22-ID-02

Committee: Infectious Disease

Title: Standardized Case Definition for Surveillance of Multisystem Inflammatory Syndrome in Children Associated with SARS-CoV-2 Infection

☐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: ___N/A_____.

Synopsis: This position statement creates a standardized case definition for surveillance of multisystem inflammatory syndrome in children (MIS-C) as a rare but severe complication of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19).

I. Statement of the Problem

MIS-C associated with SARS-CoV-2 infection is a severe delayed hyperinflammatory condition in children and adolescents occurring 2–6 weeks after antecedent SARS-CoV-2 infection.[1,2] In May 2020, CDC issued a health advisory asking clinicians to report suspected cases to local and state health departments according to a clinical case definition.[3] This case definition, based on limited data from early case series,[4-7] was rapidly published for clinical diagnosis and reporting. In the absence of published literature on the presentation, clinical features, and pathophysiology of the new condition, the case definition was necessarily broad, prioritizing sensitivity over specificity. There is no confirmatory laboratory test available to diagnose MIS-C or to distinguish it from COVID-19 caused by acute SARS-CoV-2 infection, Kawasaki disease, toxic shock syndrome, or other hyperinflammatory syndromes, further challenging reporting.

The clinical MIS-C case definition has been instrumental in establishing national surveillance,[2] determining enrollment into prospective cohort studies,[1] estimating incidence,[8] evaluating treatment efficacy,[9] and assessing trends in characteristics and clinical outcomes over the course of the pandemic.[10] However, recent analyses have suggested it may result in misclassification, possibly including some severe cases of pediatric acute COVID-19, which can also present with multiple organ system dysfunction and elevated laboratory markers of inflammation.[11-15] Particularly among older children and adolescents, features of MIS-C may overlap with those of acute COVID-19, making appropriate classification difficult.[2,14]

Ongoing national surveillance for MIS-C associated with SARS-CoV-2 infection requires a standardized case definition that incorporates current knowledge about its cardinal features and that better distinguishes it from other hyperinflammatory syndromes in children. The standardized case definition is needed to estimate disease burden, monitor geographic trends in incidence, and characterize the demographic characteristics of persons affected by MIS-C associated with SARS-CoV-2 infection in the United States. These data are critical to inform interventions such as vaccination, non-pharmaceutical interventions, and public health messaging aimed at preventing SARS-CoV-2 infection.

II. Background and Justification

First described in the United Kingdom in April 2020, MIS-C was soon identified in the United States, affecting previously healthy children who had been infected with SARS-CoV-2.[4,5] Although acute SARS-CoV-2 infection in children is generally mild or asymptomatic,[16] associated MIS-C is characterized by fever, elevated laboratory markers of systemic inflammation, and multiple organ system dysfunction including cardiovascular, mucocutaneous, gastrointestinal, hematologic, neurologic, and renal involvement.[2,17] Some patients may also present with respiratory failure or radiographic pulmonary abnormalities, which may reflect associated pulmonary hyperinflammation, a phenotypic overlap with

COVID-19 viral pneumonia, or cardiogenic pulmonary edema.[13,15,17] Patients with MIS-C are often critically ill, with the majority requiring admission to an intensive care unit (ICU) and 1–3% requiring extracorporeal membrane oxygenation (ECMO).[2,10,17] Mortality among MIS-C patients has been estimated to be 1–2%.[10,17,18]

Using the clinical case definition released by CDC in May 2020, incidence of MIS-C in seven U.S. jurisdictions during April–June 2020 was estimated to be 5.1 cases per million person-months or 316 cases per million SARS-CoV-2 infections among persons aged <21 years.[8] Both measures of MIS-C incidence decreased with age and were higher among non-Hispanic Black, Hispanic, and non-Hispanic Asian or Pacific Islander persons, compared with non-Hispanic White persons.[8] These results corroborate other results demonstrating disproportionate MIS-C burden among Black and Hispanic persons.[19,20] However, children and adolescents diagnosed with MIS-C appear less likely to have underlying medical conditions than those diagnosed with severe COVID-19.[17] Clinical risk factors for developing MIS-C after SARS-CoV-2 infection have yet to be described.

Comparative cohort studies of MIS-C and acute pediatric COVID-19 have suggested that mucocutaneous, cardiovascular, and hematologic organ system involvement, as well as the presence of abdominal pain, vomiting, or diarrhea are features that raise the likelihood of a diagnosis of MIS-C.[11,15,17] However, the prevalence of renal and neurologic involvement appears to be similar in MIS-C and COVID-19.[17,21] Further, respiratory organ system involvement is more common in COVID-19 than in MIS-C and its inclusion in the MIS-C case definition may contribute to misclassification.[11,15]

This position statement establishes a standardized case definition for MIS-C associated with SARS-CoV-2 infection for state, local, territorial, and tribal public health departments to use for routine or targeted surveillance. The standardized case definition was developed through consultation with clinical experts, review of the published literature, and interrogation of the national MIS-C surveillance data and data collected through the Overcoming COVID-19 network MIS-C registry.[1,16]

Although this position statement does not designate MIS-C associated with SARS-CoV-2 infection as a nationally notifiable condition, public health officials can use the case definition to estimate regional burden and monitor trends in incidence, and can voluntarily report cases to CDC, allowing for surveillance of trends at the national level. This capacity will be crucial to continue surveillance as SARS-CoV-2 variants of concern emerge and circulate in the United States and vaccination recommendations expand to include younger children, potentially altering the epidemiology of MIS-C.

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

CSTE recommends the following actions:

1. Implement a standardized surveillance case definition for MIS-C associated with SARS-CoV-2 infection.
    A. Utilize standard sources (e.g., reporting*) for MIS-C associated with SARS-CoV-2 infection case ascertainment. Surveillance for MIS-C associated with SARS-CoV-2 infection should use the recommended sources of data to the extent of coverage presented in Section V.

    B. Utilize standardized criteria for MIS-C associated with SARS-CoV-2 infection case ascertainment presented in Section VI and Table VI in Technical Supplement.

    C. Utilize standardized criteria for MIS-C associated with SARS-CoV-2 infection case classification presented in Section VII and Table VII in Technical Supplement.

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

To provide a standard case definition to help standardize surveillance for states performing surveillance for MIS-C associated with SARS-CoV-2 infection. Standardized surveillance will inform assessment of incidence, demographics, severity, and outcomes of MIS-C over time. Surveillance for MIS-C associated with SARS-CoV-2 infection will facilitate interpretation of apparent increases or decreases in this condition, better define the risk factors, and improve the tracking of national trends of MIS-C.

V. Methods for Surveillance: Surveillance for MIS-C associated with SARS-CoV-2 infection should use the recommended sources of data and the extent of coverage listed in Table V.

Table V. Recommended sources of data and extent of coverage for ascertainment of cases of MIS-C.

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

The primary source of data for case ascertainment of MIS-C associated with SARS-CoV-2 infection is clinician reporting to public health authorities.

Clinicians should report cases meeting the clinical and laboratory criteria for MIS-C as described in Section VI. Data from clinicians can be supplemented using data from electronic medical records, hospital discharge or outpatient records, and death certificates.

VI. Criteria for case ascertainment

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

Report to public health authorities any illness in a person aged less than 21 years that meets:

- The clinical criteria for reporting AND the laboratory criteria for reporting;
  OR
- The clinical criteria for reporting AND the epidemiologic linkage criteria for reporting;
  OR
- The vital records criteria for reporting.

A1. Clinical Criteria for Reporting
An illness characterized by all of the following, in the absence of a more likely alternative diagnosis*:

- Subjective or documented fever (temperature ≥38.0º C)

  AND

- Clinical severity requiring hospitalization or resulting in death

  AND

- Evidence of systemic inflammation indicated by C-reactive protein ≥3.0 mg/dL (30 mg/L)

  AND

- New onset manifestations in at least two of the following categories:
  1. Cardiac involvement indicated by:
     - Left ventricular ejection fraction <55%, OR
     - Coronary artery dilatation, aneurysm, or ectasia, OR
     - Troponin elevated above laboratory normal range, or indicated as elevated in a clinical note
  2. Mucocutaneous involvement indicated by:
     - Rash, OR
     - Inflammation of the oral mucosa (e.g., mucosal erythema or swelling, drying or fissuring of the lips, strawberry tongue), OR
     - Conjunctivitis or conjunctival injection (redness of the eyes), OR
     - Extremity findings (e.g., erythema [redness] or edema [swelling] of the hands or feet)
  3. Shock**
  4. Gastrointestinal involvement indicated by:
     - Abdominal pain, OR
     - Vomiting, OR
     - Diarrhea
  5. Hematologic involvement indicated by:
     - Platelet count <150,000 cells/μL, OR
     - Absolute lymphocyte count (ALC) <1,000 cells/μL

**If documented by the clinical treatment team, a final diagnosis of Kawasaki Disease should be considered an alternative diagnosis. These cases should not be reported to national MIS-C surveillance.*
*** Clinician documentation of shock meets this criterion.*

A2. Laboratory Criteria for Reporting

- Detection of SARS-CoV-2 RNA in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen using a diagnostic molecular amplification test (e.g., polymerase chain reaction [PCR]), OR
- Detection of SARS-CoV-2 specific antigen in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen, OR
- Detection of SARS-CoV-2 specific antibodies^ in serum, plasma, or whole blood associated with current illness resulting in or during hospitalization

****Positive molecular or antigen results from self-administered testing using over-the-counter test kits meet laboratory criteria.*
^Includes a positive serology test regardless of COVID-19 vaccination status. Detection of anti-nucleocapsid antibody is indicative of SARS-CoV-2 infection, while anti-spike protein antibody may be induced either by COVID-19 vaccination or by SARS-CoV-2 infection.

A3. Epidemiologic Linkage Criteria for Reporting

Close contact‡ with a confirmed or probable case of COVID-19 disease in the 60 days prior to hospitalization.

‡*Close contact is generally defined as being within 6 feet for at least 15 minutes (cumulative over a 24-hour period). However, it depends on the exposure level and setting; for example, in the setting of an aerosol-generating procedure in healthcare settings without proper personal protective equipment (PPE), this may be defined as any duration.*

A4. Vital Records Criteria for Reporting
A person whose death certificate lists MIS-C or multisystem inflammatory syndrome as an underlying cause of death or a significant condition contributing to death.

B. Disease-specific data elements to be included in the initial report

In addition to patient demographics, the following disease-specific data elements are expected to be included in all reports to public health agencies:

Clinical information
- Date of illness onset
- Date of hospitalization, if applicable
- Date of death, if applicable
- Description of clinical symptoms and signs of illness
- Underlying medical conditions
- COVID-19 vaccination history
- Results of select clinical laboratory and imaging studies
- Complications and secondary diagnoses
- Treatments received

SARS-CoV-2 laboratory information
- Date of SARS-CoV-2 nucleic acid detection, if any
- Date of SARS-CoV-2 antigen detection, if any
- Date and type of SARS-CoV-2 antibody detection, if any (e.g., anti-spike protein antibody, anti-nucleocapsid protein antibody)

Epidemiologic information
- Known close contact to a COVID-19 case

VII. Case Definition for Case Classification

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

A1. Clinical Criteria
An illness in a person aged <21 years characterized by all of the following, in the absence of a more likely alternative diagnosis*:

- Subjective or documented fever (temperature ≥38.0º C)

  AND

- Clinical severity requiring hospitalization or resulting in death

  AND

- Evidence of systemic inflammation indicated by C-reactive protein ≥3.0 mg/dL (30 mg/L)

  AND

- New onset manifestations in at least two of the following categories:
    1. Cardiac involvement indicated by:
        - Left ventricular ejection fraction <55%, OR
        - Coronary artery dilatation, aneurysm, or ectasia, OR
        - Troponin elevated above laboratory normal range, or indicated as elevated in a clinical note
    2. Mucocutaneous involvement indicated by:
        - Rash, OR
        - Inflammation of the oral mucosa (e.g., mucosal erythema or swelling, drying or fissuring of the lips, strawberry tongue), OR
        - Conjunctivitis or conjunctival injection (redness of the eyes), OR
        - Extremity findings (e.g., erythema [redness] or edema [swelling] of the hands or feet)
    3. Shock**
    4. Gastrointestinal involvement indicated by:
        - Abdominal pain, OR
        - Vomiting, OR
        - Diarrhea
    5. Hematologic involvement indicated by:
        - Platelet count <150,000 cells/μL, OR
        - Absolute lymphocyte count (ALC) <1,000 cells/μL

**If documented by the clinical treatment team, a final diagnosis of Kawasaki Disease should be considered an alternative diagnosis. These cases should not be reported to national MIS-C surveillance.*
*** Clinician documentation of shock meets this criterion.*

A2. Laboratory Criteria

Confirmatory laboratory evidence:

- Detection of SARS-CoV-2 RNA in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen using a diagnostic molecular amplification test (e.g., polymerase chain reaction [PCR]), OR
- Detection of SARS-CoV-2 specific antigen in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen, OR
- Detection of SARS-CoV-2 specific antibodies^ in serum, plasma, or whole blood associated with current illness resulting in or during hospitalization

Presumptive laboratory evidence: N/A

Supportive laboratory evidence: N/A

****Positive molecular or antigen results from self-administered testing using over-the-counter test kits meet laboratory criteria.*
^Includes a positive serology test regardless of COVID-19 vaccination status. Detection of anti-nucleocapsid antibody is indicative of SARS-CoV-2 infection, while anti-spike protein antibody may be induced either by COVID-19 vaccination or by SARS-CoV-2 infection.

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.

A3. Epidemiologic Linkage Criteria
Close contact‡ with a confirmed or probable case of COVID-19 disease in the 60 days prior to hospitalization.

‡Close contact is generally defined as being within 6 feet for at least 15 minutes (cumulative over a 24-hour period). However, it depends on the exposure level and setting; for example, in the setting of an aerosol-generating procedure in healthcare settings without proper personal protective equipment (PPE), this may be defined as any duration.

A4. Vital Records Criteria
A person aged <21 years whose death certificate lists MIS-C or multisystem inflammatory syndrome as an underlying cause of death or a significant condition contributing to death.

A5. Case Classifications

Confirmed:
- Meets the clinical criteria AND the confirmatory laboratory evidence.

Probable:
- Meets the clinical criteria AND the epidemiologic linkage criteria.

Suspect:
- Meets the vital records criteria.

Note: For cases initially identified as suspect, jurisdictions may conduct investigation of clinical and laboratory records to determine if confirmed or probable case criteria are met.

Comment: To provide consistency in case classification, review of case information and assignment of final case classification for all suspected MIS-C cases will be done by experts in national MIS-C surveillance.

B. 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
A case should be enumerated as a new case if the person had never previously been enumerated as a case OR if the person was most recently enumerated as a case with illness onset date (if available) or hospital admission date >90 days prior.

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 the 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.

X. Revision History

N/A. This is the first standardized surveillance position statement for MIS-C.

XI. References

1. Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *N Engl J Med* 2020; **383**(4): 334-46.
2. Belay ED, Abrams J, Oster ME, et al. Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic. *JAMA Pediatr* 2021.
3. Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19): HAN00432. 2020.
4. Dufort EM, Koumans EH, Chow EJ, et al. Multisystem Inflammatory Syndrome in Children in New York State. *N Engl J Med* 2020; **383**(4): 347-58.
5. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet* 2020; **395**(10237): 1607-8.
6. Toubiana J, Poirault C, Corsia A, et al. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. *BMJ* 2020; **369**: m2094.
7. Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet* 2020; **395**(10239): 1771-8.
8. Payne AB, Gilani Z, Godfred-Cato S, et al. Incidence of Multisystem Inflammatory Syndrome in Children Among US Persons Infected With SARS-CoV-2. *JAMA Network Open* 2021; **4**(6): e2116420-e.
9. Son MBF, Murray N, Friedman K, et al. Multisystem Inflammatory Syndrome in Children - Initial Therapy and Outcomes. *N Engl J Med* 2021; **385**(1): 23-34.
10. Miller AD, Zambrano LD, Yousaf AR, et al. Multisystem Inflammatory Syndrome in Children-United States, February 2020-July 2021. *Clin Infect Dis* 2021.
11. Geva A, Patel MM, Newhams MM, et al. Data-driven clustering identifies features distinguishing multisystem inflammatory syndrome from acute COVID-19 in children and adolescents. *EClinicalMedicine* 2021; **40**: 101112.
12. Consiglio CR, Cotugno N, Sardh F, et al. The Immunology of Multisystem Inflammatory Syndrome in Children with COVID-19. *Cell* 2020; **183**(4): 968-81 e7.
13. Gotzinger F, Santiago-Garcia B, Noguera-Julian A, et al. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. *Lancet Child Adolesc Health* 2020; **4**(9): 653-61.
14. Godfred-Cato S, Bryant B, Leung J, et al. COVID-19-Associated Multisystem Inflammatory Syndrome in Children - United States, March-July 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69**(32): 1074-80.

15. Godfred-Cato S, Abrams JY, Balachandran N, et al. Distinguishing Multisystem Inflammatory Syndrome in Children From COVID-19, Kawasaki Disease and Toxic Shock Syndrome. *Pediatr Infect Dis J* 2022; **41**(4): 315-23.
16. Castagnoli R, Votto M, Licari A, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents: A Systematic Review. *JAMA Pediatr* 2020; **174**(9): 882-9.
17. Feldstein LR, Tenforde MW, Friedman KG, et al. Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19. *JAMA* 2021; **325**(11): 1074-87.
18. Bowen A, Miller AD, Zambrano LD, et al. Demographic and Clinical Factors Associated With Death Among Persons <21 Years Old With Multisystem Inflammatory Syndrome in Children-United States, February 2020-March 2021. *Open Forum Infect Dis* 2021; **8**(8): ofab388.
19. Lee EH, Kepler KL, Geevarughese A, et al. Race/Ethnicity Among Children With COVID-19-Associated Multisystem Inflammatory Syndrome. *JAMA Netw Open* 2020; **3**(11): e2030280.
20. Javalkar K, Robson VK, Gaffney L, et al. Socioeconomic and Racial and/or Ethnic Disparities in Multisystem Inflammatory Syndrome. *Pediatrics* 2021; **147**(5).
21. LaRovere KL, Riggs BJ, Poussaint TY, et al. Neurologic Involvement in Children and Adolescents Hospitalized in the United States for COVID-19 or Multisystem Inflammatory Syndrome. *JAMA Neurol* 2021; **78**(5): 536-47.

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

Criterion	MIS-C associated with SARS-CoV-2 infection																				
General Clinical Criteria for Reporting																					
Patient age <21 years	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Subjective fever or temperature ≥38.0º C	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Clinical severity requiring hospitalization or resulting in death	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
C-reactive protein ≥3.0 mg/dL (30 mg/L)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Absence of a more likely alternative diagnosis*	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Cardiac Clinical Criteria for Reporting																					
At least one of the following findings: • Left ventricular ejection fraction <55% • Coronary artery dilatation, aneurysm, or ectasia • Troponin elevated above laboratory normal range, or indicated as elevated in a clinical note	N	N	N	N							N	N	N	N							
Mucocutaneous Clinical Criteria for Reporting																					
At least one of the following findings: • Rash • Inflammation of the oral mucosa • Conjunctivitis or conjunctival injection • Extremity findings (e.g., erythema or edema of the hands or feet)	N				N	N	N				N				N	N	N				
Shock Clinical Criteria for Reporting																					
Shock**		N			N			N	N			N			N			N	N		
Gastrointestinal Clinical Criteria for Reporting																					
At least one of the following findings: • Abdominal pain • Vomiting • Diarrhea			N			N		N		N			N			N		N		N	
Hematologic Clinical Criteria for Reporting																					
At least one of the following findings: • Platelet count <150,000 cells/µL • Absolute lymphocyte count <1,000 cells/µL				N			N		N	N				N			N		N	N	
Laboratory Criteria for Reporting																					
Detection of SARS-CoV-2 RNA in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen using a diagnostic molecular amplification test	O	O	O	O	O	O	O	O	O	O											
Detection of SARS-CoV-2 specific antigen in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen	O	O	O	O	O	O	O	O	O	O											

Detection of SARS-CoV-2 specific antibodies^ in serum, plasma, or whole blood associated with current illness resulting in or during hospitalization	O	O	O	O	O	O	O	O	O	O											
Epidemiologic Linkage Criteria for Reporting																					
Close contact‡ with a confirmed or probable case of COVID-19 disease in the 60 days prior to hospitalization											N	N	N	N	N	N	N	N	N	N	
Vital Records Criteria for Reporting																					
A person whose death certificate lists MIS-C or multisystem inflammatory syndrome as an underlying cause of death or a significant condition contributing to death.																					N

Notes:
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=sets of clinical criteria, laboratory criteria, epi linkage criteria, vital records criteria) **in the same column**—in conjunction with all "N" criteria in the same column—is required to report a case.
** If documented by the clinical treatment team, a final diagnosis of Kawasaki Disease should be considered an alternative diagnosis. These cases should not be reported to national MIS-C surveillance.*
*** Clinician documentation of shock meets this criterion.*
****Positive molecular or antigen results from self-administered testing using over-the-counter test kits are considered to meet laboratory criteria.*
^Includes a positive serology test regardless of COVID-19 vaccination status. Detection of anti-nucleocapsid antibody is indicative of SARS-CoV-2 infection, while anti-spike protein antibody may be induced either by COVID-19 vaccination or by SARS-CoV-2 infection.
‡Close contact is generally defined as being within 6 feet for at least 15 minutes (cumulative over a 24-hour period). However, it depends on the exposure level and setting; for example, in the setting of an aerosol-generating procedure in healthcare settings without proper personal protective equipment (PPE), this may be defined as any duration.

Table VII. Classification Table: Criteria for defining a case of MIS-C.

Criterion	**MIS-C associated with SARS-CoV-2 infection**																				
General Clinical Evidence	Confirmed										Probable										Suspect
Patient age <21 years	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Subjective fever or temperature ≥38.0º C	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Clinical severity requiring hospitalization or resulting in death	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
C-reactive protein ≥3.0 mg/dL (30 mg/L)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Absence of a more likely alternative diagnosis*	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Cardiac Clinical Evidence																					
At least one of the following findings: • Left ventricular ejection fraction <55% • Coronary artery dilatation, aneurysm, or ectasia • Troponin elevated above laboratory normal range, or indicated as elevated in a clinical note	N	N	N	N							N	N	N	N							
Mucocutaneous Clinical Evidence																					
At least one of the following findings: • Rash • Inflammation of the oral mucosa • Conjunctivitis or conjunctival injection • Extremity findings (e.g., erythema or edema of the hands or feet)	N				N	N	N				N				N	N	N				

Shock Clinical Evidence																					
Shock**		N			N			N	N			N			N			N	N		
Gastrointestinal Clinical Evidence																					
At least one of the following findings: • Abdominal pain • Vomiting • Diarrhea			N			N		N		N			N			N		N		N	
Hematologic Clinical Evidence																					
At least one of the following findings: • Platelet count <150,000 cells/μL • Absolute lymphocyte count <1,000 cells/μL				N			N		N	N				N			N		N	N	
Laboratory Evidence																					
Detection of SARS-CoV-2 RNA in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen using a diagnostic molecular amplification test	O	O	O	O	O	O	O	O	O	O											
Detection of SARS-CoV-2 specific antigen in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen	O	O	O	O	O	O	O	O	O	O											
Detection of SARS-CoV-2 specific antibodies^ in serum, plasma, or whole blood associated with current illness resulting in or during hospitalization	O	O	O	O	O	O	O	O	O	O											
Epidemiologic Linkage Evidence																					
Close contact‡ with a confirmed or probable case of COVID-19 disease during the 60 days prior to hospitalization											N	N	N	N	N	N	N	N	N	N	
Vital Records Evidence																					
A person whose death certificate lists MIS-C or multisystem inflammatory syndrome as an underlying cause of death or a significant condition contributing to death.																					N
Criteria to distinguish a new case:																					
Person has never previously been enumerated as a case	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
Person was most recently enumerated as a case with illness onset date (if available) or hospital admission date >90 days prior	O	O	O	O	O	O	O	O	O	O	O	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.

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

**If documented by the clinical treatment team, a final diagnosis of Kawasaki Disease should be considered an alternative diagnosis. These cases should not be reported to national MIS-C surveillance.*

*** Clinician documentation of shock meets this criterion.*

****Positive molecular or antigen results from self-administered testing using over-the-counter test kits are considered to meet laboratory criteria.*

^Includes a positive serology test regardless of COVID-19 vaccination status. Detection of anti-nucleocapsid antibody is indicative of SARS-CoV-2 infection, while anti-spike protein antibody may be induced either by COVID-19 vaccination or by SARS-CoV-2 infection.

‡Close contact is generally defined as being within 6 feet for at least 15 minutes (cumulative over a 24-hour period). However, it depends on the exposure level and setting; for example, in the setting of an aerosol-generating procedure in healthcare settings without proper personal protective equipment (PPE), this may be defined as any duration.