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Background

In 2014, EFSA received a mandate from the European Commission (EC) to assess the risk and consequences of introduction of new vector-borne diseases (VBDs), and to determine if further measures were needed. The goal was to assist the Commission in prioritising the use of resources for preventive actions against animal diseases, and covered 36 VBDs (Table 1) in 18 host mammalian species (Table 3) for which the risk of entry, transmission, establishment and persistence in the EU was assessed. Cocal virus and Semliki Forest virus, not in Table 1, were considered at first but later dropped due to a lack of evidence in scientific literature to inform the risk assessments.

To support the work, a comprehensive and systematic extraction of data from the literature was conducted, covering characteristics of the pathogens and the diseases they cause, as well as information on diagnostic test performance and efficacy of curative and preventive treatments, including vaccines. Furthermore, EFSA carried out similar work in-house with focus on the geographical distribution of the VBDs. The information extracted was subsequently used both for the opinion and for the production of 36 web-based, so called, story-maps.

The methodology for literature review has since been further consolidated, and the literature reviews were updated covering scientific evidence published for the 36 VBDs, in seven specific areas of knowledge (experimental infections, pathogen survival, diagnostic tests performance, vaccines, preventive and curative treatments, vector treatments and geographical distribution) up to 2017.

Regular updates of this corpus of scientific evidence are needed to support risk assessments on vector borne diseases, which are often complex with multifactorial and interdisciplinary aspects, yet needed within short deadlines and with limited resources.

The foundation set by the previous rounds of literature review for VBDs can be reused to provide efficient and reliable collection of scientific evidence to support EFSA needs in various areas of knowledge. EFSA has been requested to provide support to the European Commission (EC) via scientific opinions that would form the basis for the production of amending and implementing acts supporting Regulation 2016/429. 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) lays down rules for the prevention and control of animal diseases which are transmissible to animals or to humans.

To support EFSA in keeping the story-maps as an up-to-date source of information for risk assessors, and in providing scientific opinions in matters related to Regulation 2016/429, this project aims to:

> *Collect, collate, review, analyse and visualise information in story-maps, to provide up-to-date, evidence-based and user-friendly characterisations of pathogens affecting animal health in an interactive on-line platform.*
>
> *This document describes the methodology to conduct* ***systematic literature reviews (SLRs) that will support this aim. The SLRs will cover the following scope****:*
>
> - *The* ***36 vector-borne pathogens*** *agreed with the European Commission for which the risk of entry, transmission, establishment and persistence in the EU has been assessed by EFSA (EFSA, 2017) and characterised in story-maps – Table 1.*
> - *Diseases listed in Regulation 2016/429 (further referred to as "****Animal Health Law****" abbreviated by AHL) as* ***category A diseases*** *– Table 2.*

The list of ***target hosts*** is presented in Table 3.

Further details related to the objective, eligibility criteria and methodology of each SLR objective are provided in this document.

The SLRs will be conducted by the ***CoVetLab consortium,*** formally represented by the National Veterinary Institute, Sweden (SVA), and further composed of the Wageningen Bioveterinary Research (WBVR), The Netherlands; the Animal and Plant Health Agency (APHA), United Kingdom; and the University of Surrey (UoS), United Kingdom.

Table 1. *Vector-borne disease (VBD) agents included in the SLRs.*

Abbreviation	Vector-borne disease agent
AHFV	Alkhurma haemorrhagic fever virus
AHSV	African horse sickness virus *Pestis Equorum; Peste Equina*
AINOV	Aino virus
AKAV	Akabane virus
ASFV	African swine fever virus *Warthog disease*
BEFV	Bovine ephemeral fever virus *Bovine Epizootic Fever*
BHAV	Bhanja virus
BTV	Bluetongue virus *Pseudo Foot and mouth disease*
CCHFV	Crimean-Congo haemorrhagic fever virus *Congo Fever; Cache Valley fever*
CVV	Bunyamwera virus
EEEV	Eastern equine encephalitis virus *Equine encephalomyelitis*
EEV	Equine encephalosis virus
EHD/IBAV	Epizootic hemorrhagic disease virus *Ibaraki disease*
GETV	Getah virus
HJV	Highlands J virus
JEV	Japanese encephalitis virus
KASV	Palyam virus *Kasba virus*
KOTV	Kotonkon virus
MDV	Main drain virus
MIDV	Middelburg virus
NSDV	Nairobi sheep disease virus
PHSV	Peruvian horse sickness virus
RVFV	Rift Valley fever virus
SBV	Schmallenberg virus
SHUV	Shuni virus *Semliki forest*
SLEV	St. Louis encephalitis virus
THOV	Thogoto virus
VEE	Venezuelan equine encephalitis virus
VSAV VSIV VSNJV	Vesicular stomatitis viruses
WEEV	Western equine encephalitis virus
WNV	West Nile virus
YUOV	Yunnan orbivirus
WSLV	Wesselsbron virus
Cowdr	Ehrlichia ruminantium (formerly Cowdria ruminantium)
hepat	Hepatozoon canis
CanL	Leishmania infantum

Table 2. *AHL category A diseases which hosts are terrestrial animals.*

African swine fever*
African horse sickness*
Classical Swine Fever
Contagious bovine pleuropneumonia
Contagious caprine pleuropneumonia
Foot and Mouth
Glanders
HPAI
Lumpy skin
Newcastle
Peste des petit ruminants
Rift Valley fever*
Rinderpest
Sheep and got pox

* diseases which agents are also included in the VBDs listed in Table 1.

Table 3. *Terrestrial animal species included as hosts.*

Mammal Species	**Genus**	**MTX**
Humans	Homo	A056J
Buffalo	Bubalus	A057C
Cattle	Bos	A057E
Yak	Bos	A057J
Goat	Capra	A057P
Sheep	Ovis	A057G
Pig	Suidae	A057F
Ass	Equus	A057Q
Horse	Equus	A0B9Z
Bactrian Camel	Camelus	A057L
Dromedary	Camelus	A057M
Alpaca	Vicugna	---
Llama	Lama	A057N
Vicuna	Vicugna	---
Deer (family)	Cervidae (family)	A056M
Rabbit	Leporidae (family)	A057T
Cat	Felis	A0CNM
Dog	Canis	A0CNL
Zebra	Equus	

Bird species	**Genus**	**MTX**
Chickens	Gallus	A057Z
Turkeys	Meleagridis	A058A
Ducks	Anatidae	A058B
Pigeons	Columbidae	A058H
Parrots	Psittacidae	A057X
Parakeets	Psittaculidae	
Ostriches	Struthio	A058D
Birds of prey	Tytonidae, Strigidae, Cathartidae, Sagittariidae, Pandionidae, Accipitridae, and Falconidade	

Objectives

The scientific evidence needed to support EFSA's mandates and the construction of story maps was divided into seven main knowledge areas. From now on, these will be referred to as seven individual scientific literature reviews (SLRs):

1) Experimental infection studies;
2) Pathogen survival studies;
3) Diagnostic test performance evaluations;
4) Vaccines;
5) Treatments (preventive and curative);
6) Vector control;
7) Geographical distribution.

For each of these 7 SLRs, this document describes in details the review questions; eligibility criteria; and protocols for literature search, screening and paper selection, and data collection.

This project will fulfil 3 main objectives:

1) Update SLRs 1-6 for disease agents listed in Table 1, in the host species listed in Table 3, which were last performed including papers published until December 2017.
2) Perform SLRs 1-6 to extract evidence from scientific literature published since 1990 for all diseases listed in Table 2, for the host species listed in Table 3. Diseases listed in Table 2 which are also VBDs will only be subjected to an update, as per objective 1) above.
3) Collect evidence on the geographical distribution of diseases listed in Tables 1 and 2, in the host species listed in Table 3, from peer review literature published since 1970.

From here on we will refer to the pathogenic agents in Table 1, those causing the vector-borne diseases in scope, as "***VBD agents***", and the associated diseases as the "***VBDs***". Diseases in Table 2 will be referred to as "***AHL-A diseases***", and their pathogens as "***AHL-A disease agents***". All terrestrial animal species listed in Table 3 will be simple referred to as "***host species***".

Review questions and eligibility criteria

1) Experimental infection studies

This SLR aims to gather all scientific evidence available regarding incubation period, infectious period, characterisation of clinical signs, and mortality and morbidity rates for the diseases in scope (VBDs and AHL-A diseases listed in Tables 1 and 2).

Review questions for experimental infection studies

What is the effect of an exposure in susceptible hosts - being experimentally infected with an agent - on these specific outcomes relating to the pathogenesis of the disease:

→ What is the minimum and maximum time post inoculation to observe clinical signs?

→ What is the minimum and maximum minimum infectious period in days?

→ What is the minimum and maximum mortality rate?

→ What is the minimum and maximum morbidity rate?

→ What are the main clinical signs?

Study eligibility criteria for experimental infection studies

Element	Criteria	Level of screening
Publication type	Primary research publications	Title and abstract
Language	English	Title and abstract Full-text
Study type	Experimental infections	Title and abstract
Study design	• Experimental study design • Susceptible hosts must be experimentally exposed to the pathogen, either by inoculation, or direct or indirect contact transmission • Only a single exposure with an 'outbreak strain' or 'wild type strain' of the agent (VBD agent of AHL-A disease agent), in not-immunised or not-vaccinated or not-treated hosts, will be considered.	Title and abstract Full-text
Population	The susceptible host species (the species in which the pathogen replicates) should be listed in Table 3 or be classified as part of a genus listed in Table 3. (All studies identifying susceptible species outside of this list will be flagged and saved for potential use by EFSA at a later date)	Title and abstract Full text
Exposure	• Exposure of susceptible species with one of the VBD agents listed in Table 1 or AHL-A disease agents listed in Table 2. • Agent infection should be confirmed by an established test	Title and abstract Full-text
Outcome of interest	• The article is excluded if there is no description of one of the outcomes of interest, i.e. time of detection of the pathogen after exposure, number of positive or dead animals, or the clinical signs	Full-text
Publishing date	Specific for each SLR, depending on the project year conducted and the agents covered. Please refer to **Annex I** for a table listing the publication years covered by each planned SLR.	Title and abstract

2) Pathogen survival studies

Aims at collecting data relating to the survival time of the disease agents in scope (VBD and AHL-A agents listed in Tables 1 and 2). Information should concern the persistence of the pathogen in different matrices.

Review questions for agent survival studies

What is the minimum and maximum number of days post inoculation to detect active pathogen in different relevant matrices?

Study eligibility criteria for agent survival studies

Element	Criteria	Level of screening
Publication type	Primary research publications	Title and abstract
Language	English	Title and abstract Full-text
Study type	Pathogen survival experiments	Title and abstract

Study design	The study should provide details on the strain/isolate of the pathogen, the dose (in case of experimentally infected animals), and the temperature at which the matrix is stored	Title and abstract Full-text
Exposure	Matrices of susceptible species exposed with one of the VBD or AHL-A disease agents listed in Tables 1 and 2. Alternatively, matrices can be experimentally contaminated (spiked) with one of the agents in scope.	Title and abstract Full-text
Outcome of interest	The article is excluded if there is no description of one of the outcomes of interest, i.e. pathogen survival time	Full-text
Publishing date	Specific for each SLR, depending on the project year conducted and the agents covered. Please refer to **Annex I** for a table listing the publication years covered by each planned SLR.	Title and abstract

3) Diagnostic tests evaluation studies

Aims at collecting data relating to the performance of diagnostic tools intended to either demonstrate the presence or absence of infection (e.g. PCR, isolation of the pathogen), or detect evidence of a previous infection (e.g. antibodies).

The scope of the diagnostic tests applied for agents listed in Tables 1 and 2, in host species listed in Table 3, is further restricted to diagnostic tests approved for use within the EU, or approved for testing prior to importation in the EU. **The diagnostic tests eligible for this SLR are listed in Annex II**.

Relevant studies should evaluate the operational characteristics of tests, namely sensitivity (i.e. the probability that a truly infected individual will test positive) and specificity (i.e. the probability that a truly uninfected individual will test negative).

Review question for diagnostic test studies

What is the estimated specificity and sensitivity of index diagnostic tests?

Study eligibility criteria for diagnostic test studies

Element	Criteria	Level of screening
Publication type	Primary research publications	Title and abstract
Language	English	Title and abstract Full-text
Study type	Cross sectional, prospective or retrospective	Full-text
Study design	The studies should assess diagnostic accuracy or compare accuracy between tests	Title and abstract Full-text
Population	The susceptible host species (the species in which the pathogen replicates) should be listed in Table 3 or be classified as part of a genus listed in Table 3.	Title and abstract Full text
Study characteristics	The study population should be clearly defined i.e. at least species information. The study should specify the sample type used in the diagnostic test e.g. tissue and test target (e.g. antibody, virus particle).	Full text
Exposure	The target population can be infected by natural or experimental means. The target population should be exposed to one of the agents listed in Annex II (VBDs for which testing is required upon importation to the EU, or AHL-A disease agents).	Title and abstract Full-text

	Infection should be confirmed by an established test.	
Outcome of interest	The study should report test sensitivity and/or test specificity for one of the specific tests listed in Annex II, or provide enough data for those values to be calculated.	Full-text
Time	The study duration should be specified i.e. beginning and end dates of when sampling took place.	Full-text
Publishing date	Specific for each SLR, depending on the project year conducted and the agents covered. Please refer to **Annex I** for a table listing the publication years covered by each planned SLR.	Title and abstract

4) Vaccine efficacy studies

Aims at collecting data relating to the available vaccines authorized in the EU (as reported in **Annex III**) for each of the diseases and species in scope.

Research questions for vaccine studies

What is the efficacy of the vaccine (i.e. its ability to reduce disease incidence)?

Study eligibility criteria for vaccine studies

Element	Criteria	Level of screening
Publication type	Primary research publications	Title and abstract
Language	English	Title and abstract Full-text
Study type	Experimental	Title and abstract
Study design	Assessments that investigate the efficacy of a vaccine should use randomised controlled trials to determine the vaccines efficacy under laboratory conditions.	Full-text
Population	The susceptible host species (the species in which the pathogen replicates) should be listed in Table 3 or be classified as part of a genus listed in Table 3. (All studies identifying susceptible species outside of this list will be flagged and saved for potential use by EFSA at a later date)	Title and abstract Full text
Study characteristics	Only vaccines authorized in the EU (reported in Annex III) should be considered Studies must report: • the number of participants • the schedule of immunisations • the method of delivery	Full-text
Exposure	Exposure of susceptible species with one of the VBD or AHL-A disease agents listed in Tables 1 and 2. Studies must confirm pathogen infection by an established test.	Title and abstract Full-text
Outcome of interest	Studies should at least report the parameters necessary to calculate the vaccine efficacy or the value of the efficacy itself	Full-text
Intervention	Studies must provide information on: • Vaccine type • Dose • Administration method of vaccine	Full-text

	• Single vaccine or combination of vaccines	
Publishing date	Specific for each SLR, depending on the project year conducted and the agents covered. Please refer to **Annex I** for a table listing the publication years covered by each planned SLR.	Title and abstract

5) Curative and preventive treatment studies

Aims at collecting data relating to the available preventive and curative treatments for each of the diseases in scope (Tables 1 and 2), when applied to the host species listed in Table 3.

Preventive treatments will include those that can control the disease excluding vaccines. Curative treatments should focus on curing infection caused by the pathogen (e.g. antibiotics, anti-parasitic, antivirals, anti-protozoan drugs and chemotherapy).

Studies which report the use of a preventive treatment based exclusively on vector control, and report the outcome from the vector perspective (for instance prevention of infestation) will ***not*** be considered eligible, and will be included in the vector control treatment SLRs instead (see below). The use of a vector control treatment is however eligible when reported from the host perspective – for instance number of infections prevented.

The review should focus on the evaluation of such treatments in terms of efficacy (i.e. the ability to prevent or reduce exposure or cure infection in lab condition) or effectiveness (i.e. the ability to prevent or reduce exposure or cure infection in real world situations).

Review questions for treatment studies

a. What is the efficacy or effectiveness of the preventive treatment?

b. What is the efficacy or effectiveness of the curative treatment?

Study eligibility criteria for treatment studies

Element	Criteria	Level of screening
Publication type	Primary research publications	Title and abstract
Language	English	Title and abstract Full-text
Study type	The study must assess the efficacy or effectiveness of a treatment against a VBD listed in Table 1 or an AHL-A disease listed in Table 2.	Title and abstract
Study design	Assessments that investigate the efficacy of a treatment (laboratory conditions) should employ randomised controlled trials in order to determine efficacy under laboratory conditions. Studies assessing the effectiveness of a treatment (field and semi-field conditions) should be observational studies i.e. prospective cohort study, retrospective case-control cohort study or cross-sectional studies.	Full-text
Population	The susceptible host species (the species in which the pathogen replicates) should be listed in Table 3 or be classified as part of a genus listed in Table 3. (All studies identifying susceptible species outside of this list will be flagged and saved for potential use by EFSA at a later date)	Title and abstract
Study characteristics	Studies should contain a control/comparative group, and report on number of participants.	Full-text

Exposure	Exposure of susceptible species with one of the VBDs agents listed in Table 1 or the agent of an AHL-A disease listed in Table 2. Studies must confirm pathogen infection by an established test. For experimental studies, the means of exposure to the pathogen should be reported (e.g. injection).	Title and abstract Full-text
Outcome of interest	Studies should at least report on the efficacy or effectiveness of a treatment/combination of treatments, such as one of the following: • Number of infected that are cured/not cured • Number of infections prevented compared to a control/comparative group • Dose-response information on efficacy • Proportion of cured or protected Other valuable information is: • Adverse effects • Number of adverse events • Efficacy and safety in treatment-naïve patients • Efficacy and safety in selected subgroups of patients	Title and abstract Full-text
Intervention	Studies must provide information on: • Treatment type • Dose • Administration method of treatment • Treatment used alone or in combination with other treatments • the schedule of treatments	Full-text
Publishing date	Specific for each SLR, depending on the project year conducted and the agents covered. Please refer to **Annex I** for a table listing the publication years covered by each planned SLR.	Title and abstract

6) Vector control treatment studies

Aims at collecting data relating to the available vector control measures for the following vector groups (preventive only): mosquitoes, sand-flies, ticks and culicoides.

The review should report evaluations of vector mortality or prevented vector infestations in hosts in Table 3, in laboratory or real world situations.

Review questions for vector control treatments

c. What is the vector mortality after applying the vector control strategy

d. What is the efficacy or effectiveness of preventing vector presence or infestation?

Study eligibility criteria for vector control treatments

Element	Criteria	Level of screening
Publication type	Primary research publications	Title and abstract
Language	English	Title and abstract Full-text

Study type	The study must assess the efficacy or effectiveness of a control treatment against a vector family.	Title and abstract
Study design	Assessments that investigate the efficacy of a treatment (lab conditions) should employ randomised controlled trials in order to determine efficacy under laboratory conditions. Studies assessing the effectiveness of a treatment (field and semi-field conditions) should be observational studies i.e. prospective cohort study, retrospective case-control cohort study or cross-sectional studies.	Full-text
Population	The susceptible host species (the species in which the pathogen replicates) should be listed in Table 3 or be classified as part of a genus listed in Table 3. Studies can be just targets at one of the included vector groups, with no particular host species being involved.	Title and abstract
Study characteristics	Contains a control/comparative group. Studies should report on number of participants (when a host species is involved).	Full-text
Outcome of interest	Studies should at least report on the efficacy or effectiveness of a treatment/combination of treatments, such as one of the following: • Dose-response information on efficacy • Vector mortality • Vector presence/prevention of vector presence	Title and abstract Full-text
Intervention	Studies must provide information on: • Dose • Administration method • Control method used alone or in combination with other controls • the schedule of treatments	Full-text
Publishing date	Specific for each SLR, depending on the project year conducted and the agents covered. Please refer to **Annex I** for a table listing the publication years covered by each planned SLR.	Title and abstract

7) Geographical distribution documentation

Aims at collecting data relating to the geographical distribution of the agents in scope.

For AHL-A diseases (Table 2) this will be performed for the first time.

For the VBDs listed in Table 1, this search was previously carried out by EFSA, and then reviewed systematically for papers published from January 1st, 2005 to January 31st, 2017. This project will review the search strings used, in particular to tailor the SLR for each specific disease. More details can be found in the search strategy section. All reviews will be updated, and when judged necessary, performed again for papers published from 1970. The database already available in Distiller will be used to ensure that papers already screened will be identified and not screened again.

Review questions for geographical distribution studies

In which countries have these pathogens been reported, and what are the epidemiological measures of disease presence known, e.g.:

→ In which country and in which animal population was the disease occurrence reported?

→ When was the occurrence observed (start and duration)?

→ In which phase of an outbreak was the study conducted?

→ What were the reported prevalence and/or incidence and/or number of animals/farms affected?

Study eligibility criteria for geographical distribution studies

Element	Criteria	Level of screening
Publication type	Primary research publications	Title and abstract
Language	English	Title and abstract Full-text
Population	The susceptible host species should be listed in Table 3 or be classified as part of a genus listed in Table 3. (All studies identifying susceptible species outside of this list will be flagged and saved for potential use by EFSA at a later date)	Title and abstract Full text
Outcome of interest	The article is excluded if there is no description of one of the outcomes of interest, i.e. number of animals affected, incidence, prevalence, basic reproduction number, population affected, country affected, time of disease occurrence.	Full-text
Publishing date	Specific for each SLR, depending on the project year conducted and the agents covered. Please refer to **Annex I** for a table listing the publication years covered by each planned SLR.	Title and abstract

Methods for searching the results

Information sources

Scopus will be used as the primary platform for literature searches.

Restrictions

Only primary research studies (i.e. no review papers) published in English will be considered for potential inclusion in the reviews. All literature that are indexed in the databases will be included in the search, irrespective of whether they are e-pubs or corrected proofs.

Retrieval of full-texts will be performed using the combined literature access of all CoVetLab members (SVA, APHA, WBVR and UoS). Articles will be kept in shared repositories accessible by all team members only for the duration of the project, and not shared outside the consortium.

The limitations concerning the year of publication listed in Annex I will be applied. **Publication date restrictions are only actually applied to the year where the search begins, with open end "up to now".** For example, if a SLR is to be carried out in 2021, and meant to retrieve all relevant papers published since 1990, in Annex I we wrote the years covered by the SLR as 1990-2020, because 2020 is the last year which we are certain to have covered in full. However, the search string is implemented as "*PUBYEAR > 1989*". This will retrieve papers published from 1990 onwards, up to the day when the search was implemented in Scopus. In this specific example, papers published in 2021, the year of SLR execution, will not be excluded. When the SLR is updated in the future, it should then be planned to start with year 2021 (*PUBYEAR > 2020*), overlapping somewhat with the original search. Any duplicated references will be detected by DistillerSR®, and the screening already performed for these papers preserved. The overlap will therefore *not* compromise future updates, and the open ended limit of the date interval will ensure that all SLRs reflect current knowledge up to the review time.

Reference management

Full references and abstracts will be downloaded from Scopus in the RIS format and uploaded into the Systematic Literature Review software DistillerSR ® (Evidence Partners).

Prioritization groups

For the work during year 1, EFSA asked the CoVetLab consortium to prioritize some diseases in order to provide timely information for specific working groups. To attend this prioritization, the AHL-A diseases listed in Table 2 were divided into 3 groups. These groups are listed in Table 4, and will be referred to when specific search strategies were tailored to them.

Table 4. *Prioritization applied to the AHL diseases during year 1.*

AHL-A diseases group 1	AHL-A diseases group 2	AHL-A diseases group 3
Rift Valley fever virus	Rinderpest	African swine fever virus
Peste des petit ruminants	Contagious bovine pleuropneumonia	Foot and Mouth
Sheep and got pox	Contagious caprine pleuropneumonia	Lumpy skin
Classical Swine Fever	Glanders	HPAI
Newcastle		African horse sickness virus

Search strategy

Several individual searches are needed in order to accommodate the complexity of the 7 SLRs detailed in this document. The SLRs cover two different groups of diseases, listed in Table 1 and Table 2. Diseases

in Table 1 were previously subjected to all 7 SLRs, while those in Table 2 were not. The SLRs will not be all carried out within the same year, as detailed in Annex I. Moreover, within the first year, the prioritization groups listed in Table 4 will be used.

The specific objectives of each of the individual queries that, collectively, cover the scope established for each of the SLRs are detailed below. Within each of those specific objectives, a*d hoc* combinations of search terms will be applied. The use of Boolean operators (AND, OR, NOT), truncation ($) and wildcard (*) symbols will assure that search terms account for synonyms, abbreviations and spelling variants, enhancing thus the sensitivity of the search strategy.

Alternative names for the diseases, when relevant, will be also considered.

Search strategies for experimental infection studies

The search strings for experimental infections are always a combination of 4 elements:

1) String I: agent/disease description. Name of the pathogen and diseases, with alternative names when relevant
2) String II: host description.
3) String III: selection of experimental studies (*Experiment* OR Inoculat**)
4) Publication years selection

These elements are joined with "AND" statements. As an example, the search string below was constructed to retrieve experimental infection studies involving sheep pox, goat pox, peste des petits ruminants and classical swine fever:

TITLE-ABS-KEY (
("Sheep pox" OR "goat pox" OR "peste des petits ruminants" OR "Classical swine fever")
AND
(Goat OR Capra OR caprine OR Sheep OR Ovis or Ovine OR Camel or Camelid OR Dromedary OR Alpaca OR Vicugna OR Llama OR Lama OR Vicuna OR Vicuña OR Deer OR Cervidae OR Pig OR Hog OR Suis OR Suidae)
AND
(Experiment* OR Inoculat*)
) ***AND*** *(PUBYEAR AFT 1989)*

Table 5 lists all individual searches planned for the SLR focused on experimental infections. The complete search strings are provided in Annex IV. Each individual search was given a unique label. All references captured within each individual search will be separately uploaded to DistillerSR® and labelled with the unique search string names provided in Table 5. This allows filtering of the references during any step of the literature review process, from screening to data retrieval.

Table 5. *Search strings for all literature retrieval queries planned within the Experimental Infection objective. Labels provided to each query will be assigned to the references uploaded to DistillerSR®.*

Planned search year	Diseases covered	Publication years covered	Individual search string label
2021	**AHL-A group 1: Rift Valley Fever** Rift Valley fever is also a VBD, and therefore had already been subjected to a SLR covering years up to 2017. It was searched separately to apply a different time window.	2018-2020	**AHL_2020_G1_RVF**
	AHL-A group 1: Newcastle disease The remaining diseases in AHL priority group 1 were split into two main host groups: birds and mammals	1990-2020	**AHL_2020_G1_birds**
	AHL-A group 1: sheep pox, goat pox, peste des petits ruminants and classical swine fever	1990-2020	**AHL_2020_G1_mammals**
	AHL group 2: Rinderpest, Contagious bovine pleuropneumonia, Contagious caprine pleuropneumonia, Glanders	1990-2020	**AHL_2020_G2**
	AHL-A group 3: African swine fever and African horse sickness These diseases are also VBDs, and therefore had already been subjected to a SLR covering years up to 2017.	2018-2020	**AHL_2020_G3_VBD**

	AHL-A group 3: HPAI Non-VBDs, bird hosts	1990-2020	**AHL_2020_G3_birds**
	AHL-A group 3: Foot and Mouth, Lumpy skin Non-VBDs, mammal (Artiodactyla) hosts	1990-2020	**AHL_2020_G3_mammals**
	VBDs: All remaining VBDs not included in the AHL-A list (see Table 1)	2018-2020	**VBD_2020**
2022	AHL-A	2021	**AHL_2021**
	VBD	2021	**VBD_2021**
2023	AHL-A	2022	**AHL_2022**
	VBD	2022	**VBD_2022**
2024	AHL-A	2023	**AHL_2023**
	VBD	2023	**VBD_2023**

Search strategies for pathogen survival studies

The search strings for pathogen survival are always a combination of 3 elements:

1) String I: agent/disease description. Name of the pathogen and diseases, with alternative names when relevant
2) String II: selection of survival experiments (*Surviv* OR Persist* OR stability OR inactivat* OR disinfect**). The abbreviation Surviv* is to include terms like Survival study, Survival experiment, Survival duration, Survival period, etc. The abbreviation Persist* is to include terms like Persistence, Persistent, etc.
3) Publication years selection

These elements are joined with "AND" statements. See example in the section describing the search strategy for experimental infections.

The search is not restricted using any species keywords, nor specific types of matrices in which the pathogens were evaluated. Instead, we will use a string to search specifically for survival experiments, as detailed above.

Table 6 below lists all individual searches planned. The complete search strings are provided in Annex IV. Each individual search was given a unique label. All references captured within each individual search will be separately uploaded to DistillerSR® and labelled with the unique search string names provided in Table 6. This allows filtering of the references during any step of the literature review process, from screening to data retrieval.

Table 6. *Search strings for all literature retrieval queries planned within the pathogen survival objective. Labels provided to each query will be assigned to the references uploaded to DistillerSR®.*

Planned search year	Diseases covered	Publication years covered	Individual search string label
2021	**AHL-A diseases which are VBDs** Rift Valley Fever, African Swine Fever and African Horse Sickness. These have already been subjected to a SLR covering years up to 2017.	2018-2020	**AHL_VBD_2020**
	AHL-A diseases which are NOT VBDs	1990-2020	**AHL_2020**
	VBDs: All remaining VBDs not included in the AHL-A list	2018-2020	**VBD_2020**
2022	AHL-A	2021	**AHL_2021**
	VBD	2021	**VBD_2021**
2023	VBD	2022	**VBD_2022**

Search strategies for diagnostic test evaluation studies

The search strings are always a combination of 3 elements:

1) String I: agent/disease description. Name of the pathogen and diseases, with alternative names when relevant
2) String II: selection of eligible diagnostic tests: based on the list of diagnostic tests eligible for each specific disease (Annex II).
3) Publication years selection

These elements are joined with "AND" statements. See example in the section describing the search strategy for experimental infections.

In year 1 (2021), AHL-A diseases will be reviewed first, respecting the prioritization order listed in Table 4. When needed, in order to adhere to the list of diagnostic tests of interest for each disease provided by EFSA (Annex II), search strings combining disease and diagnostic tests will be constructed for each disease separately. This was the case for AHL-A diseases. For VBD diseases, the searches used in previous SLRs were updated and reused (respecting the scope provided in Annex II). Searches are listed in Table 7, and transcribed in full in Annex IV. All references captured within each individual search will be separately uploaded to DistillerSR® and labelled with the unique search string names provided in Table 7. This allows filtering of the references during any step of the literature review process, from screening to data retrieval.

Table 7. *Search strings for all literature retrieval queries planned within the diagnostic tests evaluation objective. Labels provided to each query will be assigned to the references uploaded to DistillerSR®.*

Planned search year	Diseases covered	Publication years covered	Individual search string label
2021	**AHL-A group 1; VBD:** Rift Valley Fever Rift Valley fever is also a VBD, and therefore had already been subjected to a SLR covering years up to 2017.	2018-2020	**AHL_RVF_2020**
	AHL-A group 1, non-VBDs: Newcastle disease, sheep pox, goat pox, peste des petits ruminants and classical swine fever	1990-2020	**AHL_Pox_2020; AHL_CSF_2020; AHL_ND_2020; AHL_PPR_2020**
	AHL group 2: Rinderpest, Contagious bovine pleuropneumonia, Contagious caprine pleuropneumonia, Glanders	1990-2020	**AHL_Rind_2020; AHL_CBPP_2020; AHL_CCPP_2020; AHL_Gland_2020**
	AHL-A group 3, VBDs: African swine fever and African horse sickness	2018-2020	**AHL_ASF_2020; AHL_AHS_2020;**
	AHL-A group 3, non-VBDs: HPAI, Foot and Mouth, Lumpy skin	1990-2020	**AHL_HPAI_2020; AHL_FMD_2020; AHL_LSD_2020**
	VBDs: All remaining VBDs not included in the AHL-A list (see Table 1)	2018-2020	**VBD_2020**
2023	**VBDs, all listed in Table 1**	2022	**VBD_2022**

Search strategy for vaccine studies

The search strings for vaccine efficacy studies are always a combination of 5 elements:

1) String I: agent/disease description. Name of the pathogen and diseases, with alternative names when relevant
2) String II: host description.
3) String III: selection of vaccine efficacy studies (*Efficacy OR Evaluation OR Assessment*)
4) String IV: commercial names of vaccines approved for use in the EU
5) Publication years selection

These elements are joined with "AND" statements.

The list of host species was constructed based on the species for which the EU vaccines are used (Annex II)

Two searches are planned to be performed on year 3:

1) Vaccine efficacy studies for the VBD vaccines approved for use in the European Union, as listed in Table AII-1 (Annex II). This will be an update of the last SLR conducted in 2018, and cover literature published 2018-2022.
2) Vaccine efficacy studies for the AHL-A diseases vaccines approved for use in the European Union, as listed in Table AII-2 (Annex II), and published from 1990.

The complete search strings are provided in Annex IV.

Search strategy for treatment studies

The search strings for treatment efficacy studies are always a combination of 4 elements:

1) String I: agent/disease description. Name of the pathogen and diseases, with alternative names when relevant
2) String II: host description.
3) String III: selection of treatment efficacy studies (*Treatment OR prevention AND Efficacy OR infect* NOT vaccine*)
4) Publication years selection

These elements are joined with "AND" statements.

A SLR focused on the AHL-A diseases, and covering references published since 1990 is planned for year 2. This will include all AHL-A diseases, even those that are also VBDs.

An update of the latest SLR for treatments against the VBD diseases is planned for year 4.

The complete search strings are provided in Annex IV.

Search strategy for vector control studies

The vectors in scope for the SLR are the same for all diseases: mosquitoes, sandflies, ticks and biting midges. No disease restriction is applied, any disease preventive measures aimed at these vectors are considered eligible as long as the treatments are approved for use in the European Union. The search string for vector treatment studies was constructed in collaboration with EFSA in previous SLRs:

Search string I: Vectors

mosquitoes **OR** sandflies **OR** "sand flies" **OR** ticks **OR** "midges"

String II: Objective-specific search terms

Clothianidin **OR** (Z,E)-tetradeca-9,12-dienyl acetate **OR** alpha-Cypermethrin **OR** Hexaflumuron **OR** 1R-trans phenothrin **OR** DCOIT **OR** DCPP **OR** Abamectin **OR** Aluminium phosphide releasing phosphine **OR** Bendiocarb **OR** Benzoic acid **OR** Carbon dioxide **OR** Muscalure **OR** Decanoic acid **OR** Deltamethrin **OR** diflubenzuron **OR** Dinotefuran **OR** Ethyl butylacetylaminopropionate **OR** etofenprox **OR** fipronil **OR** Glutaral **OR** Glutaraldehyde **OR** hydrogen cyanide **OR** Hydrogen peroxide **OR** imidacloprid **OR** Indoxacarb **OR** Iodine **OR** lambda-cyhalothrin **OR** Lauric acid **OR** Magnesium phosphide releasing phosphine **OR** margosa extract **OR** methyl nonyl ketone **OR** Metofluthrin **OR** N,N-diethyl-meta-toluamide **OR** Nitrogen **OR** Nonanoic acid, Pelargonic acid **OR** Octanoic acid **OR** Permethrin **OR** Polyvinylpyrrolidone iodine **OR** Propan-2-ol **OR** pyriproxyfen **OR** S-Methoprene **OR** Spinosad **OR** sulfuryl fluoride **OR** Synthetic amorphous silicon dioxide **OR** thiamethoxam **OR** transfluthrin

These two search strings will be combined (using AND) with the publication year restriction to perform two literature searches:

1) In project year 2, covering publications from 2018 to 2021;
2) The SLR will be updated again in year 4 (2024), covering publications from 2022 on.

Search strategy for Geographical distribution studies

The geographical distribution SLR will be updated every for both sets of diseases, VBD and AHL. This will also be complemented with information from official notification sources.

The experience from previous SLRs demonstrated that having a general search string for all diseases in scope does not work when the objective is to review the geographical occurrence of these diseases. It is particularly hard to filter studies that demonstrate the occurrence of a disease or agent based on search strings alone. The use of the keyword “detect” to look for reported detections of an agent, for instance, results in a large number of papers studying diagnostic tests, which need to be screened out. The use of the root “epidem*” to search for reported epidemics also was responsible for a lot of noise associated with the word “epidemiology”, while the use of the word “endemic” retrieves a lot of papers that use that word when giving general background knowledge about a disease.

Because the keywords we would need to use are so unspecific, the resulting noise that needs to be screened out varies greatly depending on how well the disease is studied, and how many references can be expected to be retrieved. The main lessons learned are that: 1) rather than having a search that is as specific as possible, we may need to have broad searches, and expect a lower rate of acceptance during level 1 screening; 2) the searches need to be tailored for specific diseases (or at least very small groups of diseases) and adjusted finely using scoping exercises.

The geographical distribution searches will be performed following the structure below:

1) String I: agent/disease description. Name of the pathogen and diseases, with alternative names when relevant
2) String II: host description.
3) String III: geographical occurrence (reports of disease/agent occurrence in an area, outbreak investigations, case reports, prevalence or incidence studies, or studies of disease transmission in an area reporting the reproductive number).
4) Publication years selection

String III will be constructed as a bespoken search for each disease, considering factors such as how well the disease is studied and how prevalent it is. For less well-known diseases, and/or of rare occurrence, we may use very few restrictions or even no specific geographical occurrence string, and rely on screening to select the relevant papers.

The publication year selection will be aimed for any publication from 1970 in the first year, followed by yearly updates. The time window will be reduced to keep the review manageable for diseases where the number of published papers is too large. For those diseases, however, evidence from other sources of reporting (such as reports to the World Animal Health Organisation – OIE) is expected to be much more complete.

Considering this need to continuous fine tuning and adjustment, the search strings will be kept in an updatable document online. This will serve two main purposes: 1) it will ensure that the reader can always access the most up to date search string; 2) any adjustments and improvements in the search strings will be documented with version control.

The permanent address for downloading the most up to date search strings is: https://svastatichosting.z6.web.core.windows.net/storymaps/ASF/DiseaseProfiling_GeoDistribution_SLR_SearchString.csv

Methods for study selection

Each of the SLR objectives will be conducted independently. Seven projects already exist in Distiller®, under the license owned by EFSA, containing all data collected in previous DACRAH projects (RC_EFSA_ALPHA_2015_03; RC_EFSA_ALPHA_2017_09, DACRAH-2; and RC_EFSA_ALPHA_2018_01, DACRAH-3). EFSA will be responsible for creating copies of these projects into which the CoVetLab consortium will build upon.

An overview of the systematic literature review process is provided in Figure 1.

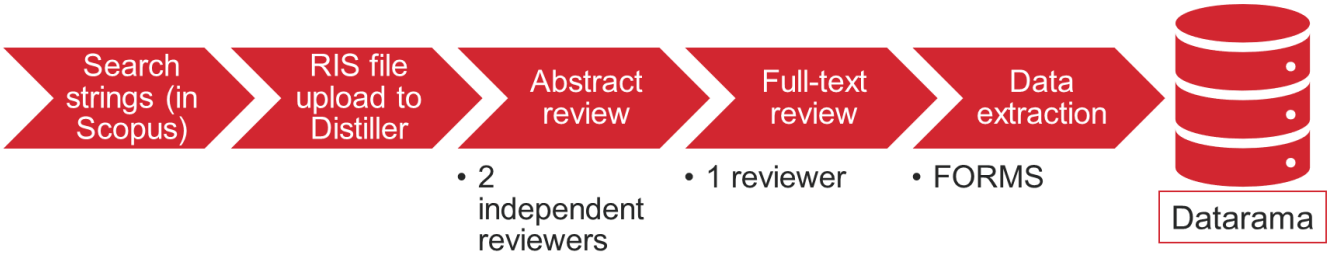

Figure 1. *Overview of the systematic literature revie process. Datarama is DistillerSR®'s database, from which data can be exported for manipulation.*

After the search strings are applied in Scopus, a RIS file containing all results is uploaded to Distiller. These files will be uploaded to the seven existing projects.

After uploading the references to Distiller, a duplicate detection will be performed. In case of literature review updates (same scope, only adding more years), Distiller can perform a "smart duplicate quarantine", in which references added in the update which are detected to already having been subjected to screening are automatically quarantine.

In this project, when we add references for AHL-A diseases to the existing projects, all detected duplicates will be reviewed manually before labelling them duplicates and subjecting them to quarantine. This will be done to ensure that papers addressing diseases or host species not in scope when the SLRs were limited to VBDs, but which are in scope now, will be subjected to a new screening.

Selection procedure

The level 1 selection process (title and abstract review) will involve the screening of title and abstract using a screening check list developed according to the eligibility criteria defined in the relevant section above. The checklists already setup in Distiller for previous VBD reviews will be reused, and adapted as needed to extend the scope to the AHL-A diseases.

If the information contained in the title or abstract is not relevant for the research objectives (any f the eligibility criteria are not met), the article will not be selected for full text assessment. The first level of screening will be performed independently and blindly by two researchers (i.e. two reviewers per study). Publications judged to be relevant by at least one reviewer will be automatically selected for further screening, while only publications rejected by both reviewers will be excluded. References without abstract will be carried over to level 2 screening, unless the title is explicit enough to make clear the lack of compliance to one or more eligibility criteria. Eligible studies in species other than those listed in Table 3 will be flagged, but not included in level 2.

Level 2 screening will involve the screening of full text articles identified in level 1, one reviewer per study, based on reading the full-text. Both level 1 and level 2 screenings will involve an initial phase of harmonisation and training regarding the assessment of study eligibility criteria, across all screeners of each objective.

Attempts will be made to obtain electronic versions of the full papers for all references that fulfil the eligibility and relevance criteria (i.e. those passing Level 1 screening). The CoVetLab's joint access to bibliographic resources are extensive but it is not possible, at the outset, to have a full overview of what journals eligible papers have been published in. Furthermore, the extent to which older publications are available in electronic format differs between publishers. In line with what was offered we will not account for requisition of publications that are not accessible through our existing channels, and/or publications that implies an extra cost for acquisition.

Documenting the selection

The study selection process will be fully documented in Distiller, allowing tracking and reporting of:

- Number of records identified through each electronic database or other source
- Total number of unique records (title/abstracts) identified through electronic search
- Number of records excluded after level 1 screening
- Records (full text) potentially eligible
- Number of records excluded after level 2 screening (by reason for exclusion)
- Final number of studies included in the review

Methods for data collection

Data collection will be performed using forms set up in Distiller® during previous SLRs. The structure of data collection has been extensively detailed at the end of the DACRAH3 project (RC_EFSA_ALPHA_2018_01). The documentation available for the data structure of each SLR is provided in Annex V.

These forms ensure that data validity checks are performed during data collection, in particular compliance to the data types specified in Annex V.

It is not expected that extensive adjustments in the data collection forms will be needed in order to accommodate for the AHL-A diseases scope. Changes to the existing forms will be avoided to ensure that all data collected are compatible with the data already collected in previous SLRs. We will however strive for maximum value in the data collection, and if adjustments or improvements to the data collection structure provided in Annex V are shown to be needed, those will be thoroughly documented during the course of the project.

One reviewer per study will individually extract data from studies that have passed screening for relevance, but a quality assurance process will be applied, as detailed below.

Authors of primary studies will not be contacted to provide missing or additional data.

Data quality assurance

After having performed these SLRs in previous DACRAH projects, the CoVetLab consortium has developed a few data quality assurance practices:

1) New reviewers are always trained by a reviewer experienced in the process
2) Harmonization rounds are performed in the beginning of each screening level, with reviewers sharing notes and thoughts on some common papers before working independently
3) A “helpsheet” is developed for each SLR containing detailing instructions for the screening process. When a reviewer has questions about the eligibility or the format of data collection for any specific paper, the question is shared among the entire group by email, providing the paper refID so that the group can consult the reference in Distiller and discuss the question. If needed, the question is forwarded to the EFSA scientific team, who can choose to forward to relevant expert working groups. Once consensus is reached, the specific questions and the reached agreement are documented in the helpsheet for future reference.
4) One project leader experience in the review is responsible for regularly reviewing the progress of the screening, and running data validation checks directly in Distiller (using the datarama) or exporting the data.
5) In the data collection step, a free-text box is provided at the end of every form. Reviewers can use this box to take any notes on study quality issues notes, relevant data which couldn’t be captured, or any other discrepancies or points worth noting. All forms with note in this box are reviewed by the project manager.