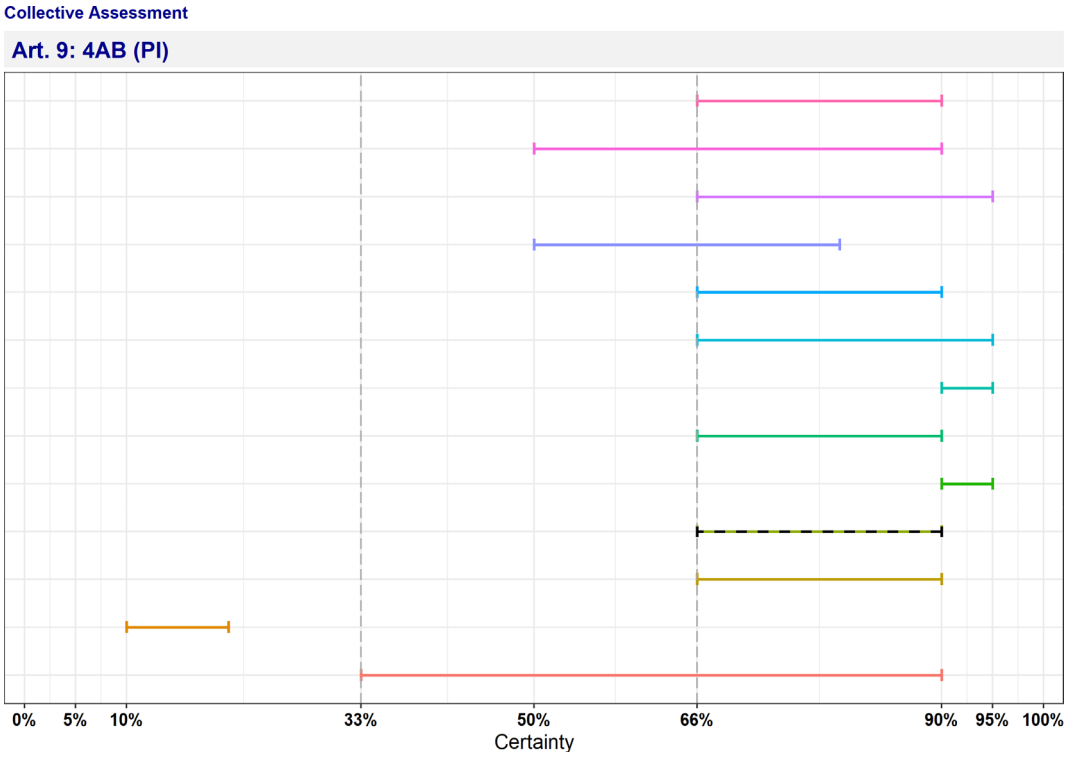
The median range is displayed as a dashed line.

Figure A.16: Individual probability ranges reflecting 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



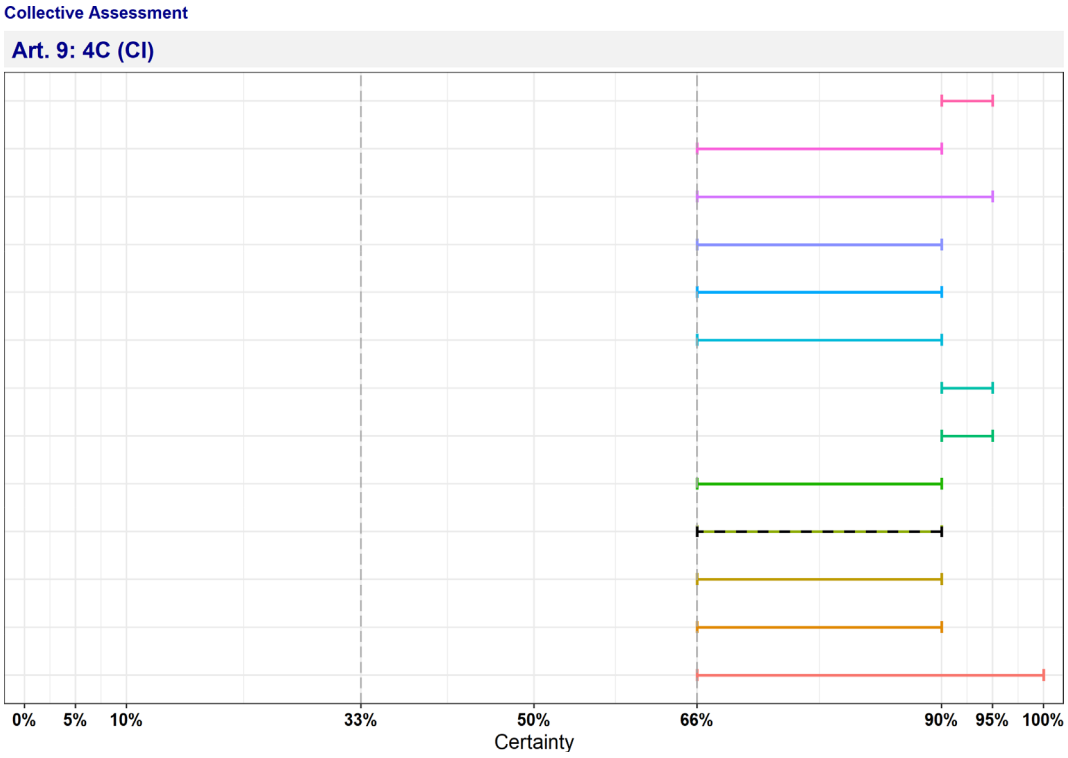
CI: current impact.
The median range is displayed as a dashed line.

Figure A.17: Individual probability ranges reflecting 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



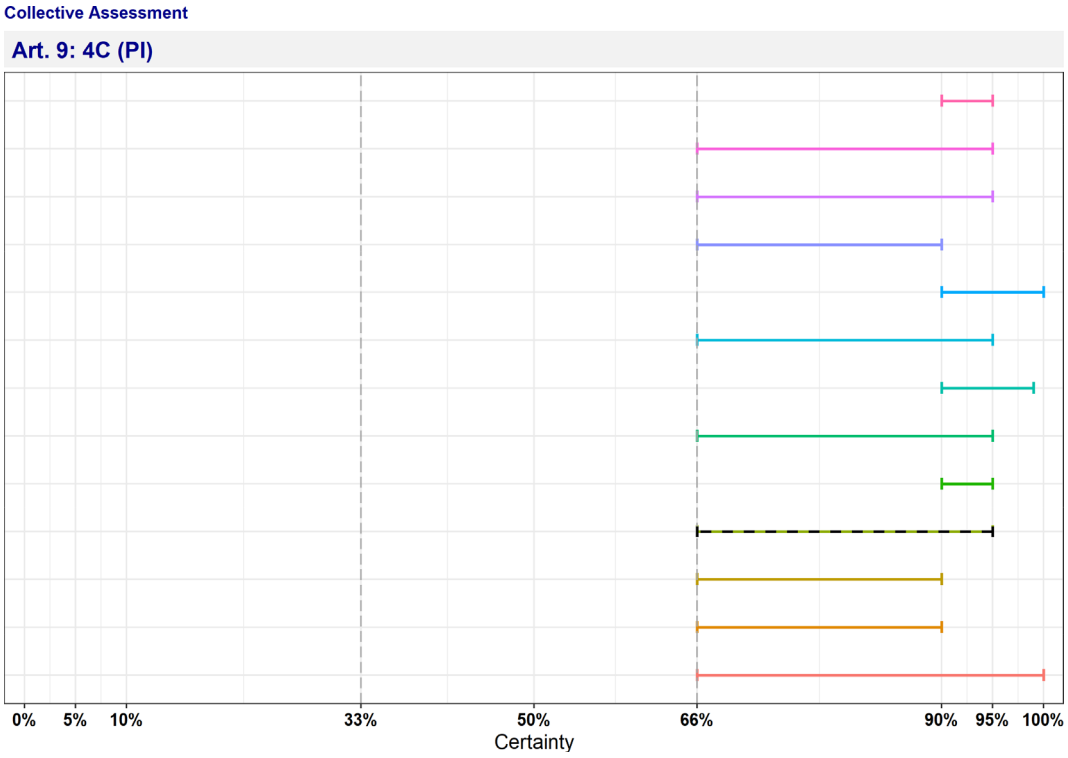
PI: potential impact.
The median range is displayed as a dashed line.

Figure A.18: Individual probability ranges reflecting fulfilment of 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



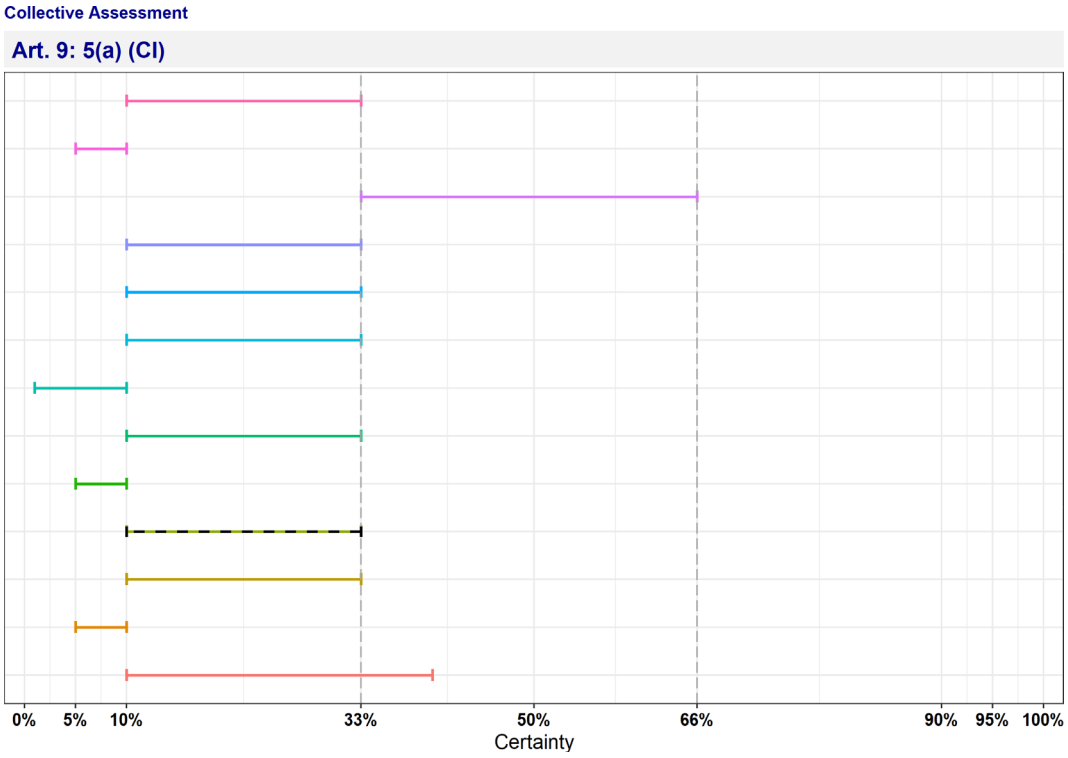
CI: current impact.
The median range is displayed as a dashed line.

Figure A.19: Individual probability ranges reflecting 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



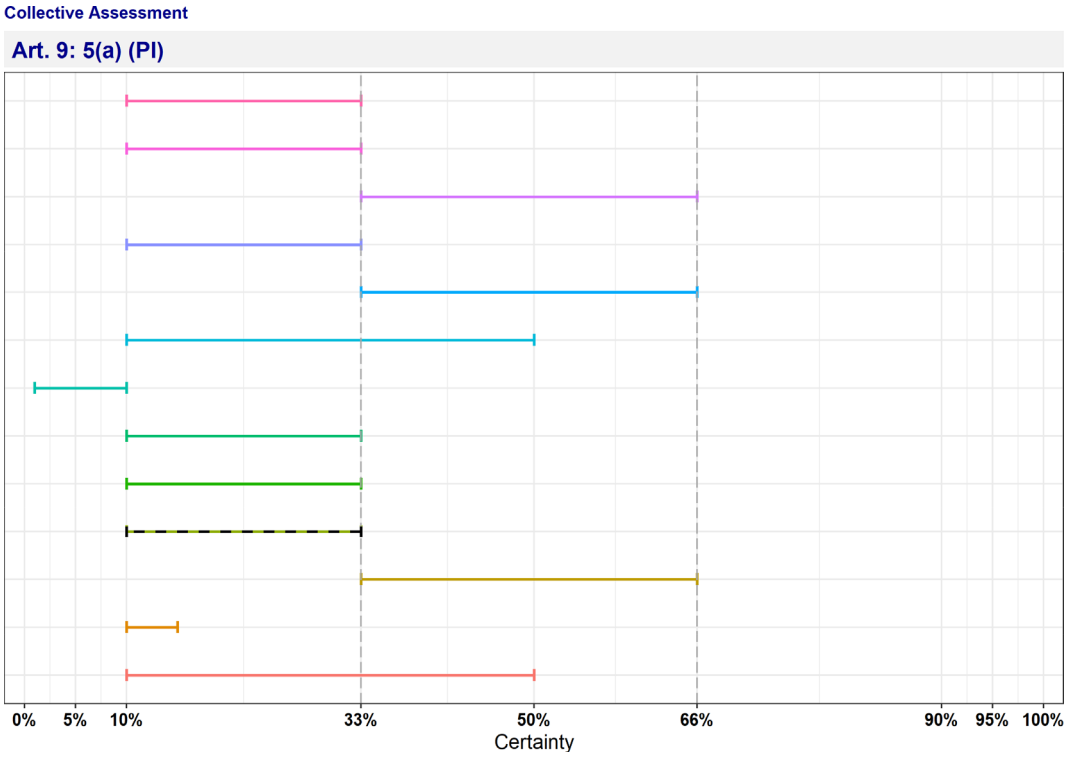
PI: potential impact.
The median range is displayed as a dashed line.

Figure A.20: Individual probability ranges reflecting fulfilment of 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



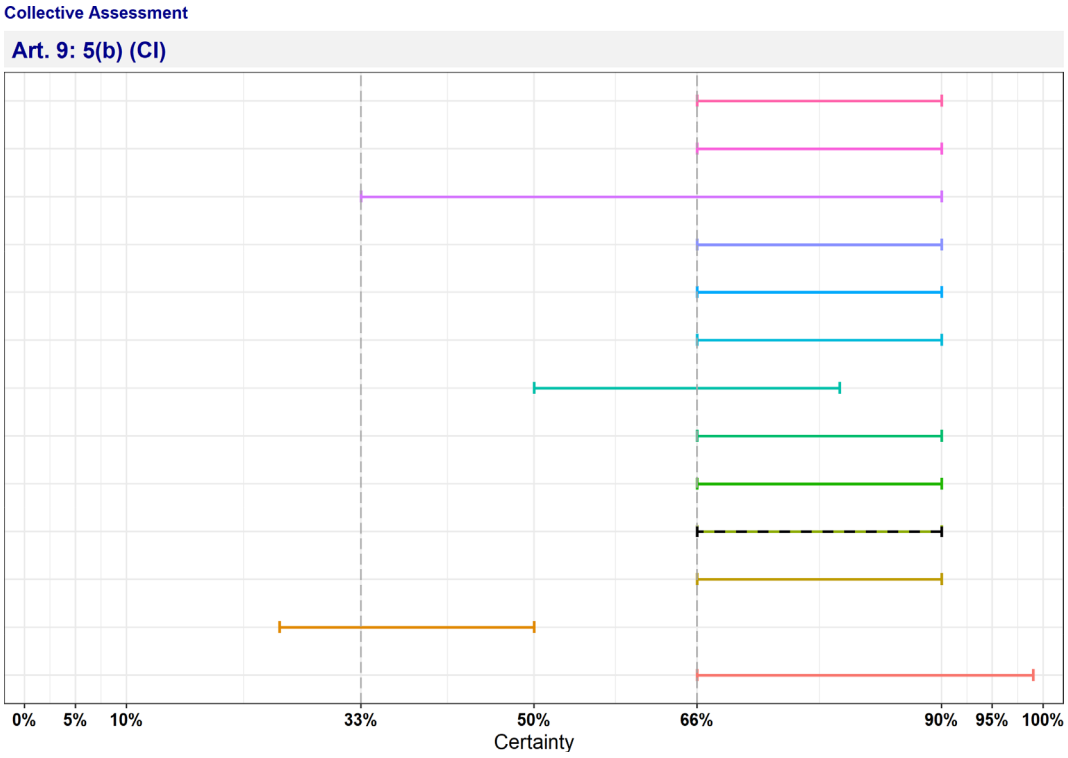
CI: current impact.
The median range is displayed as a dashed line.

Figure A.21: 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



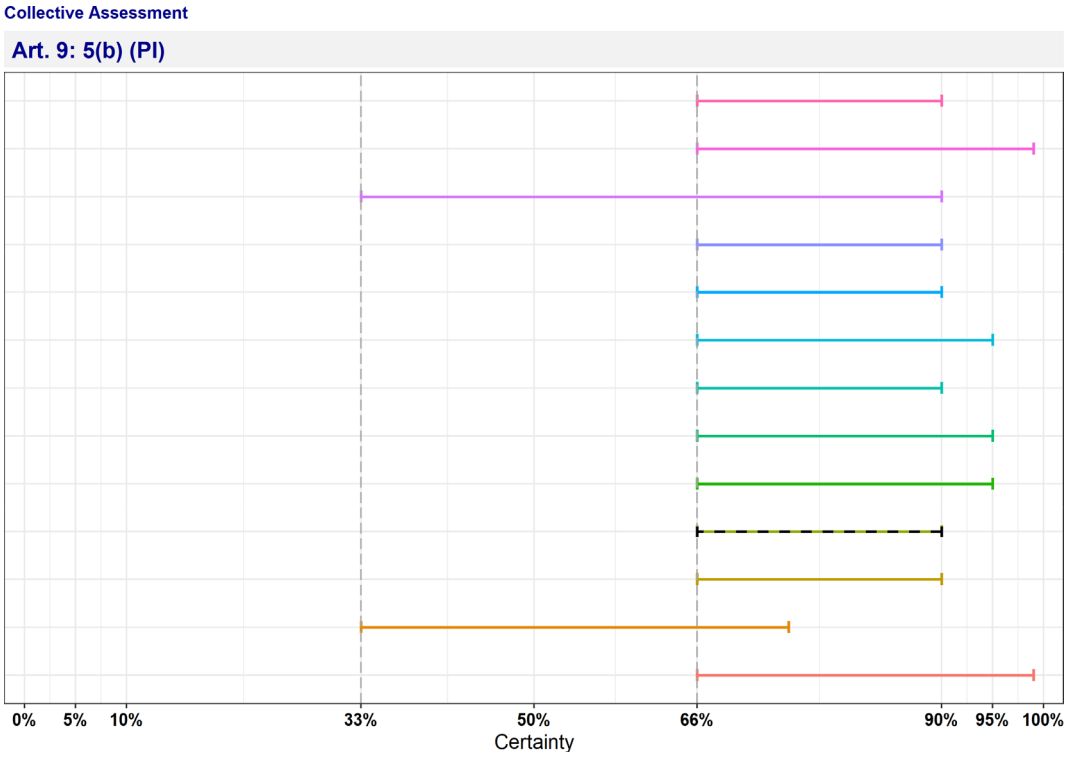
PI: potential impact.
The median range is displayed as a dashed line.

Figure A.22: 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



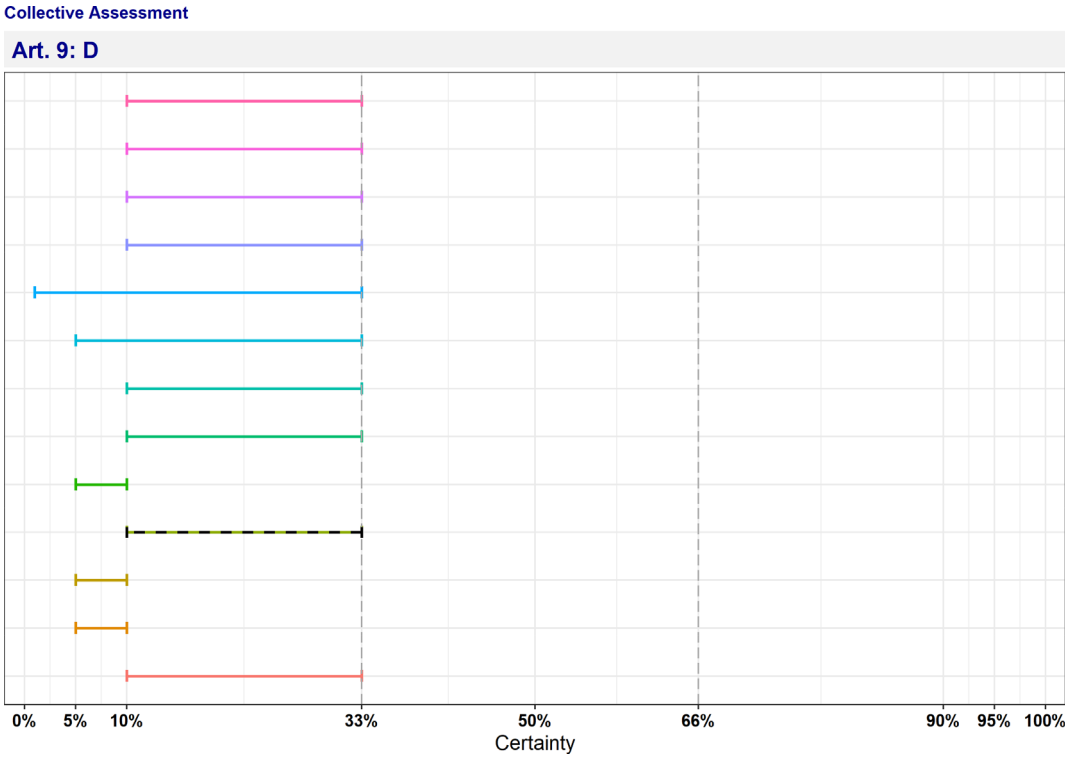
CI: current impact.
The median range is displayed as a dashed line.

Figure A.23: Individual probability ranges reflecting 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



PI: potential impact.
The median range is displayed as a dashed line.

Figure A.24: Individual probability ranges reflecting fulfilment of 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

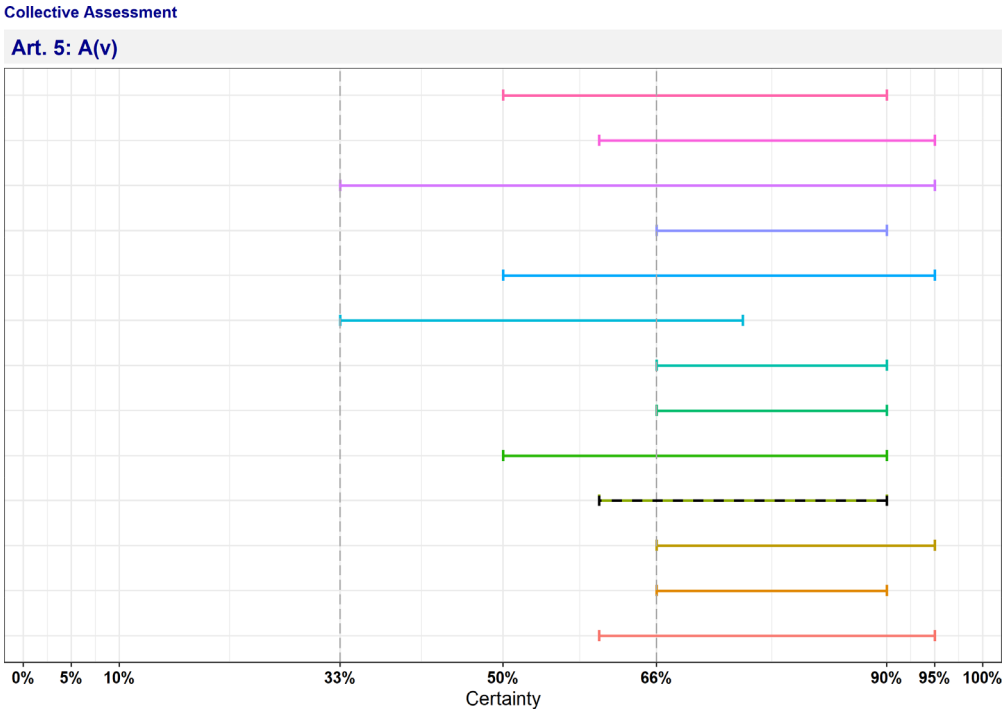


The median range is displayed as a dashed line.

Figure A.25: Individual probability ranges reflecting non-fulfilment of 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

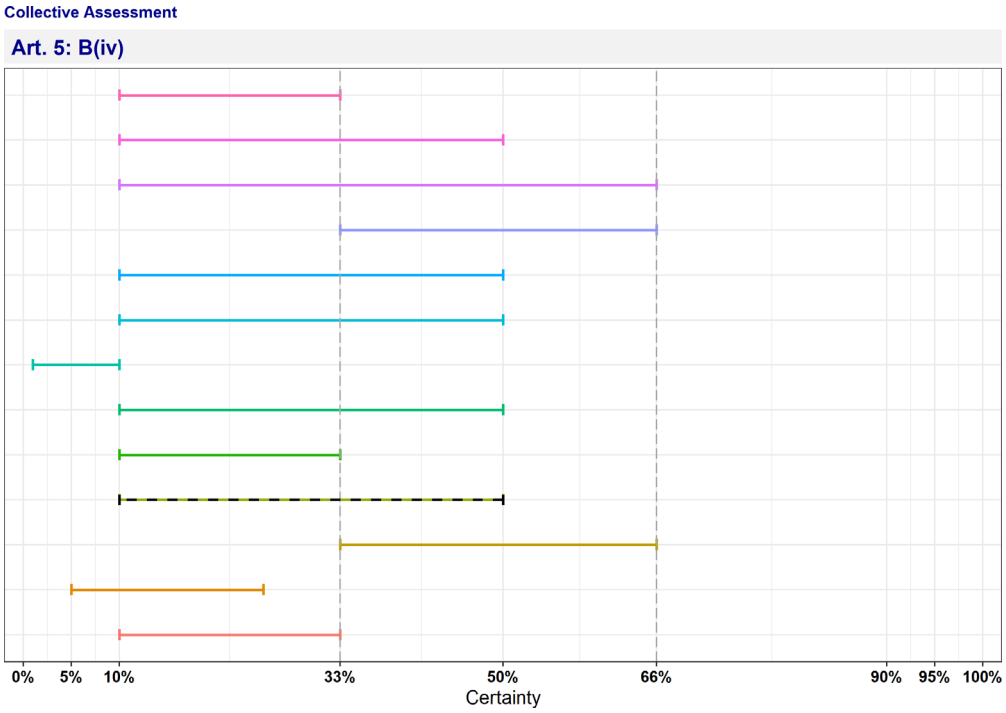
Appendix B – Criteria with uncertain outcome

B.1. Article 5 criteria



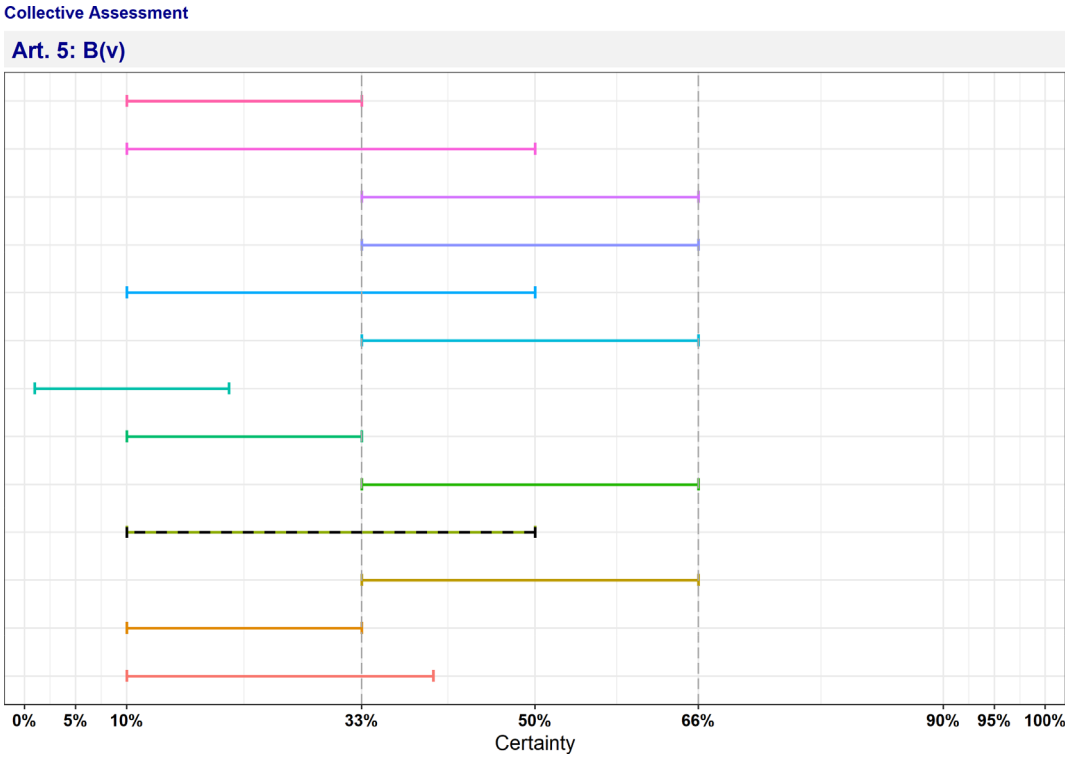
The median range is displayed as a dashed line.

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.

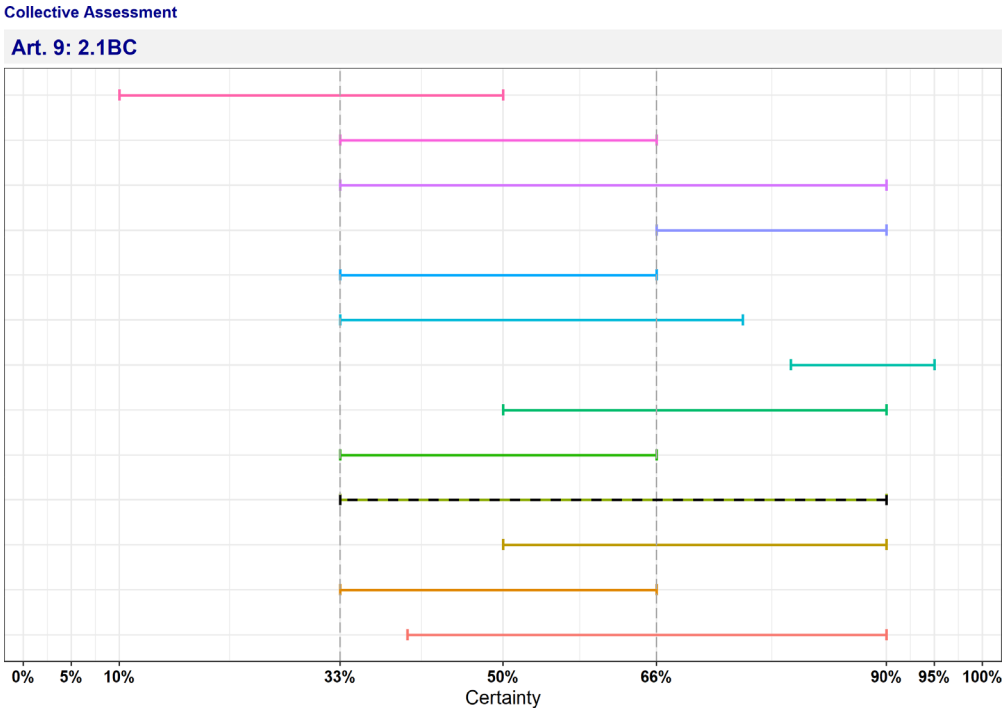
Figure B.2: Individual probability ranges reflecting uncertain outcome on Criterion B(iv) (the disease has the potential to generate a crisis or the disease agent could be used for the purpose of bioterrorism) after the collective judgement



The median range is displayed as a dashed line.

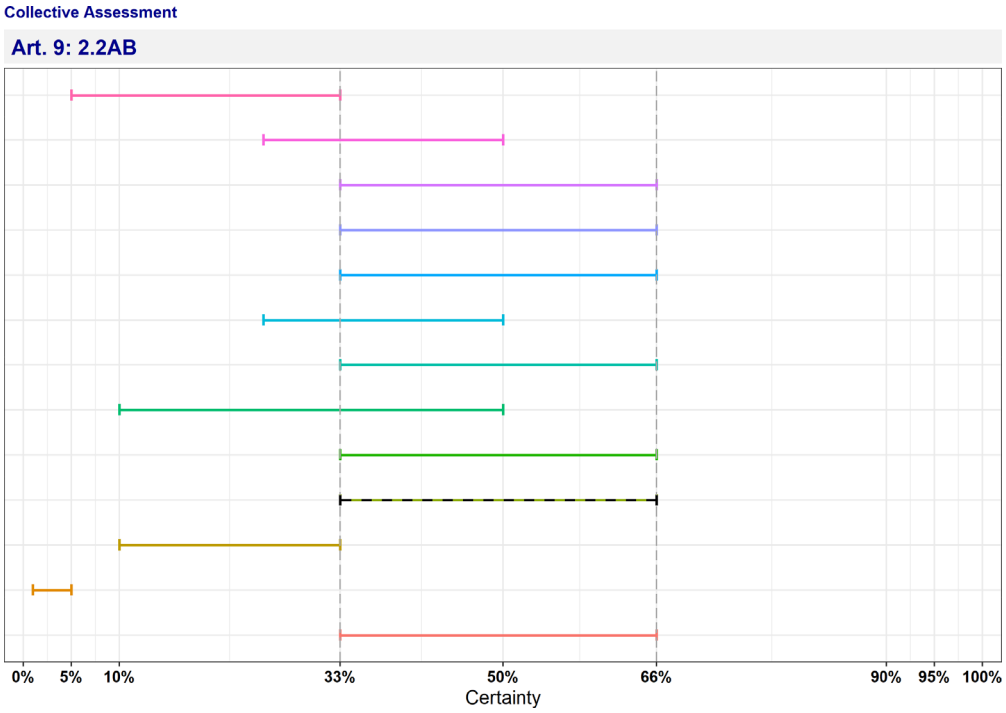
Figure B.3: Individual probability ranges reflecting uncertain outcome on Criterion B(v) (the disease has or could have a significant negative impact on the environment, including biodiversity, of the Union) after the collective judgement

B.2. Article 9 criteria



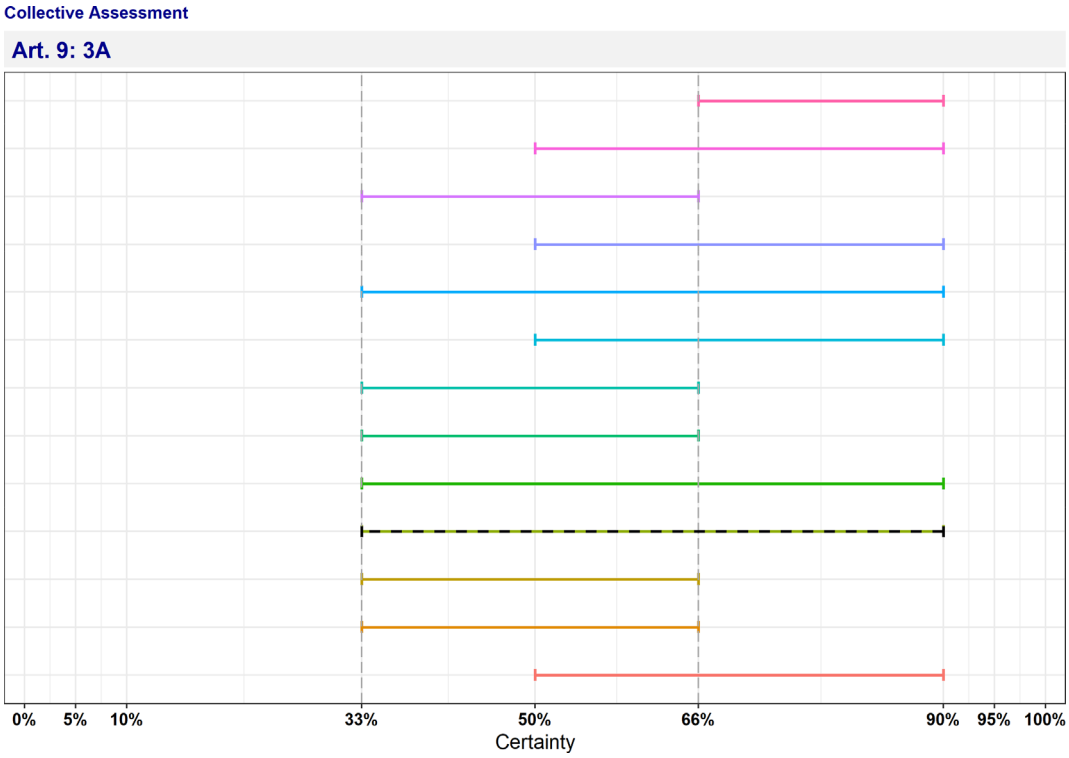
The median range is displayed as a dashed line.

Figure B.4: Individual probability ranges reflecting uncertain outcome on Criterion 2.1BC (the disease is moderately to highly transmissible) after the collective judgement



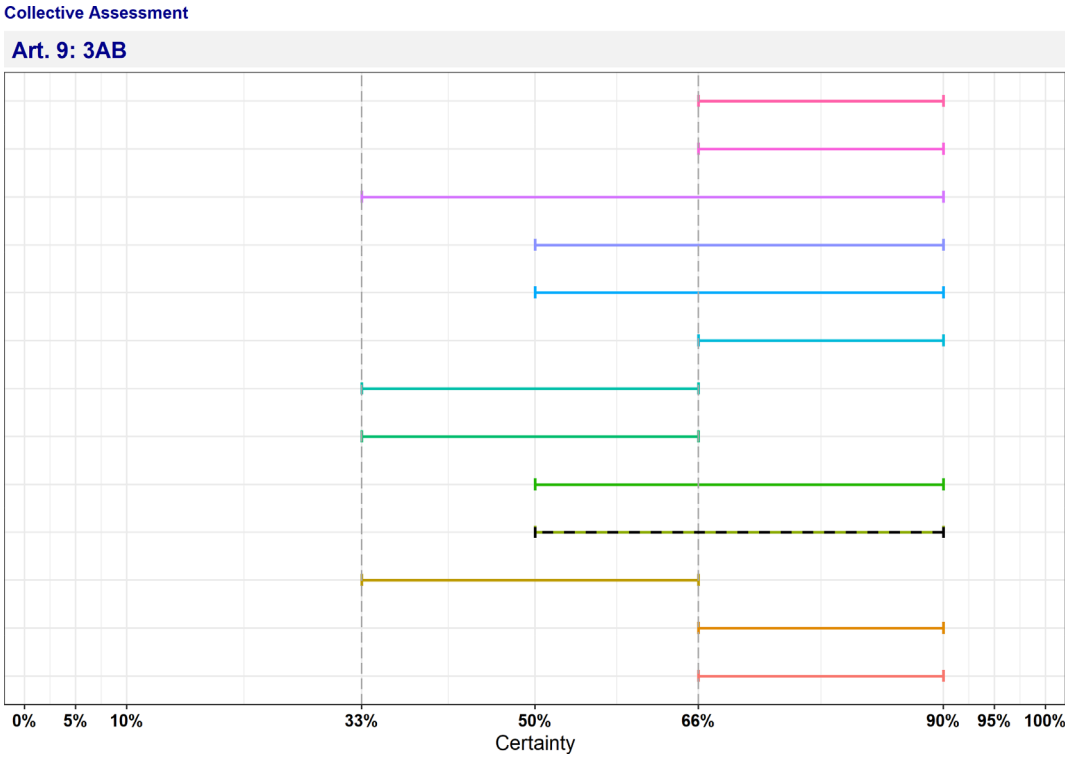
The median range is displayed as a dashed line.

Figure B.5: 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



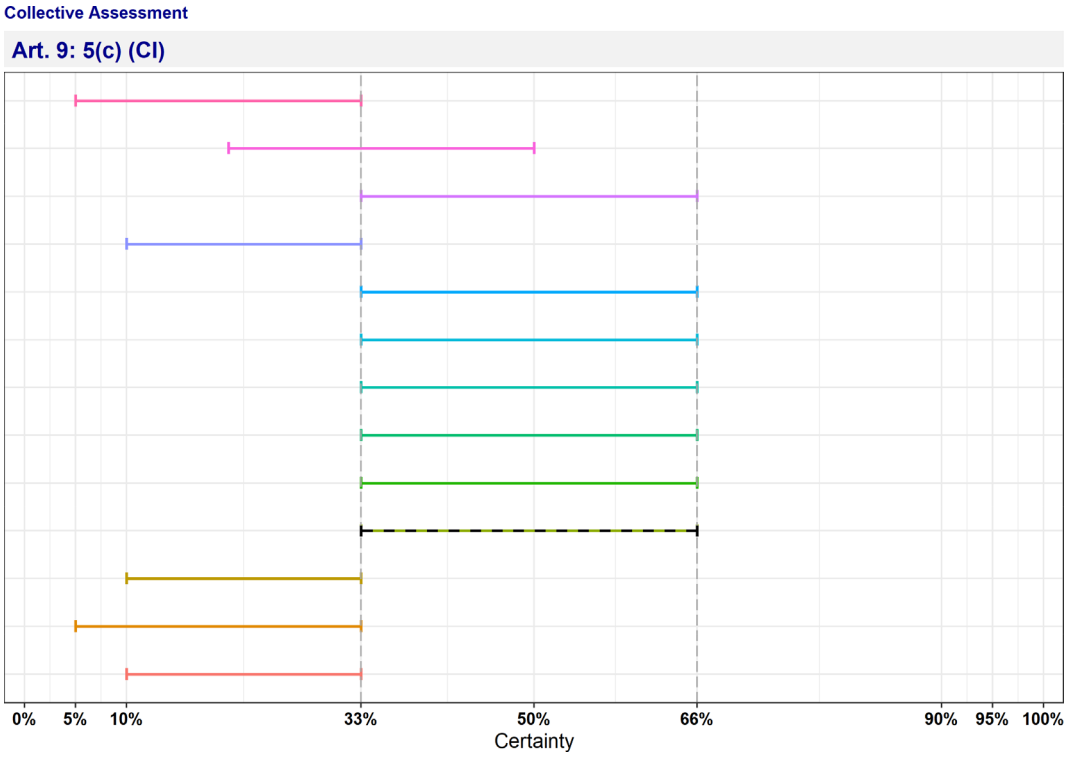
The median range is displayed as a dashed line.

Figure B.6: Individual probability ranges reflecting uncertain outcome on 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



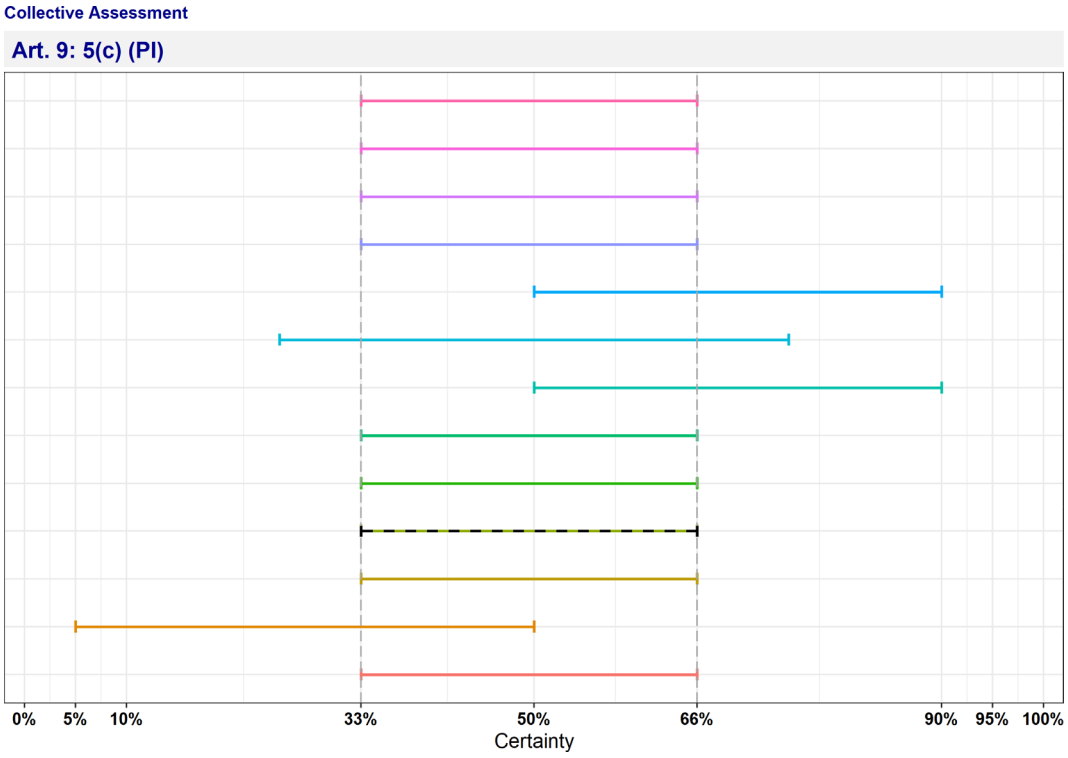
The median range is displayed as a dashed line.

Figure B.7: Individual probability ranges reflecting uncertain outcome on 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



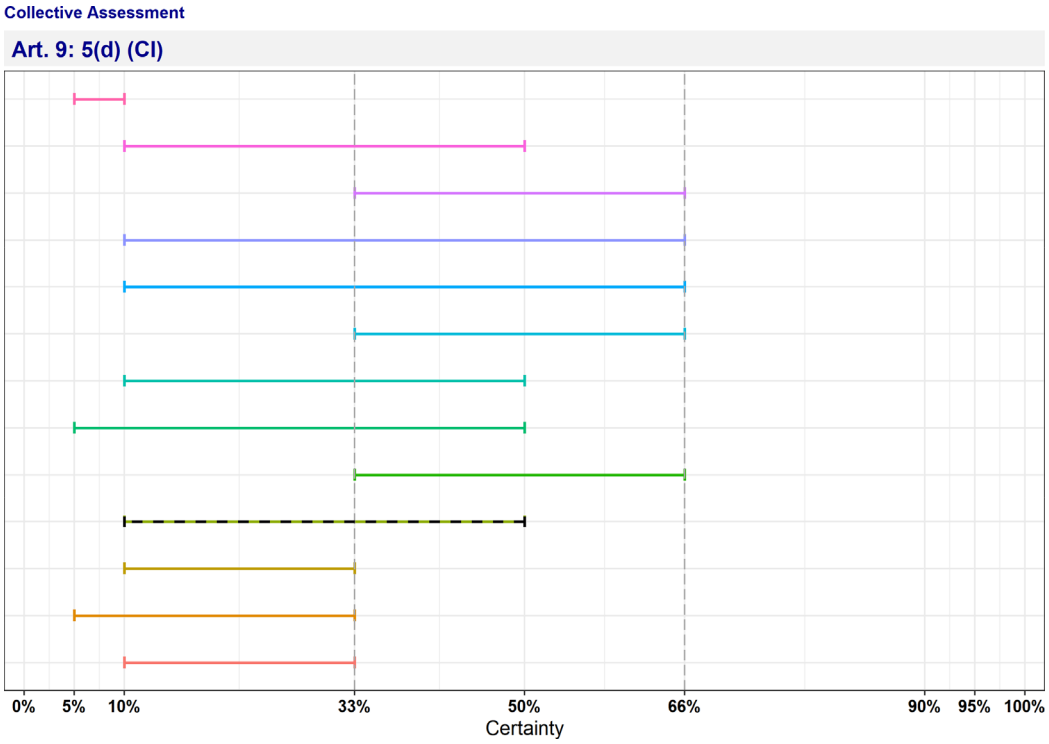
CI: current impact.
The median range is displayed as a dashed line.

Figure B.8: Individual probability ranges reflecting uncertain outcome on 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



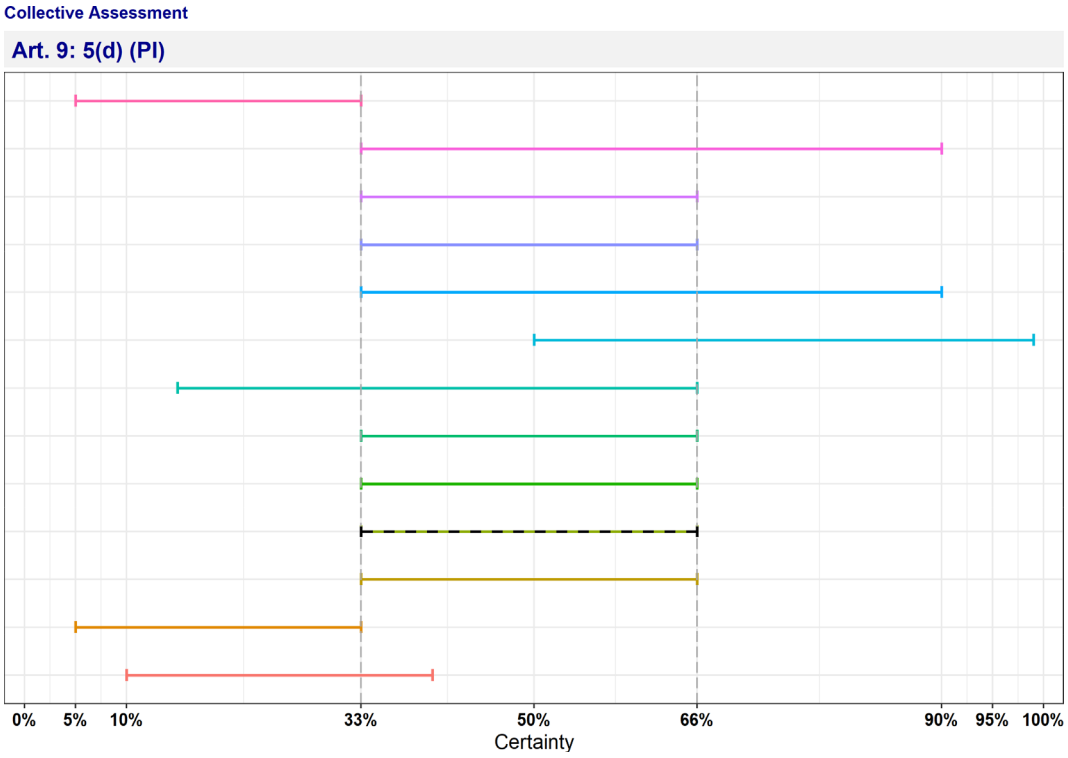
PI: potential impact.
The median range is displayed as a dashed line.

Figure B.9: Individual probability ranges reflecting uncertain outcome on 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



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

Figure B.10: Individual probability ranges reflecting uncertain outcome on 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



PI: potential impact.
The median range is displayed as a dashed line.

Figure B.11: 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