A PRACTICAL FRAMEWORK FOR DEVELOPING CASE DEFINITIONS FOR ANIMAL DISEASES

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INTRODUCTION

For infectious diseases, a **case definition** is a set of specific criteria used to distinguish between *an epidemiological unit (e.g., individual, cage, farm) infected by a pathogenic agent* (a case), and one that is not infected (non-case) in a given place at a given time. A case may or may not show clinical signs (Gardner et al., 2011; Laurin et al., 2018).

Case definitions are useful for establishing equivalent approaches for disease surveillance, response, and reporting purposes. Each case definition will be dependent on the purpose for which it will be used; and on the case category. For various purposes, case categories might include suspect, presumptive positive, confirmed positive, confirmed negative, exposed or recovered. Various epidemiological factors such as the pathogen attributes, clinical disease patterns, animal type, management or housing unit, and geographic location, population disease prevalence and distribution; and diagnostic testing technologies impact the case definition. As such, one disease may have several case definitions developed.

The objective of this document is to lay out a standardized approach for developing case definitions that can be used for veterinary disease surveillance and response.

Specifically, the framework will help support:

- Consistent reporting and communication for regulated, zoonotic, and other endemic diseases,
- Estimation of incidence levels, trends, and signals for improved detection of disease,
- Identification and management of disease outbreaks,
- Identification of new and emerging patterns.

Developing a standardized case definition is a multi-stage process (Figure 1) that may require collaboration from various stakeholders (e.g. epidemiologists, laboratorians, government and private veterinarians, commodity groups). Any case definition must be subject to periodic review to evaluate for changes related to risk factors, diagnostic advances, and updated epidemiological knowledge base.

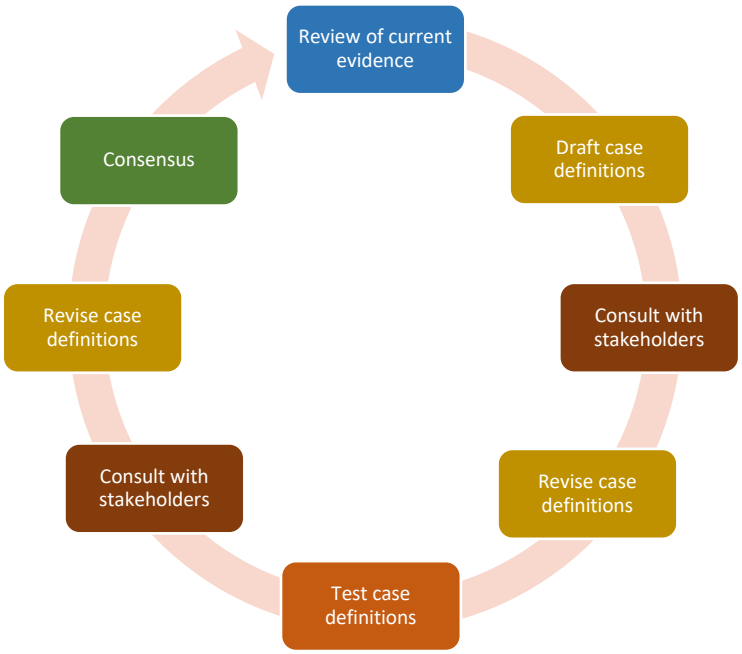
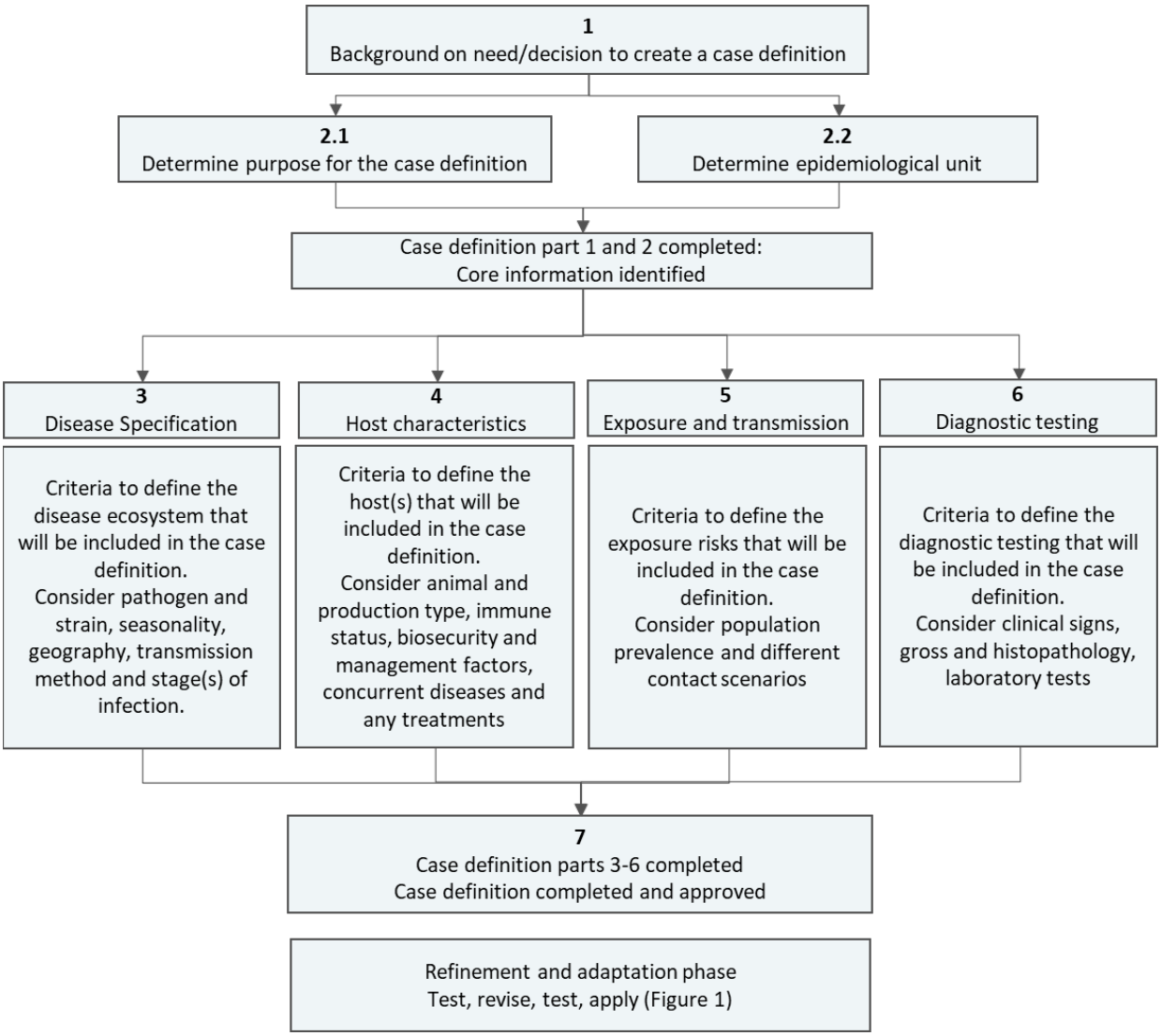


Figure 1. Multi-stage process for developing, reviewing, and updating veterinary case definitions

The working pages of the framework are presented below. These pages are designed to be filled in by users as they develop a case definition for veterinary surveillance. The framework is divided into 6 sections; background; primary criteria (purpose, epidemiological unit), disease specification, host characteristics, exposure and transmission, and diagnostic testing. Each section includes multiple criteria that the user can consider for inclusion in the case definition. It is important to note that the framework is intended to provide a comprehensive list of criteria that might be included in a case definition, but most case definitions will not require inclusion of all criteria. For example, the definition of a confirmed case may be focused on criteria related to diagnostic testing, while definitions for a suspect or exposed case may include criteria related to host characteristics, clinical signs, exposure and transmission. Figure 2 provides a visual overview of how sections of the case definition table framework intend to be completed, as well as identify interactions between the sections.

Figure 2. Flowchart showing the order and interaction of filling in the sections of the case definition table



CASE DEFINITION FRAMEWORK

SECTION 1. BACKGROUND

1. What are the circumstances that led to the need for a case definition?

2. Who is developing the case definition?

3. List pre-existing case definitions relevant to this situation:

SECTION 2. PRIMARY CRITERIA TO BE CONSIDERED FOR THE CASE DEFINITION

4. What is the name of the disease or syndrome? Include all scientific and common names.

5. What is the purpose for which the case definition is being developed? (check one)

Early disease detection		**Comments:**
Endemic disease monitoring		
Outbreak response		
Control or eradication		
Freedom from disease		
Other		

6. What is the epidemiological unit for which the case definition is being developed? (check one)

Individual		**Comments: (if group is selected, describe specifics. This should include the boundaries or criteria that define it as a group such as pen, barn, premises, flock etc.)**
Group		

7. For the disease, purpose, and epidemiologic unit stated above, which case categories are relevant? (check one or more)

Suspect		**Comments:**
Presumptive positive		
Confirmed positive		
Confirmed negative		
Exposed		
Recovered		
Other		

SECTION 3. DECISION TABLE FOR INCLUSION/EXCLUSION OF DISEASE SPECIFICATION CRITERIA

For each criterion, consider if it should be included as part of the case definition (select no, yes, or maybe) for the documented disease, purpose, and epidemiological unit and then fill out the respective columns.

Criterion	**Is this criterion included in the case definition?**	**If the criterion is considered to be a part of the case definition, (yes or maybe), what specifics should be:**		**If maybe, describe uncertainty and evidence?**	**Other additional comments:**
		Included	Excluded		
Etiological agent(s)	no/yes/maybe				
Specific strain(s)	no/yes/maybe				
Genetic characteristics	no/yes/maybe				
Geography	no/yes/maybe				
Season	no/yes/maybe				
Method of infection	no/yes/maybe				
Stage(s) of infection	no/yes/maybe				
Additional comments for the section:					

SECTION 4. DECISION TABLE FOR INCLUSION/EXCLUSION OF HOST CHARACTERISTICS CRITERIA

For each criterion, consider if it should be included as part of the case definition (select no, yes, or maybe) for the documented disease, purpose, and epidemiological unit and then fill out the respective columns.

Criterion	**Is this criterion included in the case definition?**	**If the criterion is considered to be a part of the case definition, (yes or maybe), what specifics should be:**		**If maybe, describe uncertainty and evidence?**	**Other additional comments.**
		Included	Excluded		
Animal species/ type	no/yes/maybe				
Sex	no/yes/maybe				
Age	no/yes/maybe				
Production stage/type	no/yes/maybe				
Vaccination/Immunity	no/yes/maybe				
Concurrent illness/disease	no/yes/maybe				
Other stressors	no/yes/maybe				
Biosecurity/ Quarantine	no/yes/maybe				
Specific management factors	no/yes/maybe				
Treatments	no/yes/maybe				
Additional comments for the section:					

SECTION 5. DECISION TABLE FOR INCLUSION/EXCLUSION OF EXPOSURE RISK CRITERIA

For each criterion, consider if it should be included as part of the case definition (select no, yes, or maybe) for the documented disease, purpose, and epidemiological unit and then fill out the respective columns.

Criterion	**Is this criterion relevant for the case definition?**	**If the criterion is considered to be a part of the case definition, (yes or maybe), what specifics should be:**		**If maybe, describe uncertainty and evidence?**	**Other additional comments:**
		Included	Excluded		
Prevalence of disease in contact populations	no/yes/maybe				
Contact: **Animal, direct**	no/yes/maybe				
with known or suspect infected / infectious animal	no/yes/maybe				
with same or different animal species	no/yes/maybe				
frequency and duration of contact	no/yes/maybe				
Contact: **Human, direct**	no/yes/maybe				
with known or suspect infected / infectious human	no/yes/maybe				
frequency and duration of contact	no/yes/maybe				
Contact: **Human originated, indirect**	no/yes/maybe				

with known or suspect contamination by humans	no/yes/maybe				
key indirect contact types	no/yes/maybe				
frequency and duration of contact	no/yes/maybe				
Contact: **environmental, geospatial**					
proximity to known or suspect infected / infectious animal or human or contamination	no/yes/maybe				
population density (of epidemiological units)	no/yes/maybe				
frequency and duration of exposure	no/yes/maybe				
uncontrolled contamination	no/yes/maybe				
key contact types	no/yes/maybe				
Additional comments for the section:					

SECTION 6. DECISION TABLE FOR INCLUSION/EXCLUSION OF DIAGNOSTIC TESTING CRITERIA

For each criterion, consider if it should be included as part of the case definition (select no, yes, or maybe) for the documented disease, purpose, and epidemiological unit and then fill out the respective columns.

Criterion	**Is this criterion included in the case definition?**	**If the criterion is considered to be a part of the case definition, (yes or maybe), what specifics should be:**		**If maybe, describe uncertainty and evidence?**	**Other additional comments.**
		Included	Excluded		
Clinical signs in individual animals	no/yes/maybe				
Population-level measures of disease	no/yes/maybe				
Pathological findings	no/yes/maybe				
Sample types	no/yes/maybe				
Diagnostic test(s)	no/yes/maybe				
Sample size	no/yes/maybe				
Sample Pooling	no/yes/maybe				
Sample handling/ contamination	no/yes/maybe				
Additional comments for the section:					

SECTION 7. CASE DEFINITION

Final Case Definition(s)

CASE DEFINITION FRAMEWORK MANUAL

The manual provides additional information to help users work through the case definition case definition framework.

It is recommended that users develop the case definition in order from sections 1 to 6, as each step's information will be selected based on the previous step.

SECTION 1: BACKGROUND

This section provides context and historical information for future users of the case definition to refer to.

SECTION 2: PRIMARY CRITERIA

NAME OF DISEASE

State any common and/or scientific names and any applicable details for the variations in disease names.

PURPOSE

Surveillance is the monitoring of disease over time with measurable action points; passive systems involve observer-initiated data collection; active systems involve investigator-initiated data collection.

The main applications for case definitions are:

Early detection: The disease is absent, and there is value in identifying a case quickly should the disease emerge. Ideally includes extensive testing and observation coverage of the population.

Endemic disease monitoring: The disease is present and common to the area and there is value in detecting changes in disease prevalence and/or epidemiological patterns over time or space. Often involves planned testing of a representative sample of the population(s)

Outbreak response: There is a need to detect new cases of an exotic disease (known disease but not previously found in the area) or an emerging disease (disease is new to the area and has unknown scientific information) or an endemic disease that is highly transmissible and can result in a surge of new infections under appropriate conditions. It may involve a combination of several types of surveillance

Control or eradication: There is a plan to eradicate or control a disease of concern. It can involve a combination of several types of surveillance

Freedom from disease: There is a need to demonstrate that a disease is absent or no longer present in a particular location ("proof of freedom"). Can include active testing (representative or risk-based) of a sample of the population, but could also integrate other surveillance components to increase confidence at reduced cost.

Choose "other" if the purpose required does not fall under one of the above-mentioned purposes and provide explanation and applicable details in the comment space. Hoinville et al. (2013) lists various surveillance types for animal health scenarios.

Choose one purpose for which the CD will be used. In situations where there may be more than one purpose, it is recommended that separate CD(s) be created for each purpose.

EPIDEMIOLOGICAL UNIT

The epidemiological unit is the unit for which criteria (e.g. test specifications, interpretations, analyses, management, environment) apply. The primary unit will usually be the one that has the greatest risk of disease spread.

Choose one epidemiological unit for which the CD will be used. Include any additional comments as required for why the unit is chosen and if any particular situations apply. If a population-level unit is chosen, specify details about the population such as pen or cage level, herd level, farm level, etc. Be as specific as needed to describe the level, include number of animal(s) per unit if required to describe the unit accurately. As there may be more than one epidemiological unit of interest, it can be necessary to create separate CD(s) for each. Alternatively, an addendum to the CD, stating the changes (e.g., diagnostic requirements, clinical presentation, epidemiological information) that must be considered due to the additional unit.

SECTION 3: DISEASE SPECIFICATION

For each disease specification criterion, consider if it is relevant to the case definition (select: no, yes, or maybe). Refer to the disease, purpose, and epidemiological unit to help guide decisions. For criteria determined to be relevant, document specific inclusion and exclusion elements. Where "maybe" is selected initially, effort may be needed to determine reasons for uncertainty and justification/evidence for inclusion so that the maybe can be adjusted to a yes or no decision.

ETIOLOGICAL AGENT(S)

Identify the etiological (cause of disease) agent(s) if known, including relevant naming conventions?, such as bacterium, virus, fungus, parasite, or toxin.

SPECIFIC STRAIN AND GENETIC CRITERIA

Provide information about specific strains, if applicable. Include relevant genetic information, (strain, sequence), linkages to source description of the pathogenic agent, etc. If required, separate case definitions can be created for specific strains or sequences.

GEOGRAPHY AND SEASONALITY

Include any information about the geographic location of the disease agent (including whether it is local, provincial, regional, national, international) and the seasonality (time of year or production cycle).

METHOD AND STAGE OF INFECTION

Infectious refers to infected animal(s) that shed the disease agent and able to transmit it to other animal(s). Consider if shedding occurs during preclinical or clinical stages and whether it is intermittent, seasonal, age-related, or continuous. Also include details of how they are infectious (e.g. fecal-oral, blood, saliva, droplets, skin or fur, etc.). Include information about relevant (to the purpose and epidemiological unit) method(s) of infection (e.g., fecal-oral, trans-placental, body fluids, airborne) and stage(s) of infection.

Stage of infection refers to whether the animal is non-infected, exposed, infected with no clinical signs (pre or subclinical), infected with clinical signs (showing observable or measurable signs or symptoms), infectious (able to

transmit the disease). If applicable, include a statement in the comments about preclinical stages and incubation periods. Consider any standardized methods for subjective and/or objective measurement of disease stage.

SECTION 4: HOST CHARACTERISTICS

For each host characteristic criterion, consider if it is relevant to the case definition (select: no, yes, or maybe). Refer to the disease, purpose, and epidemiological unit to help guide decisions. For criteria determined to be relevant, document specific inclusion and exclusion elements. Where "maybe" is selected initially, effort may be needed to determine reasons for uncertainty and justification/evidence for inclusion so that the maybe can be adjusted to a yes or no decision.

SPECIES

In this section, list the animal types or species (one or multiple) to be included. In the comments section, can describe why a species or animal type was included given for the selected purpose of the CD (e.g., susceptibility, transmission, zoonosis, etc.). Also, if applicable list primary breed(s).

SEX

To be used if the case definition includes or excludes based on sex.

AGE AND/OR PRODUCTION STAGE

If life stage is a relevant factor for the CD of the disease and purpose in question and to better describe the details of the epidemiological unit, select yes. If yes, then list the life stage (one or multiple to be included. Life stages may be dependent on animal type and production system but could include: neonatal, weaning, growing, immature, mature, broiler, pullet, reproductive (non-active, active, never bred yet but intact, open, in heat, bred, post-partum, lactating, spayed or castrated, pre or post breeding), egg, fry, larval, juvenile, adult, etc.

VACCINATION/IMMUNITY

Immunity is an animal's inherent ability to resist infection from a pathogenic agent or toxin. Immunity refers the stage of immunity for the epidemiological unit of concern for the purpose, disease, and species of concern. If this is a relevant factor for the case definition under development, then list the type(s) of immunity that are included and excluded. It may be necessary to discuss how natural variation on the degree of immunity in nay population might impact categorization.

Immunity stages might include: maternal (the naturally acquired immunity (maternal antibodies) a fetal/neonatal animal receives from it mother), vaccinated (acquired immunity from vaccines), carrier (harbors a pathogenic agent and may or may not show clinical signs but may be able to transmit the disease at certain times), reservoir (animal(s) that are immune to a pathogenic agent but able to transmit it directly or indirectly) , recovered (had the disease but from treatment or immune response able to rid the body completely of the disease and is now back to a normal healthy state) recent, recovered historical, immune-compromised (an immune system that is impaired and at increased risk for infection), naïve (never been exposed to the pathogenic agent), etc.

Determine whether vaccination status impacts the case definition. If there is a vaccine, consider the type of vaccine, source of vaccine, if the vaccine is readily available, and any estimate on vaccine usage and effectiveness.

Figure 3 provides an overview of typical stages on susceptibility and immunity to infectious agents that can be used to consider if immunity status should be considered for the case definition in question.

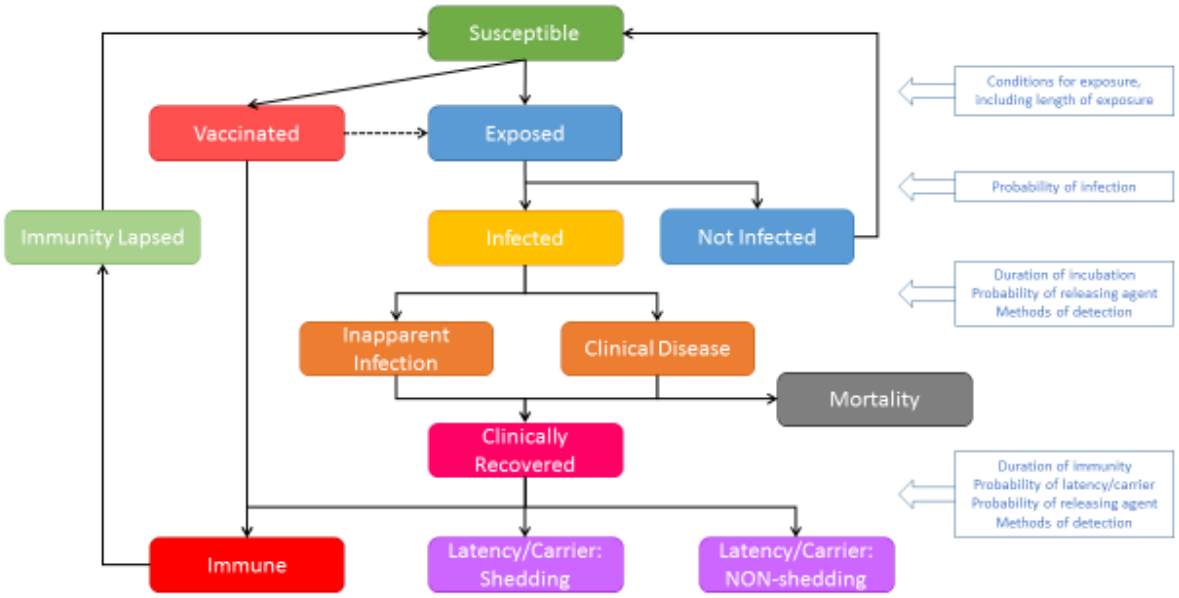


Figure 3. Typical stages of susceptibility and immunity to infectious agents

CONCURRENT DISEASE

Consider if the presence of other disease(s) or illness can impact the case definition. Discuss the importance and order of importance of any concurrent diseases and any applicable details regarding the time, degree, and stage of infection with the concurrent disease(s) to the disease in question.

OTHER STRESSORS

Stressors refer to factors that can increase the stress level of animal(s), thereby decreasing their immune responses. If additional stressors are relevant criteria, then describe the details as to the primary stressors of importance, the time since the stress, and the degree of stress level.

BIOSECURITY/QUARANTINE

Biosecurity refers to specific practices and area designations applied to the premises where the epidemiological unit is located and implemented under specific formal protocols that are meant to prevent exposure of the epidemiological unit to the disease. Any informal, “biosecurity-like” practices would fall under management instead.

Select whether having biosecurity practices in place is relevant to the CD.

Quarantine is a specific type of biosecurity measure that refers to whether the animal(s) at risk are suspected to be or at risk to be exposed and are quarantined. It is a state of separating or isolating an animal or group of animals that are infected, potentially infected, and pending confirmation of infection, or at high risk of exposure to avoid

spread of disease to or from the isolated animal(s). If this is relevant, describe length of quarantine time and any requirements for repeat quarantining, etc. Note quarantines may be regulatory or voluntary. The type of quarantine likely to be used should be captured.

SPECIFIC MANAGEMENT FACTORS

Management refers to animal management or care factors that may increase or decrease risks for disease exposure. These are factors that would apply at the epidemiological unit level. If management is selected as a relevant factor in the CD, then describe the primary details of importance.

TREATMENTS

Treatment(s) are any medicinal or non-medicinal interventions to decrease the effect or rid the animal of the infectious or pathogenic agent. If this is a relevant criterion for the CD, list in as much detail as required the specific treatment(s) modality, method, time, source, and frequency, as applicable.

SECTION 5: EXPOSURE RISKS

For each exposure risk criterion, consider if it is relevant to the case definition (select: no, yes, or maybe). Refer to the disease, purpose, and epidemiological unit to help guide decisions. For criteria determined to be relevant, document specific inclusion and exclusion elements. Where “maybe” is selected initially, effort may be needed to determine reasons for uncertainty and justification/evidence for inclusion so that the maybe can be adjusted to a yes or no decision.

PREVALENCE

Prevalence is a measure (expressed as a ratio) of how common a disease is in a particular population; it is the number of infected animals at a designated time divided by the total number of animals in that population at that same time. Prevalence of disease can affect the risk of exposure and the interpretation of test results. It may be useful to describe the presumed level (percentage) of prevalence in as much detail as can be justified with evidence-based information. Example prevalence levels: very low (<5%), low (<10%), moderate (10-50%), high (>50%), free (0%), unknown.

DIRECT ANIMAL CONTACT

Direct animal contact refers to the risk of direct exposure to an epidemiological unit from one or more susceptible animal hosts. It may be useful to describe whether the relevant contact is from a confirmed or suspect case, and whether it is from the same or different species.

Note: Horizontal contact refers to transmission of disease agents from one animal directly to another, but not through a parent-offspring relationship. Vertical transmission refers to transmission of disease agents from mother to offspring during gestation or in the period during and immediately after birth.

DIRECT HUMAN CONTACT

Direct human contact refers to the risk of direct exposure between humans and the epidemiological unit where humans are known susceptible hosts.

INDIRECT HUMAN-ORIGINATED CONTACT

Indirect human-originated contact refers to the risk of exposures from inanimate objects or materials that may carry the infectious agent and are placed in contact with the epidemiological unit due to human activities (fomites). Examples include feed, transport, equipment, supplies, clothing, footwear & other fomites. Describe the details of the risk of exposure from human activity. Include as much detail as required, including supporting evidence on probability of contamination with the infectious agent and the probability of transmission.

INDIRECT ENVIRONMENTAL/GEOSPATIAL

Indirect environmental contact refers to exposure of the epidemiological unit to a pathogenic or infectious agent through the environmental pathways. This includes agent transmission via physical movement by pests (insects, rodents, etc.), flooding, aerosol transmission and other pathways not related directly to human activity. It is important to recognize the difference in terminology for pests (or other uninfected animals) and vectors. Pests physically carry an agent but are not infected with the agent. Vectors are infected with the pathogen, often as part of a necessary stage in a complex infectious agent life cycle.

If one or more of these exposure pathways are relevant, then describe the specifics of the pathway (i.e. which types of pests, what types of weather conditions), the magnitude of the exposure (i.e. level of pest infiltration) and the expected durations (i.e. single vs multiple weather events) that are estimated for effective transmission.

The exposure risks associated with vector-borne diseases are included with environmental risks. It is recognized that these are specific risks, and the definition will need to recognize vector life cycle and factors that support vector contact.

SECTION 6: DIAGNOSTIC TESTING

CLINICAL SIGNS

Clinical signs are observable signs or symptoms of disease in a live animal. If clinical signs are relevant, provide applicable details in the inclusion and exclusion columns that refer to the organ system(s) affected (gastrointestinal, respiratory, reproductive, circulatory, nervous system, dermatological, musculoskeletal, ocular, mucus membranes), including the order of importance, whether the signs are expected to be mild, moderate, or severe, and any additional details. Also, if applicable, include a standardized method for identifying and reporting clinical signs.

Differential diagnoses are a list of other potential diseases that can have similar clinical signs or stage(s) of disease and/or gross pathology. In the comments space here, list the most important differential diagnoses, in the order of importance, and if required, a guide to the potential follow-up procedures, treatments, or tests that are required to reach a confirmed diagnosis.

POPULATION-LEVEL MEASURES OF DISEASE

This section refers to additional criteria that define disease presence at the population-level, including mortality, morbidity, social interaction, feeding behaviours, production factors, level of the population affected, etc.Include specific evidence-based information if available (e.g., drop in egg production of 50%, feed consumption drop of 10%, etc.).

Mortality refers to the state of death in animal(s), and particularly as it pertains numerically to a population, location, or time period. If this is a relevant factor, describe the level of mortality as applicable to the

epidemiological unit of concern, as well as the rate of mortality if known. Justify specific rates and percentages with evidence-based information, if available.

Morbidity refers to the state of being diseased in animal(s), and particularly as it pertains numerically to a population, location, or time period. If this is a relevant factor, describe the number or percent (of the total population) of morbidity as applicable to the epidemiological unit of concern, as well as the rate of morbidity if known. Justify specific rates and percentages with evidence-based information, if available.

PATHOLOGY

Pathology refers to gross and histopathological findings for the different body systems (gastrointestinal, respiratory, reproductive, circulatory, nervous system, dermatological, musculoskeletal, ocular, mucus membranes). A standardized method for describing pathological findings may be beneficial.

SAMPLE TYPE

The sampling process is very important in regard to interpreting test results. Different purposes, prevalence of disease, and epidemiological units may require different sampling protocols.

The target tissue or sample is the one in which the infectious or pathogenic agent is expected to be present, dependent on purpose, species, disease, and disease stage. Select if this is a relevant factor and then describe the sample(s) that should be targeted for collection. Also include details as to what part(s) of the organ(s) or tissue(s) should be collected (whole, infected, infected with margins, etc.)according to the gross pathology and pathogenesis of the disease agent. Include information about a standardized recommended method for sample collection and handling in the field.

DIAGNOSTIC TEST(S)

This section refers to diagnostic testing options. Use standard tests that have been evaluated for evidence-based diagnostic test characteristics for the disease, or tests that are recommended by regulatory bodies. It may be useful to describe which tests are recommended and the standard method for performing the tests (provide citation for recommended standard operating principles).

If relevant, according to the purpose of test (screening, confirmatory, etc. (see OIE, 2019)), describe the known (provide evidence-based citation or expert opinion) diagnostic sensitivity (DSe) and diagnostic specificity (DSp) of the recommended test. DSe is the diagnostic accuracy estimate for a test to identify truly infected animals as infected or positive. DSp is the diagnostic accuracy estimate for a test to identify truly non-infected animals as not infected or negative. A screening test is an early detection test that is used as a first step; it typically has a lower cost and quicker time to results; but it can have lower DSe and DSp and is often followed up with confirmatory test for diagnostic purposes. A confirmatory test is a diagnostic test used to confirm the results of another test (usually a screening test); typically has high DSe and DSp; usually costlier and can be more time and labor intensive.

If the epidemiological unit is the herd or pool level, then describe the HSe/HSp or PSe/PSp, if these are available and able to be justified. Also consider gathering information about any reference or benchmark tests that are used to calculate the stated diagnostic accuracy estimates and those test(s)'s validation level, or if Bayesian methods were used. For more information on how to calculate these, refer to peer-reviewed reporting standards, including (Branscum et al., 2005; Gardner et al., 2011, 2016; Kostoulas et al., 2017; Laurin et al., 2018).

Bias can occur in which a result is misclassified as either a false positive (FP, a positive test result that is incorrect (the animal is truly not infected) that results from lower DSp) or false negative (FN), a negative test result that is incorrect (the animal is truly infected) that results from lower DSe. It may be of value to describe potential causes for the bias occurring. Refer to the previously mentioned citations for information about reporting biases relevant to diagnostic tests. Include any recommendations and reasons why a test should be performed at a specific time, either temporally or in reference to the stage of infection, stage of production, or time since sample collection.

List important specifics as to how a test result is interpreted (negative, inconclusive, weak positive, strong positive) and the recommended reporting of results (e.g., copy numbers, colony forming units, cycle threshold, etc.) including recommended cut-offs and the standardized method for dealing with inconclusive results (reclassifying and/or retesting). An inconclusive result is a test result that cannot be classified as either positive or negative and often is retested again; standard operating protocols should be in place to determine the procedure for dealing with inconclusive results before a decision is made concerning it. For additional definitions on reporting and analyzing inconclusive results, review Shinkins et al., 2013.

SAMPLE SIZE

Sample size is the number of samples that are collected. For some purposes (e.g. determining prevalence, freedom for disease) statistical calculations can be done to identify the required number of samples that should be collected to accurately interpret results with appropriate confidence and power at the population level. Describe if the samples are collected randomly from the entire population or purposively (e.g. risk based, convenience), and the disease stage(s) of the samples to be collected.

POOLING

Pooling refers to mixing one or more specimens from the same animal or from multiple animals into one test, often to decrease costs and time required to test large numbers of animals. If sample pooling is a consideration, describe the methods of pooling and the pool size (how many animals or specimens mixed). Interpretation of test results from pooled samples is dependent on various factors, including prevalence, load of target analyte, and the test's diagnostic accuracy estimates. For example, pooling can potentially result in false negative results due to dilution of the target agent, and number of positives per pool, and load of the agent in those positives. For more information about pooling for surveillance testing, review Laurin et al., 2019.

SAMPLE HANDLING/CONTAMINATION

Is sample collection, transport, and storage of samples relevant to the definition? If yes or maybe, specify recommended handling details for the samples, including standardized methods and potential for biased test results. Contamination of samples can occur during collection in the field or handling in the laboratory. Contamination can bias the interpretation of test results. If this is relevant, list the type of agent(s) with which the specimen is likely to be contaminated, and the level of contamination that is expected (likely, mild, strong). In the space provided, also describe any further details regarding contamination of the specimens and when it is more likely to occur.

SECTION 7: WRITING A CASE DEFINITION

Combining the information from Sections 1-6 will allow to write a concise case definition.

Background

A short paragraph or table should describe the following (includes information from sections 1, 2 and 3)

1. Background information if needed
2. Disease (include name of pathogen and strain if appropriate)
3. Purpose of CD
4. Epidemiological unit

Example:
The following case definition for clinical cases of West Nile virus (WNV) in horses was developed for the purpose of national case reporting in Canada.

The case definition is a stepwise process where a case (epidemiological unit) may be considered suspect and/or presumptive positive, and confirmed positive or negative.

Suspect case

Considering environmental (geography and seasonality if applicable) (section 3)

1. Describe expected clinical manifestation (section 6) and pertinent host characteristics (susceptible species, age, vaccination etc) (section 4).
2. A suspect case may also target the unit of interest epidemiologically linked to a case (section 5). Again pertinent host characteristics should be described here (section 4)

Example:
Suspect case of WNV: A horse displaying compatible clinical signs that include ataxia (including stumbling, staggering, wobbly gait, or incoordination) or at least two of the following: circling, hind limb weakness, inability to stand, multiple limb paralysis, muscle fasciculation, proprioceptive deficits, blindness, lip droop/paralysis, teeth grinding, fever, acute death.) during the vector season (mid-April to November) in Canada.

Probable/presumptive positive

A presumptive case has a higher degree of probability of being a case than a suspect case. It is a suspect case that has additional support for being a case such as : screening diagnostic testing (section 6) , significant exposure (section 5) , epidemiological presentation (mortality) or link with a confirmed case.

Example:
An horse with compatible clinical signs (Suspect case) with an

- *elevated titre to WNV antibody by SN test in serum or positive IgG ELISA test, but only one sample is available;*
- *static IgG titres to WNV (SN test or ELISA) in appropriately-timed paired sera.*

Confirmed positive

A confirmed case is a suspect or a presumptive case that has been confirmed through:

1. an epidemiological investigation confirming exposure (section 5) to a confirmed case, or
2. Confirmatory laboratory testing with a testing scheme providing a high diagnostic specificity (Section 6)

Example:

Suspect or presumptive positive case with

- *Detection of viral antigen by virus isolation, positive immuno-histochemistry (IHC) for WNV antigen or Polymerase chain reaction (PCR) in tissue and appropriate histological changes.*

OR

- *detection of IgM antibody to WNV by ELISA testing in serum or cerebrospinal fluid (CSF). Vaccination may lead to a low IgM response and vaccine history must be taken into account;*

OR

- *an associated 4-fold or greater change in IgG ELISA testing or sero neutralization (SN) test antibody titre to WNV in appropriately-timed (>10-14 days apart), paired sera;*

Confirmed Negative (if necessary)

A confirmed negative case will be a suspect or presumptive positive case that has failed to be confirmed by diagnostic testing scheme with a high diagnostic sensitivity.

APPENDIX 1- METHODS AND RESULTS OF RESEARCH TO DEVELOP FRAMEWORK

METHODS

SHORT SCOPING REVIEW

Prior to developing the framework, literature was reviewed to identify any and/or different approaches for case definition development and required criteria for each approach. The scoping review was performed using PubMed. Terms searched included "surveillance" and "case definition." The only filters applied were for "other animals" and "English." Also, a general Google search was also performed for the same terms as well as the term "case definition framework." All results (websites, grey literature, peer-reviewed literature) were reviewed by one author (Dr. Emilie Laurin, Atlantic Veterinary College (AVC), Canada). For PubMed results, titles and abstracts were first reviewed, and only those results that specifically discussed a case definition protocol underwent a full paper review. All relevant literature was summarized and gaps were identified regarding case definition development or differences between approaches and why.

The scoping literature review included a background research and technical review to determine if case definition frameworks have been developed in regions of Canada or in countries with similar animal agricultural systems, and what might be learned from published frameworks and case definition processes. The review included assessing for the following:

- what attributes are included
- for what are the definitions typically used
- what are the identifiable gaps.

CRITERIA SELECTION

A list of required core principles, criteria, and sub-criteria to be included in the framework was compiled based on evidence identified during the scoping review; further discussions amongst all authors; and additional literature suggested by co-authors but not identified in the scoping review: Kloeze et. al. (2012), Laurin et al. (2018), Gardner et al. (2011, 2016), O'Connor et al. (2016); OIE (2018). The purpose of the list was to provide, for the framework, the broadest application across multiple systems and data sets. A priori, it was determined that the framework had to include three core principles: clinical presentation, epidemiology of animal health event, diagnostic testing/confirmation. Additional attributes (e.g., trade/market) could be included but must not take higher priority than the core attributes. In addition, criteria had to eventually support four different **c**ase classifications: suspect, probably/presumptive positive, confirmed positive, negative.

FRAMEWORK PRESENTATION

Goals of the project were that the case definition framework would be structured as a practical step-by-step framework or flowchart, and would include recommended processes by which case definitions are developed, assessed, reviewed, and updated (to streamline the collation and analyses of cases of defined diseases); and to provide the pathway for collaboration, consultation, and communication of case definitions to the broadest number of stakeholders so that a consistent approach is available for use across networks, systems, and data streams.

RESULTS

SCOPING REVIEW

A standardized case definition is useful to prevent subjective case classification and to decrease the risk of study and diagnostic biases (Begg, 1987; Laurin et al., 2018). A standardized case definition development process increases equivalency and comparability between cases regardless of who identifies the case and when and where it is identified (www.cdc.gov). Throughout all the literature reviewed, it was expressed that *core principles* of case definitions are clinical, laboratory, and epidemiological criteria and data. It was also discussed that case definitions will evolve over time as more information becomes available; therefore, modification methods must be in place.

Table 1 lists the results of the scoping review for each relevant citation, including the purpose, criteria, and gaps concerning case definition protocols discussed within each literature source. There were 18 relevant citations, including human health case definition guidelines and protocols that contained valuable information that could be utilized and adapted for animal health case definitions.

The *epidemiological unit* is important to identify, especially if the case definition applies to an individual or population(s), as criteria and interpretation can change depending on the epidemiological unit. In addition, the purpose (surveillance, outbreak, reportable) can affect the level of detail for the case definition and the timeliness of reporting stages of the case definition. However, outbreak components for the case definition can vary for each outbreak. Two types of case definitions were identified according to their purpose: (1) sensitive (broad or loose) to capture most or all of the true cases (e.g., highly transmissible, early outbreak), but also includes many differential diagnoses; (2) specific (strict) to include only confirmed cases (e.g., outbreak), but can be more time and cost prohibitive and also underestimate total cases if some are not tested. Therefore, the case definition may change during the investigation depending on purpose and disease (CDC, 1997).

Appendix Table A1. Results of scoping review for relevant literature.

	Organization	Framework*	Country	Disease	Purpose	Criteria **	Notes	Gaps	Citation
1.	USDA	Yes	US	Foreign	Prepare-response; 4 purposes: surveillance planning and implementation; disease outbreak response; National Animal Health Reporting System reporting standards; National reportable animal disease list development	General disease and pathogen information; lab criteria (tests recommended by OIE and NVSL), reporting, control and surveillance, classification	"Establish uniform criteria for reporting purposes", prepare: providing case definition to stakeholders prior to incident; response: updating case definition at regular intervals or as needed during incidents or outbreaks	Does not include negative as a class	USDA APHIS VS FAD PReP SOP 0002 v3.0: case definition development process January 2014
2	FAO	No	UN	Livestock (15 diseases). Transboundary; for food security, public health, and international trade	Define a case of disease event and reach a confirmatory diagnosis	Clinical manifestations, post-mortem findings, epidemiological investigation (morbidity, mortality, age), laboratory findings	"The purpose of preparing the case definition under the context of this manual is to help animal health personnel in the identification and prompt reporting of suspected disease occurrences in the field. In addition it enables them to follow a systematic approach when disease outbreaks are investigated."	Does not include negative as a class	USAID 2010 Case definition of livestock diseases. FAO of UN.
3	AVC, Canada	No	Fish	BKD	Farm-level and cage-level, clinical and subclinical disease	Industry records of weekly production data including mortalities, field observations using veterinary and fish health technical reports, diagnosis submissions and test results, treatment(s) used to control disease	Evaluated case definition using veterinary expert opinion as reference standard; epidemiological unit can change the criteria for a case definition (individual vs pen or more of various disease states together)		Boerlage et al. 2017 J fish dis 40:395-409
4	CDWG, AGPHL	Yes and no	AUS	Zoonotic and human, communicable	Surveillance for nationally reported disease	Laboratory, clinical, and epidemiological	Includes laboratory suggestive evidence for probable	No negative	www1.health.gov.au

						components as appropriate			
5.	DHM	Yes	US	Dairy	Understanding case definition, recording methods and benchmarking between herds	Epidemiological unit, clinical signs and target organs, veterinary opinion, diagnostic tests	Producers may record levels and clinical signs differently and based on differential diagnosis criteria	Opinion piece	Herd Health: making a case for case definitions by Mark Thomas. 2014 Dairy Herd Management
6	FAO	Yes and no	UN	Aquatic	Surveillance and design of surveillance; outbreak	Infection characteristics (disease state), local environmental factors influencing virulence, related human activities, and reliability (specificity/sensitivity) of available diagnostic tools (field information, laboratory techniques, experimental techniques (see their table 2)	"A useful approach to development of a case definition is given by Stephen and Ribble (1996)." Surveillance objective can dictate the specificity or sensitivity of the case definition: Outbreak: "Define a "case" (surveillance for exotic pathogen(s) = most sensitive definition; monitoring of endemic infections = acceptable level of infection/mortality level definition)."		FAO Fisheries Technical Paper 451: surveillance and zoning for aquatic animal diseases, 2004
7	CDC	Yes and no	US	Human	Infectious conditions under public health surveillance; nationally notifiable reportable disease	Clinical, laboratory, epidemiology (all 3 can differ dependent on syndrome or disease depending on purpose, if it is notifiable, etc)) Outbreak: clinical and confirmatory laboratory tests and criteria also include person, place, time, clinical features	1990: CDC published case definition for uniform criteria for reporting cases; "Substantial amounts of information, including results of laboratory tests, must be collected for many diseases before a final case classification is possible. State health departments should continue prompt	"The case definitions contained in this report establish uniform criteria for disease reporting and should not be used as the sole criteria for establishing clinical diagnoses, determining	1997 MMWR CDC report 46(RR10):1-55; Principles of Epidemiology in Public Health Practice 3rd ed., an introduction to applied epidemiolog

						(these should be specific to the outbreak under investigation) Clinical criteria should be simple, objective, and discriminating between diseased and not diseased; "Also, case definitions should not include risk factors that you may want to evaluate, since all of the cases would have the risk factor, and this would be misleading. A case definition is not the same as a clinical diagnosis. Case definitions are an aid to conducting an epidemiologic investigation, whereas a clinical diagnosis is used to make treatment decisions for individual patients." Can change during investigation	reporting of provisional cases to CDC, and records should be updated with the appropriate classification status when additional surveillance information becomes available. Cases should be categorized as laboratory-confirmed (a subset of all confirmed cases) only if they meet the laboratory criteria specified." Confirmed, probable, and possible	the standard of care necessary for a particular patient, setting guidelines for quality assurance, or providing standards for reimbursement. Use of additional clinical, epidemiologic, and laboratory data may enable a physician to diagnose a disease even though the formal surveillance case definition may not be met…. These case definitions are to be used for identifying and classifying cases, both of which are often done retrospectively, for national reporting purposes. They should not be used as criteria for public health action. For many conditions of public health importance, action to contain disease	y and biostatistics Lesson 1, section 5: the epidemiologic approach 2012 Outbreak Investigations: Step 3 Establish a Case Definition; Identify Cases

								should be initiated as soon as a problem is identified; in many circumstances, appropriate public health action should be undertaken even though insufficient information is available to determine whether cases meet the case definition."	
8	Not appllicable	No		Johne's disease	Different purposes (incidence, frequency distributions) and consistent classification of individual in a population	Purpose! for test-classification: dependent on test and whether test used in series or parallel; linked to pathogenesis; diagnostic tests, genetics/genomics; vaccine (especially post)	Descriptive terms for case classification are stage of the disease dependent	"Herd-level case definitions can be developed from those applied to individual animals but are not dealt with in this paper. " "However, the stringency with which a case definition can be met will differ between studies according to resources and other practical considerations, and the accuracy of animal classification (i.e. the sensitivity and specificity) will	Whittington et al 2017 BMC Vet Res 13:328

								also vary. For this reason, it is important that guidance be provided to enable self-assessment or indeed an independent assessment of the extent to which case definitions are met in any given study. “	
9	CFIA	No	Canada	Poultry, etc	Control and eradication, outbreak; OIE reporting requirements	Clinical signs or post-mortem (confirmed by veterinarian, owner, pathologist, veterinarian-in charge in collaboration with the area food-animal-disease program officer); diagnostic tests, epidemiology (contact, mortality)	Adopted OIE definitions	“The disease control activities related to the case definition may evolve in the course of an outbreak” no negatives	Authorities and Principles of Control (part of guidance document repository) 2014
10	OIE	No	International	Terrestrial, aquatic	Surveillance	Epidemiological unit and clustering and purpose is important, diagnostic tests	“Where one exists, the *case* definition in the relevant chapter of the *Terrestrial Code* should be used. If the *Terrestrial Code* does not give a *case* definition, a *case* should be defined using clear criteria for each *infection* or *infestation* under *surveillance*. For *wildlife infection* or *infestation surveillance*, it is essential to correctly identify and report host animal taxonomy, including genus and species.”		OIE 2019 Terrestrial Animal Health Code chap 1.4 Animal Health Surveillance

11	ECDC	Yes	Europe	Human	Outbreak	Time limit, place limit, person limit Also consider travel history or specific population characteristics (age group, gender, risk population) Sub-typing to differentiate strains or sub-types	Sensitive and specific purposes; Confirmed, probable, possible: these make up multiple case definitions per disease	Some investigations differ case definition depending on descriptive vs analytical epidemiology	ECDC toolbox for FWD outbreak investigations tool 3.3: Case definitions Ecdc.europa.eu 2020
12		Yes	Germany	Human	Public health surveillance	Clinical picture, laboratory detection, epidemiological confirmation Five classes: clinically diagnosed illness (no epidemiological or laboratory), clinically and epidemiologically confirmed illness (no laboratory), clinically and laboratory confirmed illness, laboratory detected infection not fulfilling clinical criteria, laboratory detected infection with unknown clinical picture	Checklist (yes/no) format had a higher reporting precision than those with a narrative description; use of a glossary; only include relevant criteria and clearly mark all additional explanatory information separately	Lacking a satisfactory reference standard can make case definition optimization difficult	Krause et al., 2006 BMC Public Health 6:129
13		Yes		Human	Diagnosis	Risk factors, Clinical, Diagnostic	Looking at diagnoses as a classification method of groups of people whose illnesses share the same causes or prognosis or response to treatment, for preventing or managing illness rather than as a disease label to improve	Issues if no reference standard	Coggon et al. 2005 Int J Epi 34:949-952

							issues with competing case definitions Optimal case definition can vary dependent on circumstances		
14	Not applicable	No	Europe	Human, Plague	Diagnosis and bioterrorism	Clinical, presumptive, diagnosis Possible, probable, confirmed Deliberate release Criteria			Bossi et al. 2005 Eurosurveillance 9(12)
15	Florida Dept of Health Bureau of Epi	Yes and no	US	Human	Reportable diseases, surveillance	Clinical, laboratory, epidemiological	Differ, some do not have confirmatory diagnosis, some have laboratory evidence part of clinical definition, some have laboratory confirmation regardless of clinical signs, some based on epidemiology alone Final case classification at state level and dependent on much information		FDH Surveillance Case definitions for select reportable diseases in Florida Version1.2 2008
16	Not applicable	Yes		Dairy, mastitis	Clinical diagnsosis	Cow-level	Simple, easy to understand by farm personnel; 3-point scale based on clinical signs (mild, moderate, severe) for practicality If severe cases >5% to 20% then it is an alert to investigate detection intensity and case definition	Rates of clinical mastitis vary a lot due to missing clinical signs and difference in detection intensity and case definition	Ruegg 2012 Mastitis in Dairy Cows, Vet Clin Food Anim Prac, p154-156

17	WHO	Yes	International	Human	Outbreak	Clinical and laboratory Defined period of time Restriction of place Restriction of person Case definition sensitivity and specificity	Working case definition when start investigating a potential outbreak		Foodborne Disease Outbreaks: Guidelines for Investigation and Control WHO book, p14-26
18	BCCDC	No	Canada	human	Define a disease	Varying dependent of disease specifics			Bccdc.ca case definition page

*yes = development process, guidelines, etc.; no = just a single use case definition for a particular disease/purpose, etc.

ADDITIONAL CRITERIA INFORMATION FOR SPECIFIC CITATIONS (NUMBER MATCHES TABLE)

1. Unites States Department of Agriculture (USDA)
    a. General disease and pathogen info: etiologic agent, distribution, culture and sensitivity, incubation period, differential diagnosis, transmission and reservoir, epidemiology
    b. Lab
    c. Class: suspect, presumptive positive, confirmed positive
    d. Reporting
    e. Control and surveillance

    Development and approval: after initial draft, each step of review and contact goes through industry then VC units, then state AH official then VS deputy and executive teams

4. Australian case definition working group (AusCDWG): give process for who and what order of people are involved in the development and review of case definition, including when cases should be reported

7. United Stated Centres for Disease Control (CDC):

- *Clinically compatible case*: a clinical syndrome generally compatible with the disease, as described in the clinical description.

- *Confirmed case*: a case that is classified as confirmed for reporting purposes.

- *Epidemiologically linked case*: a case in which a) the patient has had contact with one or more persons who either have/had the disease or have been exposed to a point source of infection (i.e., a single source of infection, such as an event leading to a foodborne-disease outbreak, to which all confirmed case-patients were exposed) and b) transmission of the agent by the usual modes of transmission is plausible. A case may be considered epidemiologically linked to a laboratory-confirmed case if at least one case in the chain of transmission is laboratory confirmed.

- *Laboratory-confirmed case*: a case that is confirmed by one or more of the laboratory methods listed in the case definition under Laboratory Criteria for Diagnosis. Although other laboratory methods can be used in clinical diagnosis, only those listed are accepted as laboratory confirmation for national reporting purposes.

- *Probable case*: a case that is classified as probable for reporting purposes.

- *Supportive or presumptive laboratory results*: specified laboratory results that are consistent with the diagnosis, yet do not meet the criteria for laboratory confirmation.

- *Suspected case*: a case that is classified as suspected for reporting purposes.

- for outbreak cd: “components of an outbreak cd vary for each outbreak!”

- "Person" describes key characteristics the patients share in common. For example, this description may include: age, sex, race, occupation and exclusion criteria (e.g., “persons with no history of X disease”).

- "Place" typically describes a specific geographic location (state, county) or facility associated with the outbreak (X nursing home, Y high school).

- "Time" is used to delineate a period of time associated with illness onset for the cases under investigation. Limiting the time period enables exclusion of similar illnesses which are unrelated to the outbreak of interest.

- Initially, "clinical features" should be simple and objective (e.g., sudden onset of fever and cough). The clinical criteria may later be characterized by the presence of specific laboratory findings.

- “Other case definitions, particularly those used in local outbreak investigations, are often tailored to the local situation. For example, a case definition developed for an outbreak of viral illness might require laboratory confirmation where such laboratory services are available, but likely would not if such services were not readily available.”

- “When everyone uses the same standard case definition and a difference is observed, the difference is likely to be real rather than the result of variation in how cases are classified.”

8. Johne’s dz: exposed, infected (clinical, subclinical), infectious, diseased (clinical, subclinical), resistant/resilient, recovered, susceptible

9. Canadian Food Inspection Agency (CFIA) Newcastle disease (ND) example: confirmed case: virus isolation, but “In circumstances wherein the virus cannot be isolated, infection with an ND virus can be confirmed through a combination of other diagnostic tools if the investigation is associated with a clinical history. This approach will be assessed by National Centre for Foreign Animal Diseases (NCFAD), in consultation with epidemiologists and review of field evidence, on a case-by-case basis.”

10. World Organisation for Animal Health (OIE):

- “The sensitivity and specificity of clinical observations are highly dependent on the criteria used to define a suspected *case*. In order to allow comparison of data, the *case* definition should be standardised. Awareness and training of potential field observers, including *animal* keepers, in the application of the *case* definition and reporting are important. Ideally, both the number of positive observations and the total number of observations should be recorded.”

- epidemiological investigations of suspected *cases* and *cases* conducted by the *Veterinary Services* in order to confirm *cases* and to acquire accurate knowledge of the situation for further action. All suspected *case* investigations should provide a result, either positive or negative. Criteria should be established in advance for a *case* definition. Confirmation can be made on clinical and post-mortem grounds, epidemiological information, laboratory test results or a combination of these, in accordance with relevant articles of the *Terrestrial Code* or *Terrestrial Manual*

17. World Health organization (WHO) outbreak:

- Start with quick assessment: check validity of info, get lab test reports, id cases and get info about then, ensure collection of appropriate clinical specimens and food samples
- Then after this validity of reporting source, get a group 5-10 people of initial cases to get more specific info (epi, lab, clinical, hx)
- See their Figure 2 and Figure 3

PRELIMINARY INFORMATION FOR CONSIDERING CASE CLASSIFICATION FOLLOWING CASE DEFINITION DEVELOPMENT AND IMPLEMENTATION

Classification can be based on the results of the information provided and selected for the previous applicable case definition sections for a subjective classification of the presence of infection. For an objective classification method, different probability methods can be utilized to assist in developing a standardized approach to classifying individuals or population as either negative, suspect case, probable/presumptive case, confirmed positive case.

NEGATIVE/NON-CASE/FREE
No exposure, no infection
Possible exposure and/or possible infection (on differential diagnosis list), after waiting/quarantine time there are either no infection signs and/or negative test results

SUSPECT
Possible exposure and/or possible infection (on differential diagnosis list)

PROBABLE/PRESUMPTIVE
Known or likely exposure and likely infection (on differential diagnosis list) or after waiting/quarantine time there are infection signs, but test (if available) specifications pending

CONFIRMED
Known exposure and infection
Known exposure and infection and positive results on test(s) (if available) and high test specifications

REFERENCES

Begg, C.B. 1987. Biases in the assessment of diagnostic tests. Statistics in Medicine, 6, 411–423.

Branscum A.J., Gardner I.A. & Johnson W.O. (2005) Estimation of diagnostic-test sensitivity and specificity through Bayesian modeling. *Preventive Veterinary Medicine* **68**:145-163.

CDC (Centers for Disease Control and Prevention). Principles of Epidemiology in Public Health Practice, Third Ed.: An Introduction to Applied Epidemiology and Biostatistics: Section 5: The Epidemiologic Approach. www.cdc.gov Accessed 23 May 2020.

Gardner, IA, SS Nielsen, RJ Whittington, MT Collins, D Bakker, B Harris, S Sreevatsan, JE Lombard, R Sweeney, DR Smith, J Gavalchin, S Eda. 2011. Consensus-based reporting standards for diagnostic test accuracy studies for paratuberculosis in ruminants. Preventive Veterinary Medicine 101:18-34.

Gardner, IA, SS Nielsen, RJ Whittington, MT Collins, D Bakker, B Harris, S Sreevatsan, JE Lombard, R Sweeney, DR Smith, J Gavalchin, S Eda. 2011. Consensus-based reporting standards for diagnostic test accuracy studies for paratuberculosis in ruminants. Preventive Veterinary Medicine 101:18-34.

Gardner, IA, RJ Whittington, CGB Caraguel, P Hick, NJG Moody, S Corbeil, KA Garver, JV Warg, I Arzul, MK Purcell, MSJ Crane, TB Waltzek, NJ Olesen, AG Lagno. 2016. Recommended reporting standards for test accuracy studies of infectious diseases of finfish, amphibians, molluscs and crustaceans: the STRADAS-aquatic checklist. Diseases of Aquatic Organisms. 118:91-111.

Hoinville, LJ, L Alban, JA Drewe, JC Gibbens, L Gustafson, B Häsler, V Saegerman, M Salman, KDC Stärk. 2013. Proposed terms and concepts for describing and evaluating animal-health surveillance systems. Preventive Veterinary Medicine 12:1-12.

Kloeze, H, J berezowski, L Bergeron, N de With, G Duizer, C Green, B McNAb, M VanderKop. 2012. A minimum data set of animal health laboratory data to allow for collation and analysis across jurisdictions for the purpose of surveillance. Transboundary and Emerging Diseases. 59:264-268.

Kostoulas P., Nielsen S.S., Branscum A.J., Johnson W.O., Dendukuri N., Dhand N.K., Toft N. & Gardner I.A. (2017) STARD-BLCM: Standards for the reporting of diagnostic accuracy studies that use Bayesian latent class models. Preventive Veterinary Medicine 138, 37-47.

Laurin, E, KK Thakur, IA Gardner, P Hick, NJG Moody, MSJ Crane, I Ernst. 2018. Design standards for experimental and field studies to evaluate diagnostic accuracy of tests for infectious diseases in aquatic animals. Journal of Fish Diseases. 41:729-749.

Laurin, E, K Thakur, PG Mohr, P Hick, MSJ Crane, IA Gardner, NJG Moody, A Colling, I Ernst. 2019. To pool or not to pool? Guidelines for pooling samples for use in surveillance testing of infectious diseases in aquatic animals. Journal of Fish Diseases 42:1471-1491]

O'Connor, AM, JM sergeant, IR Dohoo, HN Erb, M Cevallos, M Egger, AK Ersbøll, SW Martin, LR Nielsen, DL Pearl, DU Pfeiffer, J Sanchez, ME Torrence, H Vigre, C Waldner, MP Ward. 2016. Explanation and elaboration document for the STROBE-Vet Statement: strengthening the reporting of observational studies in epidemiology – veterinary extension. Journal of Veterinary Internal Medicine. 30:1896-1928.

OIE (Office International Epizooties). 2018. Terrestrial Animal Health Code. Chapter 1.4: Animal Health Surveillance.

OIE. 2019. Chapter 1.1.2. Principles and methods of validation of diagnostic assays for infectious Disease, Manual of Diagnostic Tests for Aquatic Animals, available at: https://www.oie.int/index.php?id=2439&L=0&htmfile=chapitre_validation_diagnostics_assays.htm.

Shinkins, B, M Thompson, S Mallett, R Perera. 2013. Diagnostic accuracy studies: how to report and analyse inconclusive test results. BMJ 346:f2778 doi: 10.1136/bmj.f2778].