Table. 2019 Changes to the CSTE Surveillance Case Definitions for Diphtheria, Hepatitis A Acute, Listeriosis, RSV-associated Mortality, *Salmonella* Typhi/Paratyphi Infections, Yellow Fever, and Yersiniosis

Condition	Old Case Definitions	2019 Case Definitions

Diphtheria	**Diphtheria, 2010**
	
	Case Classification
	Probable
	In the absence of a more likely diagnosis, an upper respiratory tract illness with:
	• An adherent membrane of the nose, pharynx, tonsils, or larynx; **AND**
	• Absence of laboratory confirmation; **AND**
	• Lack of epidemiologic linkage to a laboratory-confirmed case of diphtheria
	Confirmed
	An upper respiratory tract illness with an adherent membrane of the nose, pharynx, tonsils, or larynx; and any of the following:
	• Isolation of *Corynebacterium diphtheriae* from the nose or throat; **OR**
	• Histopathologic diagnosis of diphtheria; **OR**
	• Epidemiologic linkage to a laboratory-confirmed case of diphtheria.
		Diphtheria, 2019
		
		Clinical Criteria
		• Upper respiratory tract illness with an adherent membrane of the nose, pharynx, tonsils, or larynx OR
		• Infection of a non-respiratory anatomical site (e.g., skin, wound, conjunctiva, ear, genital mucosa)
		Laboratory Criteria
		Confirmatory laboratory evidence:
		Isolation of *C. diphtheriae* from any site AND
		Confirmation of toxin-production by Elek test or by another validated test capable of confirming toxin-production
		Epidemiologic Linkage
		Epidemiologic linkage requires direct contact with a laboratory-confirmed case of diphtheria.
		Case Classifications
		Confirmed:
		• An upper respiratory tract illness with an adherent membrane of the nose, pharynx, tonsils, or larynx and any of the following:
		  ○ isolation of toxin-producing *Corynebacterium diphtheriae* from the nose or throat OR
		  ○ epidemiologic linkage to a laboratory-confirmed case of diphtheria OR
		• An infection at a non-respiratory anatomical site (e.g., skin, wound, conjunctiva, ear, genital mucosa) with
		  ○ isolation of toxin-producing *C. diphtheriae* from that site
		
		Suspect:
		• In the absence of a more likely diagnosis, an upper respiratory tract illness with each of the following:
		  ○ an adherent membrane of the nose, pharynx, tonsils, or larynx AND
		  ○ absence of laboratory confirmation AND
		  ○ lack of epidemiologic linkage to a laboratory-confirmed case of diphtheria OR
		• Histopathologic diagnosis
		
		Comments:
		• Cases of laboratory-confirmed, non-toxin producing *C. diphtheriae* (respiratory or non-respiratory) should not be reported by state or local health departments to CDC as diphtheria cases.
		• Negative laboratory results may be sufficient to rule-out a diagnosis of diphtheria; however, clinicians should carefully consider all lab results in the context of the patient's vaccination status, antimicrobial treatment, and other risk factors.
		• PCR and MALDI-TOF diagnostics for *C. diphtheriae*, when used alone, do not confirm toxin production. These tests, when used, should always be combined with a test that confirms toxin production, such as the Elek test.

Condition	Old Case Definitions	2019 Case Definitions
Hepatitis A, Acute	**Hepatitis A, 2012** **Clinical Description** An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain), and either a) jaundice, or b) elevated serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels **Laboratory Criteria for Diagnosis** Immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive **Case Classification** **Confirmed** • A case that meets the clinical case definition and is laboratory confirmed, **OR** A case that meets the clinical case definition and occurs in a person who has an epidemiologic link with a person who has laboratory-confirmed hepatitis A (i.e., household or sexual contact with an infected person during the 15-50 days before the onset of symptoms)	**Hepatitis A, 2019** **Clinical Criteria** An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, abdominal pain, or dark urine), **AND** a) jaundice or elevated total bilirubin levels ≥3.0 mg/dL, **OR** b) elevated serum alanine aminotransferase (ALT) levels >200 IU/L, **AND** c) the absence of a more likely diagnosis **Laboratory Criteria** *Confirmatory laboratory evidence*: • Immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive, **OR** • Nucleic acid amplification test (NAAT; such as PCR or genotyping) for hepatitis A virus RNA positive **Epidemiologic Linkage** Contact (e.g., household or sexual) with a laboratory-confirmed hepatitis A case 15-50 days prior to onset of symptoms **Case Classification** *Confirmed:* • A case that meets the clinical criteria and is IgM anti-HAV positive§, **OR** • A case that has hepatitis A virus RNA detected by NAAT (such as PCR or genotyping) **OR** • A case that meets the clinical criteria and occurs in a person who had contact (e.g., household or sexual) with a laboratory-confirmed hepatitis A case 15-50 days prior to onset of symptoms. § And not otherwise ruled out by IgM anti-HAV or NAAT for hepatitis A virus testing performed in a public health laboratory.

Condition	Old Case Definitions	2019 Case Definitions
Listeriosis	**Listeriosis, 2000** **Clinical Description** In adults, invasive disease caused by *Listeria monocytogenes* manifests most commonly as meningitis or bacteremia; infection during pregnancy may result in fetal loss through miscarriage or stillbirth, or neonatal meningitis or bacteremia. Other manifestations can also be observed. **Laboratory Criteria for Diagnosis** Isolation of *L. monocytogenes* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid) In the setting of miscarriage or stillbirth, isolation of *L. monocytogenes* from placental or fetal tissue **Case Classification** **Confirmed** A clinically compatible case that is laboratory-confirmed	**Listeriosis, 2019** **Clinical Criteria** Invasive listeriosis: • Systemic illness caused by *L. monocytogenes* manifests most commonly as bacteremia or central nervous system infection. Other manifestations can include pneumonia, peritonitis, endocarditis, and focal infections of joints and bones. • Pregnancy-associated listeriosis has generally been classified as illness occurring in a pregnant woman or in an infant aged ≤ 28 days. Listeriosis may result in pregnancy loss (fetal loss before 20 weeks gestation), intrauterine fetal demise (≥20 weeks gestation), pre-term labor, or neonatal infection, while causing minimal or no systemic symptoms in the mother. Pregnancy loss and intrauterine fetal demise are considered to be maternal outcomes. • Neonatal listeriosis commonly manifests as bacteremia, central nervous system infection, and pneumonia, and is associated with high fatality rates. Transmission of *Listeria* from mother to baby transplacentally or during delivery is almost always the source of early-onset neonatal infections (diagnosed between birth and 6 days), and the most likely source of late-onset neonatal listeriosis (diagnosed between 7–28 days). Non-invasive *Listeria* Infections: *Listeria* infection manifesting as an isolate from a non-invasive clinical specimen suggestive of a non-invasive infection; includes febrile gastroenteritis, urinary tract infection, and wound infection. **Laboratory Criteria** *Confirmatory laboratory evidence*: • Isolation of *L. monocytogenes* from a specimen collected from a normally sterile site reflective of an invasive infection (e.g., blood or cerebrospinal fluid or, less commonly: pleural, peritoneal, pericardial, hepatobiliary, or vitreous fluid; orthopedic site such as bone, bone marrow, or joint; or other sterile sites including organs such as spleen, liver, and heart, but not sources such as urine, stool, or external wounds); **OR** • For maternal isolates: In the setting of pregnancy, pregnancy loss, intrauterine fetal demise, or birth, isolation of *L. monocytogenes* from products of conception (e.g. chorionic villi, placenta, fetal tissue, umbilical cord blood, amniotic fluid) collected at the time of delivery; **OR** • For neonatal isolates: In the setting of live birth, isolation of *L. monocytogenes* from a non-sterile neonatal specimen (e.g., meconium, tracheal aspirate, but not products of conception) collected within 48 hours of delivery. *Presumptive laboratory evidence*: • Detection of *L. monocytogenes* by CIDT in a specimen collected from a normally sterile site (e.g., blood or cerebrospinal fluid or, less commonly: pleural, peritoneal, pericardial, hepatobiliary, or vitreous fluid; orthopedic site such as bone, bone marrow, or joint; or other sterile sites including organs such as spleen, liver, and heart, but not sources such as urine, stool, or external wounds); **OR** • For maternal isolates: In the setting of pregnancy, pregnancy loss, intrauterine fetal demise, or birth, detection of *L. monocytogenes* by CIDT from products of conception (e.g. chorionic villi, placenta, fetal tissue, umbilical cord blood, amniotic fluid) collected at the time of delivery; **OR** • For neonatal isolates: In the setting of live birth, detection of *L. monocytogenes* by CIDT from a non-sterile neonatal specimen (e.g., meconium, tracheal aspirate, but not products of conception) collected within 48 hours of delivery. *Supportive laboratory evidence*: • Isolation of *L. monocytogenes* from a non-invasive clinical specimen, e.g., stool, urine, wound, other than those specified under maternal and neonatal specimens in *Confirmatory laboratory evidence,* above.

Condition	Old Case Definitions	2019 Case Definitions
Listeriosis (cont'd)		**Epidemiologic Linkage** For probable maternal cases: • A mother who does not meet the confirmed case criteria, **BUT** • Who gave birth to a neonate who meets confirmatory or presumptive laboratory evidence for diagnosis, **AND** • Neonatal specimen was collected up to 28 days of birth. **OR** For probable neonatal cases: • Neonate(s) who do not meet the confirmed case criteria, **AND** • Whose mother meets confirmatory or presumptive laboratory evidence for diagnosis from products of conception, **OR** • A clinically compatible neonate whose mother meets confirmatory or presumptive laboratory evidence for diagnosis from a normally sterile site. **Case Classifications** *Confirmed:* • A person who meets confirmatory laboratory evidence. *Probable*: • A person who meets the presumptive laboratory evidence; **OR** • A mother or neonate who meets the epidemiologic linkage but who does not have confirmatory laboratory evidence. *Suspect*: • A person with supportive laboratory evidence.
RSV-Associated Mortality	None	**RSV-Associated Mortality, 2019** **Clinical Criteria** A respiratory syncytial virus (RSV)-associated death is defined for surveillance purposes as a death resulting from a clinically compatible illness that was confirmed to be RSV by an appropriate laboratory or rapid diagnostic test. There should be no period of complete recovery between the illness and death. A death should not be categorized as an RSV-associated death if: 1. There is no laboratory confirmation of RSV infection. 2. The RSV illness is followed by full recovery to baseline health status prior to death. 3. After review and consultation, it is determined that RSV infection did not contribute to death. **Laboratory Criteria** *Confirmatory laboratory evidence*: Laboratory testing for RSV infection may be done on pre- or post-mortem clinical specimens, and include identification of RSV (A, B, or unspecified) infection by a positive result by at least one of the following: a. Isolation of respiratory syncytial virus (RSV) by tissue cell culture b. Detection of respiratory syncytial virus (RSV) nucleic acid by reverse-transcriptase polymerase chain reaction (RT-PCR) or other nucleic acid detection assay c. Detection of respiratory syncytial virus (RSV) antigen by immunofluorescent antibody staining (direct or indirect) d. Detection of respiratory syncytial virus (RSV) antigens by immunochromatographic or similar rapid laboratory test e. Detection of respiratory syncytial virus (RSV) antigens from autopsy specimens by immunohistochemical (IHC) staining **Case Classification** *Confirmed:* A death meeting the clinical and laboratory criteria.

Condition	Old Case Definitions	2019 Case Definitions
***Salmonella* Typhi and Paratyphi Infections**	**Typhoid Fever, 1997** **Clinical Description** An illness caused by *Salmonella enterica* serotype Typhi that is often characterized by insidious onset of sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or diarrhea, and nonproductive cough. However, many mild and atypical infections occur. Carriage of serotype Typhi may be prolonged. **Laboratory Criteria for Diagnosis** Isolation of serotype Typhi from blood, stool, or other clinical specimen **Case Classification** **Probable** A clinically compatible case that is epidemiologically linked to a confirmed case in an outbreak **Confirmed** A clinically compatible case that is laboratory confirmed	***Salmonella* Typhi and Paratyphi Infections, 2019** **Clinical Description** Infections caused by *Salmonella enterica* serotype Typhi (*S.* Typhi) or *Salmonella enterica* serotypes Paratyphi A, B (tartrate negative), and C (*S.* Paratyphi) that are often characterized by insidious onset of sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or diarrhea, and non-productive cough. However, mild and atypical infections may occur. Carriage of *S.* Typhi and *S.* Paratyphi A, B (tartrate negative), and C may be prolonged. **Clinical Criteria** One or more of the following: Fever, Diarrhea, Abdominal cramps, Constipation, Anorexia, or Relative bradycardia **Laboratory Criteria** S. Typhi Infection *Confirmatory laboratory evidence*: • Isolation of S. Typhi from a clinical specimen. *Presumptive laboratory evidence*: • Detection of S. Typhi in a clinical specimen using a culture-independent diagnostic test (CIDT). S. Paratyphi Infection *Confirmatory laboratory evidence*: • Isolation of S. Paratyphi A, B (tartrate negative), or C from a clinical specimen. *Presumptive laboratory evidence*: • Detection of S. Paratyphi A, B (tartrate negative), or C in a clinical specimen using a CIDT. **Epidemiologic Linkage** S. Typhi Infection • Epidemiological linkage to a confirmed *S.* Typhi Infection case, or • Epidemiological linkage to a probable *S.* Typhi Infection case with laboratory evidence, or • Member of a risk group as defined by public health authorities during an outbreak. S. Paratyphi Infection • Epidemiological linkage to a confirmed *S.* Paratyphi Infection case, or • Epidemiological linkage to a probable *S.* Paratyphi Infection case with laboratory evidence, or • Member of a risk group as defined by public health authorities during an outbreak. **Case Classifications** S. Typhi Infection *Confirmed:* • A person with confirmatory laboratory evidence. *Probable*: • A clinically compatible illness in a person with presumptive laboratory evidence. • A clinically compatible illness in a person with an epidemiological linkage. S. Paratyphi Infection *Confirmed:* • A person with confirmatory laboratory evidence. *Probable*: • A clinically compatible illness in a person with presumptive laboratory evidence. • A clinically compatible illness in a person with an epidemiological linkage.

Condition	Old Case Definitions	2019 Case Definitions
Yellow Fever	**Yellow Fever,1997** **Clinical Description** A mosquito-borne viral illness characterized by acute onset and constitutional symptoms followed by a brief remission and a recurrence of fever, hepatitis, albuminuria, and symptoms and, in some instances, renal failure, shock, and generalized hemorrhages. **Laboratory Criteria For Diagnosis** Fourfold or greater rise in yellow fever antibody titer in a patient who has no history of recent yellow fever vaccination and cross-reactions to other flaviviruses have been excluded or demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid. **Case Classification** **Confirmed:** A clinically compatible case that is laboratory confirmed. **Probable**: A clinically compatible case with supportive serology (stable elevated antibody titer to yellow fever virus [e.g., greater than or equal to 32 by complement fixation, greater than or equal to 256 by immunofluorescence assay, greater than or equal to 320 by hemagglutination inhibition, greater than or equal to 160 by neutralization, or a positive serologic result by immunoglobulin M-capture enzyme immunoassay]. Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.)	**Yellow Fever, 2019** **Clinical Criteria** A clinically compatible case of yellow fever is defined as: • Acute illness with at least one of the following: fever, jaundice, or elevated total bilirubin ≥ 3 mg/dl AND • Absence of a more likely clinical explanation. **Laboratory Criteria** *Confirmatory laboratory evidence:* • Isolation of yellow fever virus from, or demonstration of yellow fever viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid. • Four-fold or greater rise or fall in yellow fever virus-specific neutralizing antibody titers in paired sera. • Yellow fever virus-specific IgM antibodies in CSF or serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen. *Presumptive laboratory evidence:* • Yellow fever virus-specific IgM antibodies in CSF or serum, and negative IgM results for other arboviruses endemic to the region where exposure occurred. **Epidemiologic Linkage** Epidemiologically linked to a confirmed yellow fever case, or visited or resided in an area with a risk of yellow fever in the 2 weeks before onset of illness. **Case Classifications** **Confirmed:** A case that meets the above clinical criteria and meets one or more of the following: • Isolation of yellow fever virus from, or demonstration of yellow fever viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, AND no history of yellow fever vaccination within 30 days before onset of illness unless there is molecular evidence of infection with wild-type yellow fever virus. • Four-fold or greater rise or fall in yellow fever virus-specific neutralizing antibody titers in paired sera, AND no history of yellow fever vaccination within 30 days before onset of illness. • Yellow fever virus-specific IgM antibodies in CSF or serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, AND no history of yellow fever vaccination. **Probable:** A case that meets the above clinical and epidemiologic linkage criteria, and meets the following: • Yellow fever virus-specific IgM antibodies in CSF or serum, AND negative IgM results for other arboviruses endemic to the region where exposure occurred, AND no history of yellow fever vaccination.

Condition	Old Case Definitions	2019 Case Definitions
Yersiniosis	None	**Yersinosis, 2019** **Clinical Criteria** An illness with either diarrhea or abdominal pain that may be severe enough to mimic appendicitis. **Laboratory Criteria** *Confirmatory laboratory evidence*: • Isolation of *Y. enterocolitica* or *Y. pseudotuberculosis* by culture from a clinical specimen. *Presumptive laboratory evidence*: • Detection of any *Yersinia* non-pestis species using a NAT CIDT. *Supportive laboratory evidence:* • N/A **Epidemiologic Linkage** A person who has had contact with a case that meets the presumptive or confirmatory laboratory criteria. **Case Classifications** *Confirmed:* • A case that meets the confirmed laboratory criteria. *Probable*: • A case that meets the presumptive laboratory criteria **OR** A clinically compatible case that is epidemiologically linked to a case meeting confirmatory or presumptive laboratory criteria