

24-ID-03

Committee: Infectious Disease

Title: Update to Public Health Reporting and National Notification for Brucellosis

☒ Check this box if this position statement is an update to an existing standardized surveillance case definition and include the most recent position statement number here: 09-ID-14.

Synopsis:

- Overarching Changes:
 - Defines brucellosis-causing *Brucella* spp. (BBS) and differentiates BBS from non-brucellosis-causing *Brucella* spp. (nBBS), including formerly *Ochrobactrum* spp.
 - Modifies clinical and laboratory criteria for case ascertainment and case classification.
 - Updates epidemiologic evidence to capture changing exposure epidemiology.
 - Adds supportive laboratory evidence to capture ELISA IgG for monitoring.
 - Adds Suspect case classification to capture cases that do not have presumptive or confirmatory laboratory evidence or meet clinical criteria.
 - Addresses surveillance enumeration in relation to relapse, reinfection, and delayed convalescence with *Brucella* spp.
- Clinical Evidence Updates
 - Removes fever as a required clinical criterion for cases with BBS cultured and identified from a clinical specimen. Fever remains required if only category 2 confirmatory laboratory evidence or presumptive laboratory evidence criteria are met.
 - Adds 'encephalitis or other neurologic abnormalities' in addition to meningitis, to more fully encompass manifestations of neurobrucellosis.
 - Adds discitis/osteomyelitis for the inclusion of common spinal manifestations of brucellosis. Adds abscess to allow brucellosis manifesting as non-specific localized infection.
- Laboratory Evidence Updates
 - Removes direct detection of *Brucella* in clinical specimens by PCR. This is due to inability to differentiate between active and prior (resolved) *Brucella* infection and a lack of sufficiently validated commercial PCR laboratory tests.
 - Clarifies that *Brucella* isolates must be identified by methods specific for BBS or whole genome sequencing from an isolate to meet confirmatory criteria.
 - Adds detection of *Brucella* IgG antibodies by ELISA as supportive laboratory evidence.

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I. Statement of the Problem

CSTE position statement 09-ID-14 developed a standardized surveillance case definition for brucellosis to facilitate state, tribal, local and territorial (STLT) national reporting. Since 2010, brucellosis epidemiology, laboratory methods, and terminology have changed, impacting current ascertainment and classification of brucellosis cases.

This position statement clarifies which *Brucella* species should be considered as causing brucellosis and are to be included as reportable to STLT public health agencies (PHAs). In 2020, a taxonomic revision reclassified *Ochrobactrum* into the genus *Brucella*. This change had significant implications for clinical practice, public health, and case-based surveillance, as misinterpretation by providers could cause inaccurate diagnoses, negative health outcomes, and reporting of non-brucellosis cases to STLT PHAs. This reclassification impacts laboratory reporting for public health surveillance, as laboratories need guidance to distinguish between brucellosis-causing *Brucella* species (BBS) and non-brucellosis causing *Brucella* species (nBBS) (1,2). Non-brucellosis causing *Brucella* species (nBBS) are excluded from this case definition.

Analysis of clinical and epidemiological data obtained by public health and current literature support updates and expansion of clinical and epidemiologic criteria associated with brucellosis for case reporting and classification. The addition of supportive laboratory criteria and a “suspect” case classification category will provide STLT PHAs a standardized method to monitor cases that do not meet the confirmed or probable case classifications.

II. Background and Justification

Brucellosis is a zoonotic disease caused by certain bacteria in the *Brucella* genus categorized as brucellosis-causing *Brucella* species (BBS). Other species of *Brucella*, including the former *Ochrobactrum* genus, are considered non-brucellosis *Brucella* species (nBBS), as they have not been shown to cause brucellosis disease (2). There are multiple BBS (listed with preferred animal host) known to infect humans, including but not limited to: *B. abortus* (cattle), *B. melitensis* (goats, sheep, camels), *B. suis* (pigs), *B. canis* (dogs), and *B. neotomae* (wood rats). *Brucella abortus*, *B. melitensis*, and *B. suis* cause most cases of brucellosis reported in the United States (U.S.). Although *B. canis* can be transmitted to humans from infected dogs, human infection is uncommon. The *Brucella abortus* cattle vaccine strain RB51 can cause disease in humans, and cases have been linked to consumption of unpasteurized dairy from previously-vaccinated hoofstock (3).

Brucella abortus has been almost completely eradicated from the domestic cattle population of the U.S., though wild animal reservoirs remain a source of infection for domestic livestock and humans. *Brucella suis* is enzootic in feral swine in parts of the U.S.

Persons are exposed to BBS through contact with infected animals or contaminated animal products, often unpasteurized dairy products. Contamination of skin wounds may be a route of infection for persons working in slaughterhouses, meat processing plants, or veterinary practices. Hunters may be infected through skin wounds or by ingesting the bacteria after butchering deer, elk, moose, or wild pigs. Inhalation is not a common infection route but can be a hazard for people working in laboratories where BBS are cultured. Rarely, transmission has occurred via organ transplantation, blood transfusion, sexual contact, breastfeeding, or transplacentally (4,5).

Human brucellosis is rare in the U.S., with 100–150 cases occurring annually; however, brucellosis can be common in countries where animal disease control programs have not reduced the prevalence of BBS among host species. Certain locally-produced cheeses, such as queso fresco or “village cheeses,” may represent a particular risk as they are commonly prepared using unpasteurized cow’s or goat’s milk.

Initial symptoms of brucellosis can include fever, night sweats, malaise, headache, anorexia, myalgia, and arthralgias. While fever remains a common symptom, a review of recent U.S. brucellosis cases showed that it was absent from a quarter of culture-confirmed cases.

Some symptoms may persist, including recurrent fevers, arthritis, spondylitis, orchitis/epididymitis, endocarditis, chronic fatigue, and hepatomegaly and/or splenomegaly. Severe complications occur in a small number of cases, including neurobrucellosis (6). Neurobrucellosis poses a diagnostic challenge for healthcare providers because of

its range of associated signs and symptoms, such as behavioral changes, disorientation, cranial nerve involvement, polyneuropathy/radiculopathy, depression, paresthesia, and/or stroke (7,8).

Brucellosis can be a challenge to diagnose as the performance of serology and culture-based tests vary depending on the stage of disease and corresponding antibody profiles that change throughout disease progression. Agglutination-based serology tests are ideal for diagnosing acute, non-complicated brucellosis when serum samples are collected within four weeks of onset. Detection of IgG antibodies by ELISA tests at commercial laboratories can provide evidence of disease with supporting clinical and epidemiological criteria. The gold standard remains obtaining a bacterial culture from biological specimens. Blood culture positivity ranges from 20% to 80%, often characterized by very low levels of bacteremia (9). This low bacteremia makes PCR detection of *Brucella* from clinical specimens unreliable. Bacterial isolates must be speciated as BBS using a validated method for reporting purposes*.

Without appropriate treatment, acute brucellosis can progress to chronic manifestations. Disease relapse is not uncommon, even after the completion of antimicrobial therapy; reinfections also occur. Brucellosis may rarely cause death, which is usually associated with endocarditis.

*See Appendix A for additional information regarding brucellosis laboratory criteria.

III. Statement of the Desired Action(s) to be Taken

CSTE recommends the following actions:

1. Implement a standardized surveillance case definition for **brucellosis**.
 - A. Utilize recommended reporting* sources for case ascertainment for **brucellosis**. Surveillance for **brucellosis** should use the recommended sources of data to the extent of coverage presented in Section V.
 - B. Utilize standardized criteria for case ascertainment for **brucellosis** presented in Section VI and Table VI in Technical Supplement.
 - C. Utilize standardized criteria for case classification for **brucellosis** presented in Section VII and Table VII in Technical Supplement.
2. Utilize standardized criteria for case ascertainment and classification (based on Sections VI and VII and Technical Supplement) for **brucellosis** and **update** brucellosis on the *Nationally Notifiable Condition List* using the following notification** timeframe:
 - ☐ Immediately notifiable, extremely urgent (within 4 hours)
 - ☒ Immediately notifiable, urgent (within 24 hours)
 - ☐ Routinely notifiable
 - ☐ No longer notifiable
3. CSTE recommends that all States and Territories enact laws (statute or rule/regulation as appropriate) to make this disease or condition reportable in their jurisdiction. Jurisdictions (e.g., States and Territories) conducting surveillance (according to these methods) should submit case notifications to CDC.
4. CSTE recommends that all jurisdictions (e.g., States, Localities, or Territories) with legal authority should conduct public health surveillance and use the case classifications included in this standardized surveillance position statement.
5. Expectations for Message Mapping Guide (MMG) development for a newly notifiable condition: the National Notifiable Diseases Surveillance System (NNDSS) is transitioning to HL7-based messages for case notifications; the specifications for these messages are presented in MMGs. When CSTE recommends a new condition be made nationally notifiable, CDC must obtain Office of Management and Budget Paperwork Reduction Act (OMB PRA) approval prior to accepting case notifications for the new

condition. Under anticipated timelines, notification using the Generic V2 MMG would support transmission of the basic demographic and epidemiologic information common to all cases and could begin with the new MMWR year following the CSTE annual conference. Input from CDC programs and CSTE would prioritize development of a disease-specific MMG for the new condition among other conditions waiting for MMGs.

6. CDC should publish data on brucellosis as appropriate (see Section IX). CSTE recommends the following case statuses be included in the CDC Print Criteria:

- ☒ Confirmed
- ☒ Probable
- ☐ Suspect
- ☐ Unknown

** Reporting: process of a healthcare provider, laboratory, or other entity submitting a report (case information) of a condition under public health surveillance to local, state, or territorial public health.*

*** Notification is the process of a local, state, or territorial public health authority submitting a report (case information) of a condition on the Nationally Notifiable Conditions List to CDC.*

IV. Goals of Surveillance

The goals of surveillance are to collect and disseminate information on the temporal, geographic, and demographic occurrence of brucellosis to facilitate its prevention and control.

V. Recommended Data Sources and Methods for Surveillance

Surveillance for brucellosis should use the following recommended sources of data and/or methodologies and the extent of coverage listed in Table V.

Table V. Recommended Sources of Data, Surveillance Methods, and Extent of Coverage for Ascertainment of Cases of Brucellosis.

Source of Data/Methodology for Case Ascertainment	Coverage	
	Population-Wide	Sentinel Sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities, specify: <ul style="list-style-type: none"> • Hospitals • Pharmacies • Poison control centers • Blood banks 	X	
Death certificates	X	
Hospital discharge or outpatient records	X	
Data from electronic medical records	X	
Telephone or online survey		
School-based survey		
Other, specify: N/A		

VI. Criteria for Case Ascertainment

Case ascertainment is the process through which public health identifies potential cases of a disease or condition using data reported or provided to public health by healthcare, laboratories, and other reporting entities. This public health reporting is triggered by the case ascertainment criteria (a single criterion or a combination of criteria) included in this position statement, and each initial report sent to public health should include common data elements and disease-specific data elements. Case ascertainment criteria are not intended to be used for clinical diagnosis purposes.

A. Narrative: A description of suggested criteria for case ascertainment of a specific condition and recommended reporting procedures.

Requirements for reporting are established under state and territorial laws and/or regulations and may differ between jurisdictions. These criteria are suggested as a standard approach to identifying cases of this condition for purposes of reporting, but reporting should follow state and territorial law/regulation if these criteria conflict with those laws/regulations.

Report any illness to public health authorities that meets any of the following criteria:

- A person meeting laboratory criteria for reporting.
- A person meeting clinical criteria for reporting AND epidemiologic linkage criteria for reporting.
- A person meeting the vital records criteria for reporting.
- A person meeting the healthcare record criteria for reporting.

A1. Clinical Criteria for Reporting*

- Acute or insidious onset of fever,
AND
- Two or more of the following signs and symptoms:
 - Night sweats
 - Arthralgia
 - Headache
 - Fatigue
 - Anorexia
 - Myalgia
 - Weight loss
 - Arthritis
 - Spondylitis
 - Meningitis, encephalitis, or other neurologic abnormalities
 - Discitis or osteomyelitis
 - Abscesses
 - Focal organ involvement (including, but not limited to: endocarditis, orchitis/epididymitis, hepatomegaly, splenomegaly).

**Clinical criteria must be paired with epidemiologic linkage criteria for reporting to trigger a report to public health.*

A2. Laboratory Criteria for Reporting**

- Culture and identification of a presumptive *Brucella* spp. from clinical specimens,
OR
- Evidence of a fourfold or greater rise in *Brucella* antibody titer between acute- and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart,
OR
- *Brucella* total antibody titer $\geq 1:160$ by standard tube agglutination (SAT) or *Brucella* microagglutination test in one or more serum samples obtained after onset of symptoms,
OR
- Detection of *Brucella* IgG antibodies by ELISA in a sample collected at least 2 weeks after onset of symptoms.

***See Appendix A for additional information regarding brucellosis laboratory criteria.*

[continued]

A3. Epidemiologic Linkage Criteria for Reporting***

- Direct contact with body fluids or tissue from a confirmed human case of brucellosis,
OR
- Veterinary occupational exposure to *Brucella* vaccine (i.e., needle stick, mucous membrane exposure),
OR
- Laboratory exposure to Brucellosis-causing *Brucella* species (BBS),
OR
- Direct contact to an animal diagnosed with a *Brucella* infection (or their fluids), as determined by a state or federal animal health official, including potential aerosol exposure,
OR
- Shared one of the following exposures with a confirmed human case of brucellosis:
 - Consumption of dairy products from a common source that were unpasteurized or of unknown pasteurization, particularly from countries lacking domestic animal health programs, OR
 - Consumption or handling of undercooked meat or carcass of an animal from a herd or of a species with a known or suspected history of *Brucella*, OR
 - Slaughtering, dressing, butchering, or having other direct contact with animals or animal tissues possibly infected with *Brucella*.

****Epidemiologic linkage criteria must be paired with clinical criteria for reporting to trigger a report to public health.*

A4. Vital Records Criteria for Reporting

A person whose death certificate lists brucellosis as a cause of death or a significant condition contributing to death.

A5. Healthcare Record Criteria for Reporting

A person whose healthcare record contains a diagnosis of brucellosis.

B. Disease-Specific Data Elements to be Included in the Initial Report

Disease-specific data elements should be included in addition to the common data elements that are to be reported for all initial individual case reports (see CSTE Position Statement 09-SI-01 “Common Core Data Elements for Case Reporting and Laboratory Result Reporting” <https://cdn.ymaws.com/www.cste.org/resource/resmgr/PS/09-SI-01.pdf>). Public health authorities do not expect that an initial report will contain all the information necessary for case investigation and case classification.

Risk Factors:

- Contact with animal or animal products:
 - Animal species
 - Exposure type (hunting, skinning, contact with birthing animal)
 - Product type
 - Exposure date
- Consumption of unpasteurized dairy (milk or milk products)
 - Animal species
 - Product type
 - Date(s) of consumption
 - Location where product was purchased or acquired
- Travel information
 - Date(s) of travel
 - Location(s) of travel

[continued]

Occupational Risk Factors

- Veterinarian/animal technician/taxidermists/meat processors or any individual having other direct contact with the carcass, tissues, or fluids from a wild or domestic animal of a known *Brucella* reservoir species.
- *Brucella* vaccine exposure
 - Vaccine type (S19, RB51, Rev1)
 - PEP received; with what antimicrobials
- Microbiological laboratory work
 - Exposure source (specimen, isolate)
 - PEP received; with what antimicrobials

VII. Case Definition for Case Classification

This case definition for case classification is intended solely for public health surveillance purposes and does not recommend criteria for clinical diagnosis purposes. Once a public health agency has ascertained data on potential cases of a disease or condition from reporting entities, the public health agency assigns case statuses based on the case classifications included within this position statement.

A. Narrative: A description of criteria to determine how public health should classify a case of brucellosis.**A1. Clinical Criteria**

- An illness characterized by acute or insidious onset of fever,
AND
- Two or more of the following signs and symptoms:
 - Night sweats
 - Arthralgia
 - Headache
 - Fatigue
 - Anorexia
 - Myalgia
 - Weight loss
 - Arthritis
 - Spondylitis
 - Meningitis, encephalitis, or other neurologic abnormalities
 - Discitis or osteomyelitis
 - Abscesses
 - Focal organ involvement (including, but not limited to: endocarditis, orchitis/epididymitis, hepatomegaly, splenomegaly).

A2. Laboratory Criteria****Confirmatory Laboratory Evidence:****Category 1:**

- Identification of a *Brucella* isolate as a brucellosis-causing *Brucella* species (BBS) by methods specific for BBS (i.e., PCR assay with documented specificity for BBS and/or biochemical tests and/or whole genome sequencing of *Brucella* isolate).

Category 2:

- Evidence of fourfold or greater rise in *Brucella* antibody titer between acute and convalescent serum specimens obtained at least 2 weeks apart.***

Presumptive Laboratory Evidence:

- *Brucella* total antibody titer $\geq 1:160$ by standard tube agglutination (SAT) or *Brucella* microagglutination test in one or more serum samples obtained after onset of symptoms.

Supportive Laboratory Evidence:

- Detection of *Brucella* IgG antibodies by ELISA in a sample collected at least 2 weeks after onset of symptoms.

** Note: The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.*

*** See Appendix A for additional information regarding brucellosis laboratory criteria.*

**** To ensure consistency with laboratory methodologies, it is recommended that paired sera testing for the purposes of confirmatory classification be conducted within the same laboratory.*

A3. Epidemiologic Linkage Criteria

- Direct contact with body fluids or tissue from a confirmed human case of brucellosis,
OR
- Veterinary occupational exposure to *Brucella* vaccine (i.e., needle stick, mucous membrane exposure),
OR
- Laboratory exposure to Brucellosis-causing *Brucella* species (BBS),
OR
- Direct contact to an animal diagnosed with a *Brucella* infection (or their fluids), as determined by a state or federal animal health official, including potential aerosol exposure,
OR
- Shared one of the following exposures with a confirmed human case of brucellosis:
 - Consumption of dairy products from a common source that were unpasteurized or of unknown pasteurization, particularly from countries lacking domestic animal health programs, OR
 - Consumption or handling of undercooked meat or carcass of an animal from a herd or of a species with a known or suspected history of *Brucella*, OR
 - Slaughtering, dressing, butchering, or having other direct contact with animals or animal tissues possibly infected with *Brucella*.

A4. Vital Records Criteria

- Death certificate lists brucellosis as a cause of death or a significant condition contributing to death.

A5. Case Classifications**Confirmed:**

- Meets confirmatory laboratory evidence category 1, OR
- Meets clinical criteria AND confirmatory laboratory evidence category 2.

Probable:

- Meets clinical criteria AND presumptive laboratory evidence, OR
- Meets clinical criteria AND meets epidemiologic linkage criteria.

Suspect:

- Meets confirmatory laboratory evidence category 2, OR
- Meets presumptive laboratory evidence, OR
- Meets supportive laboratory evidence, OR
- Meets vital records criteria.

[continued]

B. Criteria to Distinguish a New Case of Brucellosis from Reports or Notifications which Should Not be Enumerated as a New Case for Surveillance

Public health authorities should enumerate new cases of brucellosis in the following instances:

- A person should be enumerated as a case if not previously enumerated as a case,
OR
- A person who was previously enumerated as a confirmed or probable case that meets confirmatory laboratory evidence category 1, AND has an event date at least twelve months after completion of adequate antimicrobial therapy, AND has new or ongoing risk factors for brucellosis exposure**,
OR
- A person who was previously enumerated as a confirmed or probable case that meets confirmatory laboratory evidence category 1 AND determined to be infected with a different Brucellosis-causing *Brucella* species (BBS) or strain than prior infection.

A person should not be enumerated as a new case if previously enumerated as a case AND there is evidence the new report is due to one of the following: brucellosis relapse, chronic infection, or delayed convalescence.**

***Refer to Appendix B for more information regarding brucellosis case enumeration.*

VIII. Period of Surveillance

Surveillance should be ongoing.

IX. Data Sharing/Release and Print Criteria

CSTE recommends the following case statuses* be included in the 'case' count released outside of the public health agency:

- ☒ Confirmed
- ☒ Probable
- ☐ Suspect
- ☐ Unknown

**Which case statuses are included in case counts constitute the "print criteria."*

Jurisdictions (e.g., States and Territories) conducting surveillance under this case definition can voluntarily submit de-identified case information to CDC, if requested and in a mutually agreed upon format.

Production of national data summaries and national data re-release for non-NNCs:

- Prior to release of national data summaries CDC should follow the CDC/ATSDR Policy on Releasing & Sharing Data, issued on April 16, 2003 and referenced in 11-SI-01 and custodians of such data should consult the CDC-CSTE Intergovernmental Data Release Guidelines Working Group report (www.cste2.org/webpdfs/drgwgreport.pdf) which contains data release guidelines and procedures for CDC programs re-releasing state, local, or territorial-provided data.
- CDC programs have a responsibility, in collaboration with states, localities, and territories, to ensure that CDC program-specific data re-release procedures meet the needs of those responsible for protecting data in the states and territories.

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X. Revision History

Position Statement ID	Section of Document	Revision Description
24-ID-04	Section I	Background on taxonomic change, summary of changes/updates within position statement in the laboratory, clinical, and case classification.
24-ID-04	Section II	Incorporation of taxonomic change for <i>Brucella</i> , discusses updated epidemiology of <i>Brucella</i> , risk factors, addition of signs/symptoms, chronic disease, and terminology.
24-ID-04	Section V	Added poison control centers and blood banks as reporting entities.
24-ID-04	Section VI	Modified reporting criteria narrative: 1) Clinical criteria not required for laboratory criteria for reporting; Removed other recommended reporting procedures.
24-ID-04	Section VI, A1	Added encephalitis or other neurologic abnormalities to meningitis, added discitis/osteomyelitis, and abscess to clinical criteria.
24-ID-04	Section VI, A2	<ul style="list-style-type: none"> Added Detection of <i>Brucella</i> IgG antibodies by ELISA in a sample collected at least 2 weeks after onset of symptoms. Removed detection of <i>Brucella</i> DNA in a clinical specimen by PCR assay.
24-ID-04	Section VI, A3	<ul style="list-style-type: none"> Added language to clarify some of the epidemiologic criteria. Added unknown pasteurization and clarified highest risk was from countries lacking domestic animal health programs. Separated dairy products from meat products. Added direct contact with animals or animal tissues to involvement with animal processing. Incorporated direct contact with body fluids or tissue from a confirmed human case of brucellosis, including potential aerosol exposure. Added criterion for veterinary occupational exposure to <i>Brucella</i> vaccine. Removed "Direct or indirect exposure to an environment or food products that were linked to a confirmed case of brucellosis."
24-ID-04	Section VI, B	Added categories under: Veterinarian/animal technician/taxidermists/meat processors or any individual having other direct contact with the carcass, tissues, or fluids from a wild or domestic animal of a known <i>Brucella</i> reservoir species.
24-ID-04	Section VII, A1	Added encephalitis or other neurologic abnormalities to meningitis, added discitis/osteomyelitis, and abscess to clinical criteria
24-ID-04	Section VII, A2	<ul style="list-style-type: none"> Clarified language for BBS: Identification of a clinical <i>Brucella</i> isolate as a brucellosis causing <i>Brucella</i> species (BBS) by methods specific for BBS (i.e. PCR assay with documented specificity for BBS and/or biochemical tests and/or whole genome sequencing of <i>Brucella</i> isolate) Added Supportive Laboratory Evidence: "Detection of <i>Brucella</i> IgG antibodies by ELISA in a sample collected at least 2 weeks after onset of symptoms". Removed Detection of <i>Brucella</i> DNA in a clinical specimen by PCR assay
24-ID-04	Section VII, A3	<ul style="list-style-type: none"> Added language to clarify some of the epidemiologic criteria. Added unknown pasteurization and clarified highest risk was from areas lacking domestic animal health programs. Separated dairy products from meat products. Added direct contact with animals or animal tissues to involvement with animal processing. Incorporated direct contact with body fluids or tissue from a confirmed human case of brucellosis, including potential aerosol exposure. Added criterion for veterinary occupational exposure to <i>Brucella</i> vaccine. Removed "Direct or indirect exposure to an environment or food products that were linked to a confirmed case of brucellosis."
24-ID-04	Section VII, A5	<ul style="list-style-type: none"> Removes clinical criteria as a requirement for confirmatory classification with culture or isolate of BBS (category 1). Addition of a Suspect case classification to capture non-culture laboratory criteria with no or insufficient clinical information, supportive laboratory evidence with or

		without clinical symptoms, or vital records criteria with no or insufficient clinical information
24-ID-04	Section VII, B	Updated criteria for identifying new cases for surveillance purposes.
12-ID-03	Case Definition	Enhanced laboratory capability and public health reporting for <i>Brucella canis</i> infections: Recommended etiologic species be reported, development of reliable assay for <i>B. canis</i> in humans, and information regarding <i>B. canis</i> infections in humans.
09-ID-14	Position to be adopted	Public Health Reporting and National Notification for Brucellosis, adds Brucellosis to Nationally Notifiable Disease List
N/A	Case Definition	1997 Case Definition, 1990 MMWR Case Definitions for Public Health Surveillance
N/A	Case Definition	1990 Case Definition, 1990 MMWR Case Definitions for Public Health Surveillance

XI. References

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Table VI. Table of criteria to determine whether a case should be reported to public health authorities.

Criterion		Brucellosis		
Clinical Criteria for Reporting				
Acute or insidious onset of fever			N	N
Two or more of the following: <ul style="list-style-type: none">• Night Sweats• Arthralgia• Headache• Fatigue• Anorexia• Myalgia• Weight loss• Arthritis• Spondylitis• Meningitis, encephalitis, or other neurologic abnormalities• Discitis or osteomyelitis• Abscesses• Focal organ involvement (including, but not limited to: endocarditis, orchitis/epididymitis, hepatomegaly, splenomegaly)			N	N
Laboratory Criteria for Reporting*				
Culture and identification of a presumptive <i>Brucella</i> spp. from clinical specimens		S		
Evidence of fourfold or greater rise in <i>Brucella</i> antibody titer between acute- and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart		S		
<i>Brucella</i> total antibody titer ≥1:160 by standard tube agglutination (SAT) or <i>Brucella</i> microagglutination test in one or more serum samples obtained after onset of symptoms		S		
Detection of <i>Brucella</i> IgG antibodies by ELISA in a sample collected at least 2 weeks after onset of symptoms		S		
Epidemiologic Linkage Criteria for Reporting				
Direct contact with body fluids or tissue from a confirmed human case of brucellosis			O	
Veterinary occupational exposure to <i>Brucella</i> vaccine (i.e., needle stick, mucous membrane exposure)			O	
Laboratory exposure to Brucellosis-causing <i>Brucella</i> species (BBS)			O	
Direct contact to an animal diagnosed with a <i>Brucella</i> infection (or their fluids), as determined by a state or federal animal health official, including potential aerosol exposure			O	
Shared an exposure with a confirmed human case of brucellosis				N
Consumption of dairy products from a common source that were unpasteurized or of unknown pasteurization, particularly from countries lacking domestic animal health programs				O
Consumption or handling of undercooked meat or carcass of an animal from a herd or of a species with a known or suspected history of <i>Brucella</i>				O
Slaughtering, dressing, butchering, or having other direct contact with animals or animal tissues possibly infected with <i>Brucella</i>				O
Vital Record Criteria for Reporting				
A person whose death certificate lists brucellosis as a cause of death or a significant condition contributing to death		S		
Healthcare Record Criteria for Reporting				
A person whose healthcare record contains a diagnosis of brucellosis		S		

Notes:

S = This criterion alone is SUFFICIENT to report a case.

N = All "N" criteria in the same column are NECESSARY to report a case.

O = At least one of these "O" (ONE OR MORE) criteria in each category (categories=clinical, laboratory, epidemiologic linkage, vital records, etc.) in the same column—in conjunction with all "N" criteria in the same column—is required to report a case.

* See Appendix A for additional information regarding brucellosis laboratory criteria

Table VII.A. Classification Table: Criteria for defining a case of Brucellosis.

Criterion	Confirmed	Probable	Suspect
Clinical Criteria			
Acute or insidious onset of fever	N	N	N
Two or more of the following: <ul style="list-style-type: none"> Night Sweats Arthralgia Headache Fatigue Anorexia Myalgia Weight loss Arthritis Spondylitis Meningitis, encephalitis, or other neurologic abnormalities Discitis/osteomyelitis Abscesses Focal organ involvement (including, but not limited to: endocarditis, orchitis/epididymitis, hepatomegaly, splenomegaly) 	N	N	N
Laboratory Criteria*			
Identification of a <i>Brucella</i> isolate as a brucellosis-causing <i>Brucella</i> species (BBS) by methods specific for BBS (i.e., PCR assay with documented specificity for BBS and/or biochemical tests and/or whole genome sequencing of <i>Brucella</i> isolate)	S		
Evidence of fourfold or greater rise in <i>Brucella</i> antibody titer between acute and convalescent serum specimens obtained at least 2 weeks apart**	N		S
<i>Brucella</i> total antibody titer $\geq 1:160$ by standard tube agglutination (SAT) or <i>Brucella</i> microagglutination test in one or more serum samples obtained after onset of symptoms		N	S
Detection of <i>Brucella</i> IgG antibodies by ELISA in a sample collected at least 2 weeks after onset of symptoms			S
Epidemiologic Linkage Criteria			
Direct contact with body fluids or tissue from a confirmed human case of brucellosis		O	
Veterinary occupational exposure to <i>Brucella</i> vaccine (i.e., needle stick, mucous membrane exposure)		O	
Laboratory exposure to Brucellosis-causing <i>Brucella</i> species (BBS)		O	
Direct contact to an animal diagnosed with a <i>Brucella</i> infection (or their fluids), as determined by a state or federal animal health official, including potential aerosol exposure		O	
Shared an exposure with a confirmed human case of brucellosis		N	
Consumption of dairy products from a common source that were unpasteurized or of unknown pasteurization, particularly from countries lacking domestic animal health programs		O	
Consumption or handling of undercooked meat or carcass of an animal from a herd or of a species with a known or suspected history of <i>Brucella</i>		O	
Slaughtering, dressing, butchering, or having other direct contact with animals or animal tissues possibly infected with <i>Brucella</i>		O	
Vital Record Criteria			
Death certificate lists brucellosis as a cause of death or a significant condition contributing to death			S

Notes:

S = This criterion alone is SUFFICIENT to classify a case.

N = All "N" criteria in the same column are NECESSARY to classify a case.

O = At least one of these "O" (ONE OR MORE) criteria in each category (categories=clinical evidence, laboratory evidence, and epidemiologic evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to classify a case.

* See Appendix A for additional information regarding brucellosis laboratory criteria.

**To ensure consistency with laboratory methodologies, it is recommended that paired sera testing for the purposes of confirmatory classification be conducted within the same laboratory.

Table VII.B. Classification Table: Criteria to distinguish a new case of Brucellosis from reports or notifications which should not be enumerated as a new case for surveillance.

Criterion	Confirmed	Probable	Suspect
<i>Criteria to distinguish a new case</i>			
A person should be enumerated as a case if not previously enumerated as a case.	S	S	S
A person who was previously enumerated as a confirmed or probable case that meets confirmatory laboratory evidence category 1, AND an event date at least twelve months after completion of adequate antimicrobial therapy, AND has new or ongoing risk factors for brucellosis exposure**	S		
A person who was previously enumerated as a confirmed or probable case that meets confirmatory laboratory evidence category 1 AND determined to be infected with a different Brucellosis-causing <i>Brucella</i> species (BBS) or strain than prior infection.	S		

Notes:

S = This criterion alone is SUFFICIENT to enumerate as a new case.

**Refer to Appendix B for more information regarding brucellosis case enumeration.

APPENDIX A: Impact of taxonomic changes to *Brucella* genus on interpretation of brucellosis diagnostic assays

Correct diagnosis of brucellosis is crucial, especially when related to public health investigation and response. Laboratory diagnosis of brucellosis is complex, with culture and serologic methodologies as the primary tools for diagnosis. In the past 15 years, the global epidemiology of the *Brucella* genus has significantly changed. Several novel *Brucella* species with zoonotic potential have been identified in wildlife reservoirs including marine mammals, amphibians, rodents, and bats. In 2020, all *Ochrobactrum* species were taxonomically renamed into the *Brucella* genus, creating challenges for clinical laboratories to adequately differentiate between Brucellosis-causing *Brucella* species (BBS) and non-Brucellosis causing *Brucella* species (nBBS).

Due to biosafety concerns with handling *Brucella* species, most *Brucella* isolates cultured from clinical specimens are identified using the Laboratory Response Network (LRN) *Brucella* PCR, which is specific for BBS. Isolates can be further confirmed to the species level at the state or national reference laboratory levels using the LRN testing algorithm, the other assay that demonstrates specificity for BBS, or by whole genome sequence analysis against a comprehensive database of *Brucella* species genomes. At this time, there are no known commercially available, validated PCR tests that can differentiate BBS and nBBS. This is a known diagnostic limitation that deserves attention.

Direct detection of *Brucella* from clinical specimens is not recommended for diagnostic purposes due to concerns about prolonged positive molecular tests in fully recovered patients or “DNAemia” and false-negative PCR results due to low bacterial concentration in clinical specimens that may be below the limit of detection of the assay. Similarly, metagenomic tests, such as the Karius test, are becoming more available but should be considered with caution as a diagnostic tool for brucellosis as they have not been extensively validated for all infection types against gold standard diagnostic methods.

Due to the recent taxonomic changes in the *Brucella* genus, databases of automated mass-spectrometry and rapid microbial identification systems have aligned their reference libraries with current naming conventions leading to ambiguous *Brucella* identifications that do not distinguish between BBS and nBBS species and/or can misidentify BBS as nBBS due to a lack of specificity in the testing modality.

Serology, in addition to culture, is the most reliable method of diagnosing acute, non-complicated brucellosis cases. In the U.S., ELISA and agglutination tests are offered by most commercial laboratories, and the CDC conducts the *Brucella* micro-agglutination test. Clinical consultations are recommended for complicated, chronic, or relapse brucellosis cases in order to best interpret antibody profiles and clinical presentation.

Table of Currently Recognized *Brucella* Species*:

Brucellosis Causing <i>Brucella</i> species (BBS)		Non-Brucellosis causing <i>Brucella</i> species (nBBS) (previous <i>Ochrobactrum</i> spp.)	
1	<i>Brucella abortus</i> (Schmidt 1901) Meyer and Shaw 1920 (Approved Lists 1980)	1	<i>Brucella anthracis</i> (Holmes et al. 1988) Hördt et al. 2020
2	<i>Brucella canis</i> Carmichael and Bruner 1968 (Approved Lists 1980)	2	<i>Brucella ciceri</i> (Imran et al. 2010) Hördt et al. 2020
3	<i>Brucella ceti</i> Foster et al. 2007	3	<i>Brucella cytisi</i> (Zurdo-Piñero et al. 2007) Hördt et al. 2020
4	<i>Brucella inopinata</i> Scholz et al. 2010	4	<i>Brucella daejeonensis</i> (Woo et al. 2011) Hördt et al. 2020
5	<i>Brucella melitensis</i> (Hughes 1893) Meyer and Shaw 1920 (Approved Lists 1980)	5	<i>Brucella endophytica</i> (Li et al. 2016) Hördt et al. 2020
6	<i>Brucella microti</i> Scholz et al. 2008	6	<i>Brucella gallinifacis</i> (Kämpfer et al. 2003) Hördt et al. 2020
7	<i>Brucella neotomae</i> Stoenner and Lackman 1957 (Approved Lists 1980)	7	<i>Brucella grignonensis</i> (Lebuhn et al. 2000) Hördt et al. 2020
8	<i>Brucella nosferati</i> Hernández-Mora et al. 2023	8	<i>Brucella haematophila</i> (Kämpfer et al. 2007) Hördt et al. 2020
9	<i>Brucella ovis</i> Buddle 1956 (Approved Lists 1980)	9	<i>Brucella intermedia</i> (Velasco et al. 1998) Hördt et al. 2020
10	<i>Brucella pinnipedialis</i> Foster et al. 2007	10	<i>Brucella lupini</i> (Trujillo et al. 2006) Hördt et al. 2020
11	<i>Brucella papionis</i> Whatmore et al. 2014	11	<i>Brucella oryzae</i> (Tripathi et al. 2006) Hördt et al. 2020
12	<i>Brucella suis</i> Huddleson 1929 (Approved Lists 1980)	12	<i>Brucella pecoris</i> (Kämpfer et al. 2011) Hördt et al. 2020
13	<i>Brucella vulpis</i> Scholz et al. 2016	13	<i>Brucella pituitosa</i> (Huber et al. 2010) Hördt et al. 2020
		14	<i>Brucella pseudointermedia</i> (Teyssier et al. 2007) Hördt et al. 2020
		15	<i>Brucella pseudogrignonensis</i> (Kämpfer et al. 2007) Hördt et al. 2020
		16	<i>Brucella rhizosphaerae</i> (Kämpfer et al. 2008) Hördt et al. 2020
		17	<i>Brucella thiophenivorans</i> (Kämpfer et al. 2008) Hördt et al. 2020
		18	<i>Brucella tritici</i> (Lebuhn et al. 2000) Hördt et al. 2020

List of Prokaryotic names with Standing in Nomenclature (LPSN) [Search result \(dsmz.de\)](https://www.dsmz.de/en/research/research_projects/lpsn)

*Highlighted rows are the most common *Brucella* species as of April 2024.

APPENDIX B: Definitions for determining a new brucellosis case to prevent duplicative case reporting

Brucellosis may become chronic, making it difficult to differentiate between a new brucellosis case (reinfection) and chronic illness. Though there is not a universally accepted definition for chronic brucellosis, it is generally used to describe cases where signs and symptoms persist for 12 months after diagnosis. Incident BBS infection may be difficult to distinguish in patients with a prior medical history of brucellosis. This is especially true for cases where the same *Brucella* sp. is recovered from cultures taken after initial illness or if only serology is used to diagnose brucellosis. A previously reported acute brucellosis case should not be counted a second time if illness can be attributed to subsequent development of chronic illness manifestation.

Three chronic illness manifestations are recognized by the World Health Organization: relapse, chronic localized infection, and delayed convalescence.

Brucellosis relapse is a recurrence of signs and symptoms after completion of antimicrobial treatment, generally within 3-6 months post-treatment. Relapsing cases typically have objective (measurable) signs of infection such as fever and persistently elevated *Brucella* IgG serum antibody titers (4,10). Approximately 5% to 15% of brucellosis cases can relapse. Because antimicrobial resistance is rare, repeating treatment with appropriate antimicrobial therapy is recommended.

Chronic localized brucellosis infection is a recurrence of signs or symptoms due to a deep nidus of infection such as osteomyelitis, endocarditis or liver abscess, with persistently elevated *Brucella* IgG serum antibodies. *Brucella* may sometimes also be detected in cultures if relapse or chronic localized brucellosis occurs. Unlike relapse, chronic localized brucellosis may result in intermittent objective signs of infection over an extended period of time. In addition, surgical intervention may be required to remove or drain chronic localized nidus of infection in conjunction with antimicrobial treatment.

Delayed convalescence results in persistent symptoms following antimicrobial treatment, without objective signs of infection such as fever. Cultures are negative for *Brucella*, and IgG antibody titers decrease and may not be detectable. Repeat antimicrobial treatment does not appear to resolve symptoms.