16-ID-04

Committee: Infectious Disease

Title: Public Health Reporting and National Notification for Shigellosis

I. Statement of the Problem

Culture-independent diagnostic testing (CIDT), defined as the detection of antigen or nucleic acid sequences of the pathogen, is rapidly being adopted by clinical laboratories. For *Shigella*, these are generally PCR-based testing methods which do not require a stool culture and thus do not yield an isolate. While concerted efforts are being made to ensure reflexive culture is performed at the clinical laboratory or the state public health laboratory, CIDT-positive reports are not always culture-confirmed. In 2011, CSTE updated the *Shigella* case definition, classifying a positive CIDT result that is not culture-confirmed as a suspect case. Further modification of this case definition is needed to address the following three concerns:

1. These suspected cases are not being reported to national surveillance, and the number of positive CIDT reports is growing rapidly, leading to substantial under-ascertainment of laboratory-diagnosed cases.
2. Case definitions for bacterial enteric pathogens are not consistent. In the 2014 CSTE position statement for *Campylobacter*, a CIDT-positive report that is not culture-confirmed is classified as a probable case and is reported to national surveillance.
3. Some of the new multiplex PCR tests report "Shigella/EIEC" as a combined result, which is leading to confusion for disease reporting and case classification purposes and must be addressed.

To prevent an increase in underreporting of shigellosis cases and to make case definitions for enteric bacterial pathogens more consistent, this position statement proposes that:

1. Detection of *Shigella* by CIDT without culture-confirmation be classified as a probable shigellosis case.
2. Since many CIDTs cannot differentiate between *Shigella* and Enteroinvasive *Escherichia coli* (EIEC), detection of *Shigella/*EIEC should also be considered a probable shigellosis case.
3. Illnesses among persons who are epidemiologically linked to a confirmed or laboratory-diagnosed probable case will be classified as probable epidemiologically-linked cases.

II. Background and Justification
Background:

Shigella is among the most commonly reported enteric bacterial pathogens in the United States, causing approximately 500,000 illnesses each year. Transmission occurs through direct or indirect fecal-oral transmission, mainly through person-to-person spread but also through the consumption of contaminated food or water. Approximately 75% of the laboratory-confirmed *Shigella* infections are due to *S. sonnei.*

Shigellosis is characterized by diarrhea, which may be bloody, fever, nausea, and abdominal cramps. Illnesses are usually self-limited and resolve within 5 to 7 days of onset. Outbreaks of shigellosis are common and can be difficult to control, particularly in crowded settings where personal hygiene may be difficult, such as child care facilities, elementary schools, encampments for homeless persons, and prisons. Point-source outbreaks due to contaminated food or water have also occurred.

Although antimicrobial treatment is generally unnecessary for patients with uncomplicated *Shigella* infections, antimicrobials are often used to limit the duration of illness and communicability and to reduce illness severity. However, resistance to the oral antimicrobial medications ampicillin and trimethoprim/sulfamethoxazole is common among *Shigella* in the United States, and resistance to other

antibiotics, including fluoroquinolones is on the rise. In addition, recent reports of U.S. outbreaks caused by Shiga toxin-producing *Shigella sonnei* further impact treatment and surveillance decisions.

Justification:
Surveillance data are essential for monitoring trends and detecting outbreaks. Methods for surveillance must keep pace with changing laboratory diagnostic methods.

- Use of CIDT to detect *Shigella* has increased rapidly at clinical laboratories following FDA approval of several multiplex nucleic acid tests in 2014. As of March 3, 2016, FoodNet data indicate 29/426 (7%) of laboratories in the FoodNet catchment area are using CIDT. FoodNet has detected a 284% increase in the number of positive CIDT reports during 2015 (454 reports) compared with 2012-2014 (average 118/year).
- CIDT *Shigella* positive reports are not always culture-confirmed either because the culture is negative at the clinical or public health laboratory, or because culture was not attempted.
- In 2015, 454 cases of shigellosis positive (+) by CIDT and not culture-confirmed were reported to FoodNet. These cases represent 14% of all reported shigellosis cases in the FoodNet catchment area, which represents 15% of the US population.
- During 2012-2015, FoodNet received reports of 621 *Shigella* CIDT-positive results for which culture was performed. Of those, 70% were confirmed by culture. This proportion varied by the specific CIDT used.
- The current case definition for shigellosis classifies a CIDT-positive result without culture confirmation as a suspect case. These cases are not reported to CDC for use in national surveillance.
- The current (2014) case definition for campylobacteriosis classifies a CIDT-positive result without culture confirmation (PCR or antigen-based testing) as a probable case. These are transmitted to CDC for use in national surveillance.
- Some state health departments have barriers to investigating suspected cases. For example, some have rules that require local jurisdictions to investigate confirmed and select probable cases but not suspected cases. Increasing numbers of positive CIDT results that are non-culture confirmed, could affect outbreak detection and result in missed opportunities for control measures at the local level (such as childcare or worker exclusion).
- As the use of CIDT increases, counting only culture-confirmed cases will grossly undercount total number of laboratory-diagnosed shigellosis cases. Public health case definitions must keep pace or surveillance will suffer.
- Phylogenetic analyses suggest that enteroinvasive *E. coli* (EIEC) and *Shigella* are polyphyletic and also belong to the same genus; some research supports reclassifying *Shigella* as EIEC. Because at least three of the five commercially available multiplex PCR tests used by clinical laboratories cannot distinguish between EIEC and *Shigella*, we propose including diagnoses of "*Shigella*/EIEC" in the case definition for shigellosis.

This position statement proposes that:
1. Detection of *Shigella* by CIDT without culture-confirmation be classified as a probable shigellosis case.
2. Since CIDTs cannot differentiate between *Shigella* and EIEC, detection of *Shigella/*EIEC should also be considered a probable shigellosis case.
3. Illnesses among persons who are epidemiologically linked to a confirmed, or probable case with supportive laboratory evidence, will be classified as probable cases.

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

1. Utilize standard sources (e.g. reporting*) for case ascertainment for shigellosis. Surveillance for shigellosis 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 shigellosis.

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 shigellosis and <u>add</u> shigellosis 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.

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

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.

4. State health departments should create a variable to distinguish CIDT-diagnosed probable shigellosis cases from probable cases that are epidemiologically linked to a culture-confirmed or CIDT-diagnosed case. This differentiation of probable cases will facilitate assessment of the impact of CIDT on surveillance.

5. Likewise, CDC should include a variable to distinguish CIDT-diagnosed probable cases from probable cases that are epidemiologically linked in the disease-specific Message Mapping Guide (MMG), to assess the impact of CIDT on surveillance.

6. State health departments should attempt to capture the type(s) of Shigella testing performed for reported shigellosis cases. This could include surveys of laboratory testing practices, capture of LOINC and SNOMED codes from electronic laboratory reporting, or other methods.

7. When available, *Shigella* serogroup characterization should be reported.

8. Since CIDTs cannot differentiate between *Shigella* and EIEC, detection of *Shigella/*EIEC should also be considered a probable shigellosis case

IV. Goals of Surveillance

To provide information on the temporal, geographic, and demographic occurrence of shigellosis to facilitate its prevention and control.

V. Methods for Surveillance:

Surveillance for shigellosis should use the recommended sources of data and the extent of coverage listed in Table III.

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:

1. Any person with *Shigella spp.* isolated from a clinical specimen.
2. Any person with *Shigella spp.* detected in a clinical specimen using culture-independent diagnostic tests (CIDT).
3. Any person with diarrhea and who is a contact of a shigellosis case or a member of a risk group defined by public health authorities during an outbreak investigation.
4. A person whose healthcare record contains a diagnosis of shigellosis.
5. A person whose death certificate lists shigellosis as a contributing or underlying cause of death.

Other recommended reporting procedures

- All cases of shigellosis should be reported according to state regulations.
- Reporting should be on-going and routine.
- Frequency of reporting should follow the state health department's routine schedule.

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	Shigellosis	
Clinical Evidence		
Clinically compatible illness		N
Healthcare record contains a diagnosis of shigellosis	S	
Death certificate contains shigellosis as a contributing or underlying cause of death	S	
Laboratory Evidence		
Isolation of *Shigella* from a clinical specimen	S	
Detection of *Shigella spp.*or *Shigella*/EIEC in a clinical specimen using a CIDT	S	

Epidemiological Evidence		
Epidemiologically linked to a shigellosis case		O
Member of a risk group as defined by public health authorities during an outbreak investigation		O

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

Clinical Information
- Reported symptoms and signs of illness (e.g. diarrhea, bloody diarrhea, fever)
- Hospitalized

Epidemiological Risk Factors
- International travel in the 7 days prior to onsets
- Occupation/Industry/Place of Business, to include but not limited to:
    - Food handler
    - Child care center worker
    - Long term care facility worker
- Child care attendee
- Long term care facility resident
- Contact of a shigellosis case

Laboratory Information
- Method(s) of laboratory testing (e.g., culture or CIDT [FDA-approved or not FDA-approved PCR or antigen-based test])
- Name of test and manufacturer, as available

VII. Case Definition for Case Classification

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

Clinical Criteria

An illness of variable severity commonly manifested by diarrhea, fever, nausea, cramps and tenesmus. Asymptomatic infections may occur.

Laboratory Criteria

Supportive laboratory evidence: Detection of *Shigella spp.* or *Shigella/*EIEC in a clinical specimen using a CIDT.

Confirmatory laboratory evidence: Isolation of *Shigella spp.* from a clinical specimen.

Epidemiologic Linkage

A clinically compatible case that is epidemiologically linked to a case that meets the supportive or confirmatory laboratory criteria for diagnosis.

Case Classification

> **Confirmed case:** a case that meets the confirmed laboratory criteria for diagnosis.

> **Probable:** a case that meets the supportive laboratory criteria for diagnosis, OR a clinically compatible case that is epidemiologically linked to a case that meets the supportive or confirmatory laboratory criteria for diagnosis.

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 not be counted as a new case if laboratory results were reported within 90 days of a previously reported infection in the same individual.

When two or more different serotypes are identified in one or more specimens from the same individual, each should be reported as a separate case.

Comment:
The use of CIDTs as stand-alone tests for the direct detection of *Shigella/*EIEC in stool is increasing. EIEC is genetically very similar to *Shigella* and will be detected in CIDTs that detect *Shigella*. Specific performance characteristics such as sensitivity, specificity, and positive predictive value of these assays likely depend on the manufacturer and are currently unknown. It is therefore useful to collect information on the type(s) of testing performed for reported shigellosis cases. When a specimen is positive using a CIDT, it is also helpful to collect information on all culture results for the specimen, even if those results are negative.

Culture confirmation of CIDT-positive specimens is ideal, although it might not be practical in all instances. State and local public health agencies should make efforts to encourage reflexive culturing by clinical laboratories that adopt culture-independent methods, should facilitate submission of isolates/clinical material to state public health laboratories, and should be prepared to perform reflexive culture when not performed at the clinical laboratory. Isolates are currently necessary for molecular typing (PFGE and whole genome sequencing) that are essential for outbreak detection and for antimicrobial susceptibility testing, which is increasingly important because of substantial multidrug resistance among *Shigella.*

B. Classification Tables

Table VII-B. Criteria for defining a case of shigellosis.

Criterion	Probable		Confirmed
Clinical Evidence			
Clinically compatible illness	N		
Laboratory evidence			
Detection of *Shigella spp.* or *Shigella*/EIEC in a clinical specimen using a CIDT		N	
Isolation of *Shigella* from a clinical specimen.			N
Epidemiologic evidence			
Epidemiologically linked to a confirmed or probable shigellosis case with laboratory evidence	O		

Member of a risk group as defined by the public health authorities during an outbreak investigation	O		
Criteria to distinguish a new case:			
Not counted as a new case if occurred within 90 days of a previously reported infection in same individual.		N	N
Report separate serotypes as distinct cases.	N		

<div align="right">2016 Template</div>

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 should be ongoing.

IX. Data sharing/release and print criteria

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

- Data will be used to determine the burden of illness due to shigellosis, trends in illness over time, assess the effectiveness of control programs, and monitor progress toward decreasing shigellosis. Data may be used to compare cases across jurisdictions.
- Data may also be used to compare case numbers with information from other foodborne disease surveillance systems.
- Electronic reports of shigellosis cases in NNDSS are summarized weekly in the MMWR Tables. Annual case data on shigellosis is summarized in the yearly Summary of Notifiable Diseases. State-specific compiled data will continue to be published in the weekly and annual MMWR. All cases are verified with the states before publication.
- The frequency of reports/feedback to the states and territories will be dependent on the current epidemiologic situation in the country. Frequency of cases, epidemiologic distribution, importation status transmission risk, and other factors will influence communications.

X. Revision History

Position Statement ID	Section of Document	Revision Description
11-ID-19	Statement of the desired action(s) to be taken	ADDED recommendation that states and CDC add a variable to distinguish between probable cases with laboratory evidence and probable epi-linked cases. ADDED language to include *'Shigella/*EIEC' as a probable case since CIDTs cannot differentiate between *Shigella* and EIEC
11-ID-19	Section VII-A – Laboratory criteria	EDITED Detection of *Shigella spp. or Shigella*/EIEC in a clinical specimen using a CIDT will meet criteria for probable rather than suspect case.

11-ID-19	Table VII-B – Probable laboratory evidence	EDITED Detection of *Shigella* spp. or *Shigella*/EIEC in a clinical specimen using a CIDT will meet criteria for probable rather than suspect case. DELETED suspect case classification.

XI. References

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