

**16-ID-11**
**Committee:** Infectious Disease

**Title:** Revision of the Standardized Case Definition for Tularemia (*Francisella tularensis*)

**I. Statement of the Problem**

Cases of tularemia (*Francisella tularensis*) are currently reportable to the National Notifiable Disease Surveillance System (NNDSS). Surveillance is important in enabling an accurate assessment of tularemia burden and for appreciating possible bioterror threats. As molecular techniques have improved, polymerase chain reaction (PCR) testing of specimens suspected to have *F. tularensis* has become more prevalent; however, results of PCR testing are not yet considered in case classification.

**II. Background and Justification**

Tularemia is a zoonotic disease caused by the gram-negative coccobacillus *Francisella tularensis*. Tularemia characteristically presents as an acute febrile illness. Various clinical manifestations can occur depending on the route of infection and host response, including an ulcer at the site of cutaneous or mucous membrane inoculation, pharyngitis, ocular lesions, regional lymphadenopathy, and pneumonia. If untreated with appropriate antibiotics, tularemia can be fatal.

Known also as “rabbit fever” and “deer fly fever,” tularemia was first described in the United States in 1912 and has been reported from all states except Hawaii. Human infection can occur in several ways: being bitten by an infected tick, deerfly or other insect; handling infected animal carcasses (most commonly rodents, rabbits, and hares); eating or drinking contaminated food or water; and breathing in the bacterium. Tularemia is not known to be spread from person to person. Tularemia was removed from the list of nationally notifiable diseases in 1994, but increased concern about potential use of *F. tularensis* as a biological weapon led to its return in 2000.

Traditional methods of laboratory diagnosis have included culture and changes in serum antibodies. Polymerase chain reaction (PCR) testing became incorporated in testing protocols in 2014 and has been shown to be useful and accurate in establishing a presumptive diagnosis. The Laboratory Response Network (LRN) facilities routinely use PCR techniques, and more recently, commercial laboratories have adopted those techniques.

**III. Statement of the desired action(s) to be taken**

1. Utilize standard sources (e.g. reporting\*) for case ascertainment for tularemia (*Francisella tularensis*). Surveillance for tularemia should use the following recommended sources of data to the extent of coverage presented in Table III.

**Table III. Recommended sources of data and extent of coverage for ascertainment of cases of tularemia (*F. tularensis*).**

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	x	
Laboratory reporting	x	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers)	x	
Death certificates	x	
Hospital discharge or outpatient records	x	
Extracts from electronic medical records	x	
Telephone survey		
School-based survey		
Other _____		

2016 Template

2. Utilize standardized criteria for case identification and classification (Sections VI and VII) for tularemia and add tularemia to the *Nationally Notifiable Condition List*

- 2a. Immediately notifiable, extremely urgent (within 4 hours)
- 2b. Immediately notifiable, urgent (within 24 hours)
- 2c. Routinely notifiable

CSTE recommends that all States and Territories enact laws (statue 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.

Expectations for Message Mapping Guide (MMG) development for a newly notifiable condition: NNDSS is transitioning to HL7-based messages for case notifications; the specifications for these messages are presented in MMGs. When CSTE recommends that a new condition be made nationally notifiable, CDC must obtain 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.

3. CDC should publish data on tularemia (*F. tularensis*) as appropriate in *MMWR* and other venues (see Section IX).

4. CSTE requests that results from PCR testing be added to the list of laboratory criteria acceptable to classify a tularemia case as “probable.”

CSTE recommends that all jurisdictions (e.g. States or Territories) with legal authority to conduct public health surveillance follow the recommended methods as outlined above.

**Terminology:**

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

\*\*Notification: process of a local or state public health authority submitting a report (case information) of a condition on the Nationally Notifiable Condition List TO CDC.

#### **IV. Goals of Surveillance**

1. To recognize the role of molecular detection assays in classifying infectious diseases.
2. To ensure rapid methods of detecting pathogens on the Category A possible bioterrorism agent list.
3. To provide information on the temporal, geographic, and demographic occurrence of tularemia to facilitate its prevention and control.

#### **V. Methods for Surveillance: Surveillance for tularemia (*Francisella tularensis*) should use the recommended sources of data and the extent of coverage listed in Table III.**

Data sources described in Table III are standard sources and will not change as a result of this position statement.

#### **VI. Criteria for case identification**

##### **A. Narrative: A description of suggested criteria for case ascertainment of a specific condition.**

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

- A person with a clinical presentation consistent with tularemia.
- A person whose healthcare record contains a diagnosis of tularemia.
- A person whose death certificate lists tularemia as a cause of death or a significant condition contributing to death.

- Elevated serum antibody titer(s) to *F. tularensis* antigen
- Detection of *F. tularensis* in a clinical specimen by fluorescent assay or PCR
- Isolation of *F. tularensis* from a clinical specimen

*Other recommended reporting procedures*

- All cases of tularemia should be reported.
- Reporting should be on-going and routine.
- Reporting should be immediate.

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

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

Criterion	Tularemia Reporting
<i>Clinical Evidence</i>	
Clinical suspicion of tularemia	S
Health record diagnosis of tularemia	S
Death certificate lists tularemia as cause of death or significant condition contributing to death	S
<i>Laboratory Evidence</i>	
Elevated serum antibody titer(s) to <i>F. tularensis</i> antigen	S
Detection of <i>F. tularensis</i> in a clinical specimen by fluorescent assay	S
Detection of <i>F. tularensis</i> in a clinical specimen by PCR	S
Isolation of <i>F. tularensis</i> from a clinical specimen	S
<small>2016 Template</small>	

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 (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to report a case.

\* A requisition or order for any of the "S" laboratory tests is sufficient to meet the reporting criteria.

**C. Disease-specific data elements**

Epidemiological information

- Evidence or history of a tick or deerfly bite
- Exposure to tissues of a mammalian host of *F. tularensis*
- Exposure to potentially contaminated water
- Work in a laboratory that handles tularemia specimens or *F. tularensis* cultures
- Living or working in—or recently traveling to—areas of states with significant numbers of recent cases of tularemia

## VII. Case Definition for Case Classification

### A. Narrative: Description of criteria to determine how a case should be classified.

#### Clinical Criteria

An illness characterized by several distinct forms, including the following:

- Ulceroglandular: cutaneous ulcer with regional lymphadenopathy
- Glandular: regional lymphadenopathy with no ulcer
- Oculoglandular: conjunctivitis with preauricular lymphadenopathy
- Oropharyngeal: stomatitis or pharyngitis or tonsillitis and cervical lymphadenopathy
- Pneumonic: primary pulmonary disease
- Typhoidal: febrile illness without localizing signs and symptoms

#### Laboratory Criteria

##### Supportive

- Elevated serum antibody titer(s) to *F. tularensis* antigen (without documented fourfold or greater change) in a patient with no history of tularemia vaccination, **OR**
- Detection of *F. tularensis* in a clinical or autopsy specimen by fluorescent assay, **OR**
- Detection of *F. tularensis* in a clinical or autopsy specimen by a polymerase chain reaction (PCR)

##### Confirmatory

- Isolation of *F. tularensis* in a clinical or autopsy specimen, **OR**
- Fourfold or greater change in serum antibody titer to *F. tularensis* antigen between acute and convalescent specimens

#### Epidemiologic Linkage

Clinical diagnosis is supported by evidence or history of a tick or deerfly bite, exposure to tissues of a mammalian host of *F. tularensis*, including via an animal bite, or exposure to potentially contaminated water.

#### Case Classification

##### Probable Case:

A clinically-compatible case with supportive laboratory evidence.

##### Confirmed Case:

A clinically-compatible case with confirmatory laboratory evidence.

#### Criteria to distinguish a new case of this disease or condition from reports or notifications which should not be enumerated as a new case for surveillance

Serial or subsequent cases of tularemia experienced by one individual should only be counted if there is an additional epidemiologically compatible exposure and new onset of symptoms. Because the duration of antibodies to *F. tularensis* is not known, mere presence of antibodies without a clinically-compatible illness AND an epidemiologically compatible exposure within 12 months of onset may not indicate a new infection, especially among persons who live in endemic areas.

**B. Classification Tables**
**Table VII-B. Criteria for defining a case of tularemia (*Francisella tularensis*).**

Criterion	Confirmed					Probable				
<i>Clinical Evidence</i>										
Regional lymphadenopathy	N					N				
Conjunctivitis		N					N			
Preauricular lymphadenopathy		N					N			
Stomatitis			O					O		
Pharyngitis			O					O		
Tonsillitis			O					O		
Cervical lymphadenopathy			N					N		
Pleuropneumonitis				N						N
Hilar adenopathy				N						N
Fever (> 38°C)					N					N
<i>Laboratory Evidence</i>										
Elevated serum antibody titer(s) to <i>F. tularensis</i> antigen (without documented fourfold or greater change)						O	O	O	O	O
Detection of <i>F. tularensis</i> in a clinical specimen by fluorescent assay						O	O	O	O	O
Detection of <i>F. tularensis</i> in a clinical specimen by PCR						O	O	O	O	O
Isolation of <i>F. tularensis</i> from a clinical specimen	O	O	O	O	O					
Fourfold or greater change in serum antibody titer to <i>F. tularensis</i> antigen in specimens drawn at least 2 weeks apart	O	O	O	O	O					
<i>Epidemiological Evidence</i>										
Exposure to tissues from a mammalian host, including via an animal bite	O	O	O	O	O	O	O	O	O	O
Exposure to soil or water in an endemic region	O	O	O	O	O	O	O	O	O	O
Evidence of a deerfly or tick bite	O	O	O	O	O	O	O	O	O	O
No additional clinically-compatible symptoms within the past 12 months	O	O	O	O	O	O	O	O	O	O
No history of a tularemia vaccination	O	O	O	O	O	O	O	O	O	O

**Notes:**

N = All “N” criteria in the same column are Necessary to classify a case. A number following an “N” indicates that this criterion is only required for a specific disease/condition subtype (see below). If the absence of a criterion (i.e., criterion NOT present) is required for the case to meet the classification criteria, list the Absence of criterion as a Necessary component.

O = At least one of these “O” (One or more) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all “N” criteria in the same column—is required to classify a case. (These “O” criteria are alternatives, which means that a single column will have either no O criteria or multiple O criteria; no column should have only one O.) A number following an “O” indicates that this criterion is only required for a specific disease/condition subtype.

### VIII. Period of Surveillance

Surveillance is expected to be ongoing.

### IX. Data sharing/release and print criteria

Notification to CDC for confirmed and probable cases of tularemia is recommended.

- Immediate (extremely urgent) notification to CDC should occur for all suspected, probable and confirmed cases if intentional release of tularemia is suspected as the cause of infection.
- Standard notification should be used for all other cases.
- Provisional data on tularemia cases reported through NETSS/NNDS are summarized weekly in the MMWR, and finalized data are published annually in the Summary of Notifiable Diseases. Longer articles describing and interpreting national trends are published in the MMWR on an ad-hoc basis (approximately once every other year).
- State-specific compiled data will continue to be published in the weekly and annual MMWR.
- Provisional state-specific compiled data will continue to be published in the weekly reports. Finalized data will be published in the annual MMWR Surveillance Summaries, following verification by each state. The frequency of release of additional publication of this data will be dependent on the current epidemiologic situation in the country. These publications might include annual epidemiologic summaries in the MMWR or manuscripts in peer-reviewed journals.

### X. Revision History

Position Statement ID	Section of Document	Revision Description
16-ID-11	Table VII-B – Probable/Confirmed	Adding Probable case status for PCR

The 1996 case definition appearing on this page was re-published in the 1999 CSTE position statement 1999-ID-6 and the 2009 CSTE position statement 09-ID-66. Thus, the 1996, 1999, and 2010 versions of the case definition are identical.

## XI. References

1. Centers for Disease Control and Prevention (CDC). Case definitions for infectious conditions under public health surveillance. MMWR 1997;46(No. RR-10):1-57.
2. Centers for Disease Control and Prevention [Internet]. National notifiable diseases surveillance system: case definitions. Atlanta: CDC. Available from: <https://www.cdc.gov/nndss/case-definitions.html>
3. Centers for Disease Control and Prevention [Internet]. Tularemia. Atlanta: CDC. Available from: <http://www.bt.cdc.gov/agent/tularemia/>. Accessed: 2016 Mar 23.
4. Centers for Disease Control and Prevention (CDC). Tularemia – United States, 2001-2010. MMWR 2013;62(47):936-66.
5. Centers for Disease Control and Prevention (CDC). Notes from the Field: Increase in Human cases of tularemia – Colorado, Nebraska, South Dakota and Wyoming, January – September 2015. MMWR 2015;64(67):1317-18.
6. Chang M, Glynn MK, Groseclose SL. Endemic, notifiable bioterrorism-related diseases, United States, 1992-1999. Emerg Infect Dis [serial online] 2003 May. Available from: <http://www.cdc.gov/ncidod/EID/vol9no5/02-0477.htm>. Accessed: 2008 Aug 5.
7. Council of State and Territorial Epidemiologists (CSTE). Reinstating Tularemia as a nationally notifiable disease. CSTE position statement 1999-ID-6.
8. Council of State and Territorial Epidemiologists (CSTE). CSTE official list of nationally notifiable conditions. CSTE position statement 07-EC-02. Atlanta: CSTE; June 2007. Available from: <http://www.cste.org>.
9. Council of State and Territorial Epidemiologists (CSTE). Criteria for inclusion of conditions on CSTE nationally notifiable condition list and for categorization as immediately or routinely notifiable. CSTE position statement 08-EC-02. Atlanta: CSTE; June 2008. Available from: <http://www.cste.org>.
10. Council of State and Territorial Epidemiologists, Centers for Disease Control and Prevention. CDC-CSTE Intergovernmental Data Release Guidelines Working Group (DRGWG) Report: CDC-ATSDR Data Release Guidelines and Procedures for Re-release of State-Provided Data. Atlanta: CSTE; 2005.
11. Dauphin LA, Walker RE, Petersen JM, Bowen MD. [Comparative evaluation of automated and manual commercial DNA extraction methods for detection of Francisella tularensis DNA from suspensions and spiked swabs by real-time polymerase chain reaction](#). Diagn Microbiol Infect Dis 2011;70(3):299-306.
12. Dennis DT, Inglesby TV, Henderson DA, et al. Tularemia as a biological weapon: medical and public health management. JAMA. 2001;285:2763-73. Available from: <http://jama.ama-assn.org/cgi/content/full/285/21/2763>. Accessed: 2008 Aug 5.
13. Euler M, Wang Y, Otto P, Tomaso H, Escudero R, Anda P, Hufert FT, Weidmann M. [Recombinase polymerase amplification assay for rapid detection of Francisella tularensis](#). J Clin Microbiol 2012;50(7):2234-8.
14. Farlow J, Wagner DM, Dukerich M, Stanley M, Chu M, Kubota K, et al. Francisella tularensis in the United States. Emerg Infect Dis [serial on the Internet]. 2005 Dec. Available from: <http://www.cdc.gov/ncidod/EID/vol11no12/05-0728.htm>. Accessed: 2008 Aug 5.
15. Gunnell MK, Lovelace CD, Satterfield BA, Moore EA, O'Neill KL, Robison RA. [A multiplex real-time PCR assay for the detection and differentiation of Francisella tularensis subspecies](#). J Med Microbiol. 2012;61(Pt 11):1525-31.
16. Heymann DL, editor. Control of communicable diseases manual. 20th edition. Washington: American Public Health Association; 2015.
17. Penn RL. Chapter 224 – Francisella tularensis (Tularemia). In: Mandell GL, Bennett JE, Dolin R, editors. Principles and Practice of Infectious Diseases, 6th edition. Philadelphia: Churchill Livingstone; 2005.
18. Walker RE, Petersen JM, Stephens KW, Dauphin LA. [Optimal swab processing recovery method for detection of bioterrorism-related Francisella tularensis by real-time PCR](#). J Microbiol Methods 2010;83(1):42-7.

**XII. Coordination****Agencies for Response:**

- (1) Thomas R Frieden, MD, MPH  
Director  
Centers for Disease Control and Prevention  
1600 Clifton Road, NE  
Atlanta GA 30333  
(404) 639-7000  
[txf2@cdc.gov](mailto:txf2@cdc.gov)
- (2) Scott Becker, MS  
Executive Director  
Association of Public Health Laboratories (APHL)  
8515 Georgia Avenue, Suite 700  
Silver Spring, MD 20910  
(240) 485-2747  
[scott.becker@aphl.org](mailto:scott.becker@aphl.org)

**XIII. Submitting Author:**

- (1)  Active Member  Associate Member  
Louisa Castrodale, DVM, MPH  
State Public Health Veterinarian  
Alaska Section of Epidemiology  
3601 C St, Suite 540  
Anchorage, AK 99503  
907-269-8002  
[louisa.castrodale@alaska.gov](mailto:louisa.castrodale@alaska.gov)

**Co-Authors:**

- (1)  Active Member  Associate Member  
Jennifer House, DVM, MPH  
State Public Health Veterinarian  
Colorado Department of Public Health and Environment  
4300 Cherry Creek Drive South  
DCEED-EPI-A3  
Denver, CO 80246  
303-692-2700  
[jennifer.house@state.co.us](mailto:jennifer.house@state.co.us)
- (2)  Active Member  Associate Member  
Joseph McLaughlin, MD, MPH  
State Epidemiologist  
Alaska Section of Epidemiology  
3601 C St, Suite 540  
Anchorage, AK 99503  
907-269-8001  
[joseph.mclaughlin@alaska.gov](mailto:joseph.mclaughlin@alaska.gov)