# CDC’s Division of STD Prevention Ceftriaxone-Resistant Gonorrhea Outbreak Response Plan Guide

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# **Ceftriaxone-Resistant Gonorrhea Outbreak Response Plan Guide**

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## Purpose and scope of this document

The purpose of this document is to provide guidance to jurisdictions as they develop a Sexually Transmitted Disease Outbreak Response plan specific to a ceftriaxone-resistant gonorrhea outbreak. This document is intended to be used in conjunction with CDC’s Division of STD Prevention’s Sexually Transmitted Disease Outbreak Response Plan Guide. Whereas the Outbreak Response Plan Guide provides overarching guidance and considerations for developing an STD outbreak response plan, this document focuses on guidance and considerations unique to ceftriaxone-resistant gonorrhea outbreaks. This guidance is not meant to be prescriptive, but rather is meant to (1) highlight content areas and considerations that jurisdictions might choose to address in local plans and (2) spur discussions within health departments as response plans are bring crafted.

This document includes guidance on objectives and scope of a ceftriaxone-resistant gonorrhea outbreak response plan, including approaches to enhance identification of an outbreak and public health response activities to consider in the setting of the local identification of one or more cases.

## Outline for Ceftriaxone-Resistant Gonorrhea Outbreak Response Plan

1. Objectives
2. Outbreak preparedness
   1. Activation of outbreak response plan
      1. Considerations for enhancing local surveillance for ceftriaxone-resistant gonorrhea
      2. Working case definition
   2. Roles and responsibilities
   3. Additional staffing and resource capacity
   4. Data security
   5. Communication plan
   6. Identify partnerships and collaborations
3. Considerations for managing a response
   1. Management structure and staffing mix
   2. Informing, coordinating, and engaging with partners
   3. Prioritization of disease
4. Outbreak investigation and response
   1. Determine the existence of an outbreak
   2. Verify the diagnoses
   3. Establish a case definition and find cases
   4. Describe the data in terms of person, place, and time
   5. Determine who is at risk of becoming ill
   6. Data analysis and study design
   7. Implement prevention and control measures
5. Considerations for the recovery phase
6. Appendices
   1. Definitions

## Objectives of a Ceftriaxone-Resistant Outbreak Response Plan

Pro-active development of a comprehensive and well-designed ceftriaxone-resistant gonorrhea outbreak response plan, prior to identification of an outbreak, may allow a jurisdiction to

* Enhance systems to identify ceftriaxone-resistant infections in a timely manner
* Take steps to prepare for an outbreak well in advance of an actual event
* Identify gaps that can be addressed prior to an actual event
* Efficiently and rapidly organize and manage staffing and logistical support in the event of an outbreak
* Efficiently and rapidly respond to an outbreak to halt spread of disease

These plan objectives are explained in further detail on the pages hereafter.

## Outbreak Preparedness

Actions taken to enhance preparedness and bolster local surveillance may increase the likelihood of detecting a ceftriaxone-resistant gonococcal infection in a timely manner and may improve the efficiency and effectiveness of a subsequent outbreak response. Preparedness efforts, prior to an outbreak, can also include development of systems, capabilities, partnerships, or materials that may be utilized during an outbreak.

While the overall preparedness for ceftriaxone-resistant gonorrhea outbreaks are similar to any STD outbreak as described in the “STD Outbreak Response Plan Guide,” unique considerations are described below.

### **2.a.** Activation of the Outbreak Response Plan

See CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general discussion of when to activate the plan. Specific considerations for ceftriaxone-resistant gonorrhea outbreaks include:

#### Enhancing local surveillance for ceftriaxone-resistant gonorrhea

While technically not part of outbreak response, enhanced surveillance may assist local jurisdictions with timely detection of an outbreak, which will both trigger a response and, particularly if detection is timely, may increase the likelihood of an effective response.

##### Laboratory-based surveillance

* Jurisdictions may want to consider establishing ongoing surveillance of local *N. gonorrhoeae* antibiotic susceptibility patterns through the routine collection of specimens for *N. gonorrhoeae* culture and local performance of antibiotic susceptibility testing (AST). Jurisdictions may already participate in such surveillance activities as part of CDC’s GISP (Gonococcal Isolate Surveillance Project), eGISP (enhanced-GISP) programs, or SURRG (Strengthening US Response for Resistant Gonorrhea) initiatives.
* Even without ongoing surveillance via AST, jurisdictions can consider identifying local laboratories (public, academic, or commercial) with the capacity to conduct *N. gonorrhoeae* culture and AST in the case of suspected treatment failures and/or ARGC outbreaks. In the absence of such capacity, jurisdictions can consider building up such capacity at a local or state public health laboratory and/or develop memoranda of understanding with other laboratories to provide such capacity. Jurisdictions can also determine whether laboratories that can conduct culture and AST are able and willing to receive specimens from local providers.
* Community healthcare providers may not have ready access to supplies for collecting specimens for culture (such as culture plates). Jurisdictions are encouraged to provide guidance or identify strategies to increasing provider access to these culture collection supplies, and provide guidance or establish strategies for rapid transport of specimens to a laboratory that can conduct culture/AST.
* Jurisdictions can develop systems or partnerships to ensure that local laboratories that conduct AST will rapidly notify the health department STD program of isolates with elevated ceftriaxone minimum inhibitory concentrations (MICs).
* CDC is interested in exploring the use of molecular surveillance in the setting of an outbreak to define the scope and scale of the outbreak. This might involve the local development or validation of a molecular probe and associated primers that can be implemented on a real-time PCR to look for one or more specific molecular markers of ceftriaxone resistance using remnant nucleic acid amplification test (NAAT) specimens. Jurisdictions can consider collaborating with CDC to implement and/or pilot molecular surveillance. Molecular surveillance may facilitate identification of resistant infections without relying on performance of GC culture and AST.

##### Treatment failure-based surveillance

* Jurisdictions can consider establishing systems to allow providers to rapidly and easily report possible gonorrhea treatment failures to the health department STD program, including the identification of a single phone number or point of contact. Jurisdictions can determine whether reporting systems will be available after-hours and on weekends and holidays. Jurisdictions can determine if and how to make clinicians aware of the established system.
* Jurisdictions can consider developing a protocol for managing possible gonorrhea treatment failures, including:
  + Developing a set of questions that a designated point of contact will use to ascertain critical information from providers about possible treatment failures (e.g., recent testing across exposed anatomic sites, recent treatment, recent sexual history/possible re-exposure, and recent travel)
  + Guidance to clinicians on specimen collection for culture and AST, including what supplies are needed, how to obtain necessary supplies, how to collect samples, and to what laboratory to transport specimens for culture and AST.
  + Guidance for local STD clinics regarding specimen collection, as STD clinics may also be a resource for the collection of specimens for culture and AST
  + Specific roles and responsibilities for health department staff in regards to clinical management of suspected treatment failure cases, ensuring provider access to specimen collection materials, proper transport of the inoculated culture media to an appropriate laboratory for culture and AST, interpretation of AST results, and communication of AST results (with accurate interpretation and guidance on management) to relevant persons.
* Jurisdictions can develop systems to collect and manage data on suspected treatment failures so that data can be easily analyzed.
* Jurisdictions may want also to consider establishing systems to implement and track tests of cure (TOC) at the STD clinic if enhanced emphasis or recommendations for TOC are issues in an outbreak setting.

#### Developing a working case definition

Development of at least preliminary working case definitions can inform planned approaches to preparedness and surveillance, identification of an outbreak, and activation of a response plan.

Identification of a single case of ceftriaxone-resistant gonorrhea has substantial local, national, and international public health implications; jurisdictions may determine that identification of a single case of ceftriaxone-resistant gonorrhea constitutes an outbreak. Jurisdictions may want to consider case definitions based on clinical criteria (e.g., treatment failure to recommended therapy), laboratory criteria (e.g., ceftriaxone MICs ≥0.5 µg/ml), or both.

Currently, there are no fully agreed-upon definitions of ceftriaxone-resistant *Neisseria gonorrhoeae*, multidrug-resistant (MDR) gonorrhea, or extensively drug-resistant (XDR) gonorrhea. There is also a lack of data on the ceftriaxone MIC threshold that predicts unsuccessful clinical cure after treatment with CDC-recommended therapy. Available data from case reports suggest that ceftriaxone MICs ≥0.5 µg/ml may be associated with unsuccessful treatment; this MIC threshold is consistent with the Clinical and Laboratory Standards Institute (CLSI) interpretation of ceftriaxone MIC of ≤0.25 µg/ml as susceptible (and ≥0.5 µg/ml as non-susceptible).

Although there are limited data on the ceftriaxone MIC threshold that predicts unsuccessful clinical cure after treatment with CDC-recommended therapy, local jurisdictions are encouraged to develop local working case definitions for resistant infections that will trigger a local response plan.

The cephalosporin-resistant gonorrhea classifications noted below in Textbox A were adapted from CDC’s [Cephalosporin-Resistant *Neisseria gonorrhoeae* Public Health Response Plan](https://www.cdc.gov/std/treatment/Ceph-R-ResponsePlanJuly30-2012.pdf) (August, 2012) and may provide a starting point for local decision-making. Please note: Since release of CDC’s Public Health Response Plan in 2012, recent case reports have suggested that treatment failures after ceftriaxone-based treatment have been associated with ceftriaxone MICs of ≥0.5 µg/ml.

##### Textbox A

|  |
| --- |
| **Suspect Case**  A suspect case fulfills either the clinical criteria or laboratory criteria described below:  **Clinical Criteria**  The patient experienced possible treatment failure with the following specific components: |
| * + Patient had laboratory-confirmed *N. gonorrhoeae* infection, and   + Patient received CDC-recommended ceftriaxone-based antimicrobial regimen as treatment, and   + Patient subsequently had a positive *N. gonorrhoeae* test result (positive culture ≥72 hours after treatment or positive NAAT ≥8 days after treatment), and   + Patient did not engage in sexual activity after treatment   OR |

**Laboratory Criteria:**Antimicrobial susceptibility testing (AST) of pre-treatment or post-treatment isolate demonstrates ceftriaxone MIC ≥0.125 µg/ml

|  |
| --- |
| **Probable Case** A probable case fulfills the clinical criteria *and* laboratory criteria described below:  **Clinical Criteria and Laboratory Criteria** The patient experienced possible treatment failure with the following specific components: |
| * Patient had laboratory-confirmed *N. gonorrhoeae* infection, and * Patient received CDC-recommended ceftriaxone-based antimicrobial regimen as treatment, and * Patient subsequently had a positive *N. gonorrhoeae* test result (positive culture ≥72 hours after treatment or positive NAAT ≥8 days after treatment), and * Patient did not engage in sexual activity after treatment * AST of pre-treatment or post-treatment *N. gonorrhoeae* isolate demonstrates ceftriaxone MIC of ≥0.25 μg/ml |

**Please note: Jurisdictions are strongly encouraged to promptly notify CDC of any suspected or probable ceftriaxone-resistant infections at (404) 718-5447.** CDC can provide the jurisdiction with guidance on treatment and response and can assist with coordination across states. CDC will also communicate critical information about the outbreak within the US Government and when appropriate, to international partners. Additional information is available at https://www.cdc.gov/std/gonorrhea/arg/basic.htm.

### **2.b.** Roles and responsibilities

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to roles and responsibilities. When planning for an ARGC outbreak, jurisdictions may want to further describe specific roles and responsibilities in advance, such as the incident commander, epidemiology, laboratory, surveillance, partner services, STD clinic operations and clinical care, communication, finance, training, and operations. Responsibilities that may be unique to a ceftriaxone-resistant gonorrhea outbreak include

* Clinical history taking, work-up, specimen collection, and treatment
* Laboratory specimen collection, transport, and testing oversight

An example of a ceftriaxone-resistant gonorrhea response structure with specific defined roles and responsibilities is included in Appendix B.

### **2.c.** Additional staffing and resource capacity

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to additional staffing and resource capacity. Specific questions to consider for ceftriaxone-resistant gonorrhea outbreaks are listed below:

#### Laboratory staffing and supplies

* What are the available STD laboratory services and what is the workload capacity of the current laboratory workforce?
* What are the culture and antibiotic testing capabilities for the public health and other local laboratories?
* What is the estimated maximum workload (such as the number of cultures that can be processed or isolates that can undergo AST in a timely manner) of the laboratory staff?
* What additional laboratory supplies may be needed in an outbreak situation (e.g., culture collection and AST supplies including culture plates and media, culture collection transport systems, such as ESwab or Intray, specimen collection swabs, Etest™ AST strips, shipping supplies), and can they be procured quickly when needed?
* Does routine courier service exist between local STD clinic and lab that will be performing culture and AST?
* If considering molecular surveillance as part of an outbreak response (e.g., testing remnant NAAT specimens to detect molecular markers of antibiotic resistance observed in the outbreak strain), jurisdiction may want to consider these additional questions:
  + Is there capacity at the public health laboratory (PHL) or perhaps a local university lab to conduct requisite molecular testing (e.g., access to real-time PCR, capacity to develop and/or validate and run a molecular probe, staffing to coordinate collection of remnant NAAT specimens, staffing to extract DNA from remnant NAAT specimens, staffing for related coordination roles).
  + What additional staffing resources and/or relationships with other health care facilities or labs may be needed (perhaps in advance of an outbreak) to coordinate access to remnant NAAT specimens (perhaps from multiple labs) to use for the molecular surveillance, and perform associated tracking?

#### Clinical services

* Which healthcare settings are currently able to collect specimens for and/or perform GC culture and/or AST for *N. gonorrhoeae*? What is the maximum patient volume that these settings could handle if there was an outbreak?
* Which healthcare settings stock ceftriaxone and can treat patients diagnosed with gonorrhea?
* Which healthcare settings stock and can administer intramuscular gentamicin?
* If needed for very rare instances of extensively drug-resistant infections, which area hospitals could administer an IV antibiotic to patients diagnosed with gonorrhea?
* Are other healthcare settings able to rapidly establish culture for *N. gonorrhoeae* or offer gonorrhea NAAT testing if there was an outbreak?

### **2.d.** Data security

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to data security.

### **2.e.** Communications Plan

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to communication. CDC has developed a Health Alert HAN template for gonorrhea with reduced susceptibility available at <https://www.cdc.gov/std/program/outbreakresources/HANtemplate-gono.htm>. In preparing a ceftriaxone-resistant gonorrhea outbreak plan, jurisdictions may want to consider drafting a HAN template to report on a gonorrhea case(s) with known ceftriaxone resistance and treatment failure with recommended treatment, or draft outbreak-related messages to key populations.

### **2.f.** Identify partnerships and collaborations

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to partnerships and collaborations. Additional partnerships that a jurisdiction can consider strengthening or developing to respond to a ceftriaxone-resistant gonorrhea outbreak include:

* Local hospital that could administer IM gentamicin (or an IV antibiotic if recommended by CDC)
* Local laboratories for GC culture, AST, molecular detection, and access to remnant NAAT specimens for molecular detection
* Key healthcare providers (e.g., those serving large numbers of at-risk populations, such as MSM)
* Community-based organizations
* Local businesses serving at-risk populations (e.g., massage parlors or bath houses)
* Professional provider organizations
* Local laboratories
* National Network of STD Clinical Prevention Training Centers <https://nnptc.org/>

## Considerations for Managing a Response

This section covers several aspects of managing and conducting a response. This section is not meant to be template for how to conduct a response nor is it meant to be comprehensive of all aspects to consider. Rather, it is meant to highlight a few selected aspects that might be overlooked and/or are aspects of an outbreak response that might be unique to a ceftriaxone-resistant gonorrhea outbreak.

### **3.a.** Management Structure

Jurisdictions may also wish to outline whether (or under what circumstances) an incident command structure (ICS) will be established to manage a ceftriaxone-resistant gonorrhea outbreak response, and will it be established at the state and/or local level. Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to management structure.

### **3.b.** Informing, Coordinating, and Engaging with Partners

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to communication.

### **3.c.** Prioritization of disease

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to disease prioritization. In many jurisdictions DIS do not typically investigate gonorrhea cases. Jurisdictions should consider how they will quickly pivot DIS staff to focus on cases of resistant gonorrhea and/or provide updated training and support for DIS staff who may not be as familiar with gonorrhea investigations, ceftriaxone, and/or who may need to encourage and facilitate patient access to antibiotic susceptibility testing and/or tests of cure.

## Outbreak Investigation and Response

This section is not meant to be template for how to conduct a response nor is it meant to be comprehensive of all aspects to consider. Rather, it is meant to highlight a few selected aspects that might be overlooked and/or are aspects of an outbreak response that might be unique to a ceftriaxone-resistant gonorrhea outbreak.

### **4.a.** Determine the existence of an outbreak

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to determining the existence of an outbreak. See also section 2a. above on “Activation of the Outbreak Response Plan” for specific considerations for a ceftriaxone-resistant gonorrhea outbreak.

### **4b.** Verify the diagnoses

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to verifying the diagnoses. Ceftriaxone resistance can be verified via clinical examination and laboratory testing. When a patient presents with what is suspected to be treatment failure after recommended therapy, providers are encouraged to

* Ask the patient about sexual exposure following treatment (to investigate whether the patient may have been re-infected)
* Test for other STDs that may be causing persistent symptoms
* Collect specimens for culture and AST to determine the bacterial antimicrobial susceptibility profile.

### **4c.** Establish a case definition and find cases

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to establishing a case definition and finding cases. See also section 2a. above on “Developing a working case definition” for specific considerations for a ceftriaxone-resistant gonorrhea outbreak.

### **4d.** Describe the data in terms of time, place, and person

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to describing data.

### **4e.** Determine who is at risk of becoming ill

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to determining who is at risk.

### **4f.** Data analysis and Study Design

Jurisdictions may opt to outline planned epidemiological investigations and data analyses so that any new collection of supplemental epidemiological data or use of existing data sources can be conducted efficiently. Such analyses might include description of factors associated with ceftriaxone-resistant infection, such as demographics, recent travel to a specific location or recent sex with partners who traveled to a specific location, recent sex with commercial sex workers, common locations for finding partners, or geographical location of residence. Plotting of an epidemic curve and mapping of cases may provide insights into the outbreak.

### **4i.** Implement prevention and control measures

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to prevention and control measures. Below are some specific considerations for ceftriaxone-resistant gonorrhea outbreaks.

#### Clinical management of cases and sexual partners

A foundational element of an outbreak response and control efforts is likely to be clinical management of the cases and the cases’ recent sex partners. Please refer to [CDC’s STD Treatment Guidelines](https://www.cdc.gov/std/treatment/default.htm) for the latest treatment recommendations. Jurisdictions are encouraged to outline in the response plan the planned steps in clinical management of cases and partners. When developing these planned steps, jurisdictions should be aware that there remains uncertainty about the optimal approaches to testing and treating persons with ceftriaxone-resistant infections. CDC is invested in being a resource to local and state STD programs and in assisting with clinical decision-making (such as providing guidance on treatment and re-testing).

Clinicians who diagnose *N. gonorrhoeae* in a patient with suspected treatment failure should: perform specimen collection for culture and AST of relevant clinical specimens from all potentially exposed anatomic sites prior to retreatment; consult an infectious-disease specialist, STD/HIV Prevention Training Center ([www.nnptc.org](http://www.nnptc.org)), and/or CDC (Sancta St Cyr: 404.718.5447, oew3@cdc.gov) for guidance in clinical management; and report the case to CDC through state and local public health department authorities within 24 hours. Because many suspected treatment failures in the United States are due to re-infection, any suspected treatment failures should first be retreated with CDC recommended antimicrobial therapy. In cases in which treatment failure is suspected, especially if supported by AST results suggesting resistance, dual therapy with single doses of intramuscular gentamicin 240 mg plus oral azithromycin 2 g can be considered. This regimen may not successfully cure pharyngeal infections, however. A TOC with NAAT and culture at relevant clinical sites should be performed 7–14 days after retreatment. Jurisdictions may want to consider how TOC activities will be implemented and monitored in an outbreak situation.

CDC requests to be involved in decision-making regarding treatment if the above treatment options are not feasible or are unsuccessful. CDC’s Neisseria Reference Laboratory requests that isolates from infections that do not respond to CDC-recommended therapy also be sent to CDC for confirmatory testing and further characterization, including whole genome sequencing (<https://www.cdc.gov/std/gonorrhea/arg/basic.htm>).

Clinicians should ensure that the patient’s sex partners within the 60 days preceding onset of symptoms or gonorrhea diagnosis are ideally evaluated with culture and AST and presumptively treated ideally using the same regimen that successfully treated the patient. Health departments should prioritize notification and culture evaluation for the patient’s sex partner(s) from the preceding 60 days for those with suspected cephalosporin treatment failure or persons whose gonococcal isolates demonstrate reduced susceptibility to cephalosporins. In the setting of an outbreak of ceftriaxone-resistant gonorrhea, jurisdictions might opt to conduct TOC for all infected sexual partners (even if culture and AST were not able to be performed). If appropriate based on local conditions and resources, patients and partners may be offered other sexual health services, such as referral for HIV pre-exposure prophylaxis.

#### Laboratory activities

In a ceftriaxone-resistant gonorrhea outbreak situation, local or state public health laboratories may process NAAT specimens, specimens collected for culture, and perform AST (likely via Etest™). SOPs and validation studies for conducting *N. gonorrhoeae* culture and AST should ideally be completed prior to an outbreak. However, outbreak plans could include details on how to build up this capacity quickly if needed. If public health laboratories do not have the capacity to perform AST, the jurisdiction can identify another laboratory where AST can be performed and consider establishing in advance an MOU or other arrangement for rapid processing of specimens and communicating results.

It may be particularly useful in advance of an outbreak to develop a specimen flow diagram that includes NAAT and culture specimen collection and processing in health centers (or the field), specimen transport, specimen isolation and performance of AST.

Jurisdictions may opt to ask that laboratories store isolates collected during an outbreak of ceftriaxone-resistant gonorrhea, particularly those demonstrating reduced susceptibility to ceftriaxone. As noted above, CDC’s Neisseria Reference Laboratory in the Laboratory Reference and Research Branch (LRRB) requests that isolates from infections that do not respond to CDC-recommended therapy or and/or isolates demonstrating reduced susceptibility or resistance to a cephalosporin (e.g., ceftriaxone MIC ≥0.125µg/mL) also be sent to CDC for confirmatory testing and further characterization (e.g., molecular characterization) (<https://www.cdc.gov/std/gonorrhea/arg/basic.htm>), which may assist the outbreak response.

As noted above (under *Laboratory-Based Surveillance*), CDC is interested in exploring the use of molecular surveillance in the setting of an outbreak to identify define the scope and scale of the outbreak and potentially identifying additional cases. This might involve the local development or validation of a molecular probe and associated primers that can be implemented on a real-time PCR to look for one or more specific molecular markers of antibiotic resistance using remnant NAAT specimens. It also may involve coordinating access to remnant GC-positive NAATs (potentially from area public health labs in addition to other laboratories that process NAATs locally), extracting DNA from these remnant NAATs, and performing the molecular assay.Jurisdictions can consider collaborating with CDC to implement molecular surveillance.

#### Field Investigations and Partner Services

Field investigations and partner services are an important component of all STD outbreak control activities. These activities may include conducting epidemiological interviews and eliciting partners from cases, as well as partner notification, facilitation of appropriate treatment, testing and culturing, and test of cure visits for cases and their sexual contacts. Partner services can be particularly challenging when case-patients report high numbers of anonymous sexual partners or are reluctant to share names and locating information of sexual partners. As part of a ceftriaxone-resistant gonorrhea outbreak response plan, jurisdictions may want to consider how field investigations and partner services activities will be rolled out. Some questions about how such investigation protocols might differ from routine STD field investigations to consider include:

* What questions should DIS ask of cases
  + Traditional questions such as names and contact information for recent sexual partners, duration of partnerships, where patients found their partners, etc.
  + Ceftriaxone-resistant gonorrhea specific questions such as recent travel history of cases and their sex partners
* How and where will contacts be referred for testing, culturing, and treatment?
* How should information about ceftriaxone-resistant gonorrhea, the importance of naming sexual partners to prevent further spread of resistant infections, the importance of getting care at a location where specimens can be collected for culture, and the importance of a test of cure be communicated to cases and their sexual contacts?
* How many attempts at contacting cases and sexual contacts should be made and within what time frame?
* Where will field investigation data be stored?
* Will DIS hold case conferences?
* How will out of jurisdiction and/or out of state partners be handled?

#### Implementation of other control measures

Jurisdictions can consider whether additional control measures will be implemented and under what conditions. Additional measures to consider might include enhanced screening, expanded collection of specimens for culture, expanded clinic hours or establishment of healthcare settings that can provide additional testing and treatment, education around GC and promotion of condom use, enhanced partner services approaches (such as the investigation of partners of partners), expanded outreach and messaging to key providers or at-risk populations, implementation of molecular surveillance using remnant NAATs, or expansion of test of cure (TOC) recommendations (such as implementation of routine TOC in a selected subset or all patients with gonorrhea).

## Considerations for the Recovery Phase

Refer to CDC’s [STD Outbreak Response Plan Guide](https://www.cdc.gov/std/program/outbreakresources/outbreak-response-plan-guide.pdf) for general considerations related to considerations for the recovery phase and an example of a simple after action report.

The debrief or after-action meeting following a ceftriaxone-resistant gonorrhea outbreak can be a platform for discussing the response, identifying successes and challenges, and identifying opportunities for enhanced surveillance, and/or modifications to routine testing, treatment and test of cure activities, and to improve future responses and refine the outbreak response plan.

Specifically following a ceftriaxone-resistant gonorrhea outbreak, jurisdictions may want to consider evaluating: how long it took to establish systems for laboratory culture, AST, and possibly molecular surveillance; how long it took for laboratory results to reach providers and health department staff; how effective were partner services in locating, testing and treating sexual partners; what aspects of communication to the public, providers and media worked well and what could be improved)

## Appendix A

### Definitions

#### Antibiotic

A medicine that kills or inhibits the growth of bacteria. In medical usage, antibiotics refer specifically to antibacterial medicines that are produced naturally by a microorganism (such as penicillin).

#### Antibiotic-Resistant Gonorrhea (ARGC)

A general designation of a gonococcal infection that demonstrates resistance to at least one antimicrobial agent.While a useful term for communicating with the general public, the clinical and public health importance of the infection is better conveyed to providers and public health officials by labeling the infection with the specific antimicrobials to which the infection is resistant (such as ceftriaxone-resistant *Neisseria gonorrhoeae; see below*)

#### Antimicrobial

A broad category of medicines that kill or inhibit the growth of microorganisms, and includes antibacterials, antivirals, and antifungals. Antimicrobials can be produced naturally by a microorganism (referred to as antibiotics) or can be synthetically produced. “Antimicrobial” is more precise than “antibiotic” when describing cefixime, ceftriaxone, and azithromycin; however, “antimicrobial” and “antibiotic” are often used interchangeably.

#### Antibiotic Susceptibility Testing (AST)

Laboratory testing of live bacteria (isolates) that involves exposing bacteria to a series of concentrations of antimicrobials. AST is used to determine which antibiotics and at which antibiotic concentration keep a particular gonococcal infection from growing on an agar plate. Types of *N. gonorrhoeae* AST include disc diffusion, gradient strip testing such as Etest™, and agar dilution. Bacteria are considered to be susceptible to an antimicrobial agent if the bacteria do not grow in the presence of antibiotic. If bacteria grow in the presence of antibiotic, the bacteria may have reduced susceptibility to the antimicrobial agent.

#### ARLN

The Antimicrobial Regional Laboratory Network is a network of regional public health laboratories equipped to respond to emerging health threats and provide cutting-edge antimicrobial resistance laboratory support. The ARLN has capacity for culture-based antimicrobial susceptibility testing and genomic sequencing.

#### Azithromycin

A widely-used and broad-spectrum macrolide antimicrobial that is recommended for treatment of chlamydia and that was previously recommended to be administered with ceftriaxone for treatment of gonorrhea. Common brands names include Zithromax, AzaSite, and Zmax, and is often prescribed for other infectious conditions as a multiday Zpack.

#### CDC

The Centers for Disease Control and Prevention, a federal agency in the Department of Health and Human Services, provide management and financial support for the SURRG program, lead national surveillance of gonococcal resistance, and publish national treatment guidelines for STDs, including gonorrhea.

#### Cefixime

An oral cephalosporin antimicrobial that was listed as an alternative treatment for gonorrhea in CDC’s update to Treatment Guidelines for Gonococcal Infection, 2020. Until 2012, cefixime was a recommended treatment for gonorrhea. A common brand name of cefixime is Suprax.

#### Ceftriaxone

An injectable cephalosporin antimicrobial that can be delivered intramuscularly or intravenously. Ceftriaxone is the recommended treatment for gonorrhea. A common brand name is Rocephin.

#### Ceftriaxone-Resistant *Neisseria gonorrhoeae*

Although widely-agreed upon criteria for ceftriaxone resistance are lacking, preliminary/working criteria include a gonococcal infection that demonstrates laboratory-based antimicrobial resistance (as evidenced by substantially elevated minimum inhibitory concentrations by AST, such as MICs ≥1.0 µg/ml) and which may have been unsuccessfully treated with recommended ceftriaxone-based therapy.

#### Cephalosporin

A large group of broad-spectrum antimicrobials that function by inhibition of bacterial cell wall synthesis. The cephalosporin class includes third-generation cephalosporins ceftriaxone and cefixime.

#### Culture

A laboratory method of growing bacteria by letting them reproduce in culture medium under controlled laboratory conditions. Bacterial cultures are used to determine the type of organism, the abundance of organisms in the sample, and the viability of the organism (can help distinguish an active gonococcal infection from residual DNA [detected by NAAT] from a successfully treated infection). *N. gonorrhoeae* culture provides a specimen for antibiotic susceptibility testing (AST).

#### Disease Intervention Specialists (DIS)

A backbone of public health in the United States, DIS confirm treatment, conduct patient interviews, provide patient counseling, conduct partner services (locate sexual partners to cases and link them to testing and treatment), and provide a growing number of other critical public health services, such as linkage to HIV care.

#### eGISP

The Enhanced Gonococcal Isolate Surveillance Project strengthens surveillance of resistant gonorrhea and increases state and local capacity to detect and monitor it. In select STD clinics, eGISP collects samples from men with gonococcal urethritis as well as from women and extragenital sites. These specimens are sent to regional laboratories for susceptibility testing.

#### Eswab

A collection and transport system that maintains viability of bacteria at room and refrigerator temperature for up to 48 hours prior.

#### Etest

Epsilometer **test** (**Etest™**) is an ‘exponential gradient’ method of determining of antimicrobial susceptibility. Etest™ consists of a predefined gradient of antibiotic concentrations on a plastic strip and is used to determine the minimum inhibitory concentration (MIC) of antibiotics.

#### GISP

The Gonococcal Isolate Surveillance Project monitors U.S. antibiotic resistance trends in gonorrhea. Through the collaborative effort of selected STD clinics and their local laboratories, regional laboratories, and CDC, GISP data helps ensure gonorrhea receives the right antibiotic treatment. GISP monitors antimicrobial susceptibility of approximately 5,000 male gonococcal urethritis cases seen in ~26 STD clinics.

#### Health Alert Network (HAN)

CDC’s Health Alert Network (HAN) is CDC’s primary method of sharing cleared information about urgent public health incidents with public information officers; federal, state, territorial, tribal, and local public health practitioners; clinicians; and public health laboratories.

#### Incident Command Structure (ICS)

An incident management structure is a predetermined organizational structure used to manage the planning, operational, logistical, financial, and administrative components of an outbreak event. The ICS is an essential tool for command, control, and coordination of resources during an outbreak.

#### Multidrug Resistance/Extensively Drug Resistance

[Multidrug resistance is antimicrobial resistance](https://en.wikipedia.org/wiki/Antimicrobial_resistance) shown by a species of [microorganism](https://en.wikipedia.org/wiki/Microorganism), such as bacteria, to multiple [antimicrobial](https://en.wikipedia.org/wiki/Antimicrobial) drugs. Extensively drug-resistance (XDR) is a rare type of multidrug-resistance in which bacteria are resistant to first- and second-line treatment options.

#### Minimum inhibitory concentrations (MICs)

The lowest antibiotic concentration that inhibits visible growth of bacteria in the laboratory. AST by Etest™ and agar dilution generate results in MICs.

#### Nucleic Acid Amplification Testing (NAAT)

Nucleic acid amplification testing is a laboratory technique that can detect very small amounts of DNA or RNA in test samples. NAATs test this DNA or RNA to identify specific bacteria, such as *N. gonorrhoeae* and *C. trachomatis*.

#### SURRG

Strengthening the U.S. Response to Resistant Gonorrhea began in 2016 with three goals: 1) enhance domestic antibiotic-resistant gonorrhea surveillance and infrastructure; 2) build capacity for rapid detection and response to resistant gonorrhea through increased culturing and local antibiotic susceptibility testing; and 3) conduct rapid field investigations to stop the spread of resistant infections. The project also aims to gain a better understanding of the epidemiological factors contributing to resistant gonorrhea. As of 2020, eight jurisdictions collected specimens, performed local antibiotic susceptibility testing, and analyzed data as part of SURRG, helping guide national recommendations for the public health response to resistant gonorrhea.

#### Test-of-Cure (TOC)

Repeat testing for gonorrhea, either by nucleic acid amplification testing (NAAT) or culture performed within two weeks of diagnosis and treatment, to ensure that an infection was cured. TOC can identify treatment failures in asymptomatic patients.

#### Treatment failure

Unsuccessful treatment of gonorrhea despite administration of CDC-recommended treatment with ceftriaxone. Treatment failure may be evident clinically through persistence of symptoms despite treatment, or may be evident through retesting of patients with asymptomatic gonococcal infections.

## Appendix B: Example Roles and Responsibilities

Example of potential roles and responsibilities to include for an ARGC outbreak response, adapted from the Indiana State Department of Health ARGC Outbreak Response Plan

* **Surveillance**: The Surveillance Manager (identify staff/position to fill role) will
  + Store, clean, and ensure security of case data
  + Analyze ARGC case data
  + Provide epidemiology updates to the Incident Commander as needed
  + Define roles for their team members as needed
  + The Surveillance support team may include
    - County epidemiologists
    - Data entry technicians
* **Clinic:** The Clinic Manager (identify staff/position to fill role) will
  + Ensure collection of GC specimens at the STD clinic and non-STD clinic partner sites
  + Ensure collection guidelines are being followed by appropriate staff and evaluate difficult processes for areas of improvement
  + Provide policy on specimen collection technique and transportation to all relevant clinical staff
  + Report any potential treatment failures seen by their assistant managers directly to the Incident Commander
  + Define roles for their team members as needed
  + The Clinic support team may include
    - Assistant Clinic Managers and all other clinical providers at each clinic site (list all relevant sites).
* **Laboratory**: The Laboratory Manager (identify staff/position to fill role) will
  + Oversee the transporting, receiving, processing, and resulting of gonorrhea samples submitted by specified sites
  + Supervise the AST lab technician who performs the identification and AST testing for N. gonorrhoeae samples
  + Ensure reduced susceptibility samples are reported to the Incident Commander
  + Facilitate and manage any molecular assay activities (validation, acquiring and extracting DNA from remnant GC-positive NAAT specimens, processing molecular assay)
  + Define roles for their team members as needed
  + The Laboratory support team includes
    - AST Lab Technician, all other clinical lab technicians who process GC samples, and any couriers
    - AST Lab Technician will
      * Follow guidelines on the preparation of AST cultures via Etest for processing isolated ARGC cultures
      * Report MIC values for all AST results from ARGC cases to relevant staff (identify staff)
* **DIS**: The DIS Managers (identify staff/position to fill role) will
  + Oversee gonorrhea case investigations during the outbreak
  + Facilitate any needed modifications to interview questions and associated tracking systems (e.g. travel history; test of cure results); facilitate any needed additional DIS training
  + Ensure patients are treated appropriately, receive partner services, and any necessary referrals
  + Ensure partners elicited during DIS interviews are brought into the clinic for testing and preventative treatment.
  + Define roles for their team members as needed
  + The DIS support team includes
    - DIS and back-up DIS
    - DIS will
      * Locate patients that are ARGC cases and partners/social contacts per the local SOPs
      * Conduct case investigation interviews on ARGC cases, partners, and social contacts
      * Elicit partner and social contact information from ARGC cases
      * Enter case investigation information into surveillance system
      * Perform field testing and assist field clinicians in collecting GC culture swabs on mobile unit, at the discretion of the Field Operation Supervisor
* **Outreach**: The Outreach Manager (identify staff/position to fill role) will
  + Oversee the potential supplemental public health led targeted testing or educational outreach needed during an outbreak response in relation to any sub-populations that may be at high risk for ARGC as defined by the Surveillance Team
  + Provide reports to the Incident Commander from outreach testing of affected populations and
  + Define roles for their team members as needed
  + The Outreach support team may include:
    - Outreach technician, other outreach workers, and any phlebotomists or clinical staff that accompany team on target testing.
    - Health educators, epidemiologists, communications experts who may work with community health or other service providers to better reach at-risk populations