Cephalosporin-Resistant Gonorrhea Outbreak Response Protocol, Summary Document

Background

The Wisconsin Department of Health Services (DHS) strives to prevent the spread of sexually transmitted infections (STIs) and proactively prepare for emergent outbreaks of antibiotic resistant gonorrhea (ARGC). If an outbreak were to occur, rapid deployment of resources would be necessary. Thus, an outbreak response protocol (ORP) for outbreaks of ARGC has been developed to guide activities and ensure cohesive coordination of agencies. This document provides a high-level summary of DHS' Cephalosporin Resistant Gonorrhea ORP, and more detailed information is contained in the full ORP. Funding provided by the Combatting Antimicrobial Resistant Gonorrhea and Other STIs (CARGOS) Grant currently supports Wisconsin's ability to respond to ARGC outbreaks statewide, allowing for access to antimicrobial susceptibility testing at no cost to the requesting department or clinician. This work is reinforced through monitoring by local and Tribal health departments who then contact DHS about potential cases of ARGC.

Outbreak Response Protocol

1. Contact DHS to report a patient with possible ARGC and get guidance.
2. Request patient return to clinic to provide additional samples for testing.
3. Milwaukee Health Department Laboratory (MHDL) will provide specimen collection kits and handle transport back to the laboratory for testing.
4. DHS will coordinate communications between labs, clinics, and local health departments.
5. Local disease intervention specialists (DIS) or other staff handling case investigations should work to contact patient and attempt partner elicitation. All partners should have specimens collected for testing.
6. DHS and MHDL will report results of antimicrobial susceptibility testing (AST) to the requesting health department.
7. If results indicate reduced susceptibility or resistance to cephalosporins (cefixime and ceftriaxone), DHS will coordinate the response with the requesting health department and the Centers for Disease Control and Prevention (CDC).
8. Samples will be sent from MHDL to CDC for confirmatory testing.
9. If CDC reports similar findings, an outbreak response will be initiated.
10. DIS or other staff performing case management or interviews of patients will work to identify any partners and collect their contact information.
11. DHS and the local health department will coordinate to ensure all contacts of the case and partners are identified, tested, and treated with the same treatment given to the index case.
12. The local health department should work with local providers to ensure the index case and all contacts return for test of cure.
13. Outbreak response will end once all cases and contacts have been treated and receive a negative test of cure 7–14 days following treatment.
14. The local health department is advised to continue monitor for suspected treatment failures.

About Suspected Treatment Failure

- Suspected treatment failure (STF) should be considered if a patient treated with the CDC recommended regimen still reports symptoms about 3–5 days following treatment.
- A positive test of cure 7–14 days after treatment may also be indicative of a treatment failure.
- In both instances, it is necessary to rule out possible reinfection (for example, Was the patient's partner treated? Did the patient report any new sexual contact after treatment?).

ARGC Case Definition

Case Definitions for Levels of Suspected Treatment Failure to Indicate Reduced Susceptible or Antibiotic Resistant Gonorrhea		
Level	**Clinical Criteria**	**Laboratory Criteria**
Suspect Case (Patient fulfills **either** the Clinical Criteria **or** Laboratory Criteria) Probable Case (Patient fulfills **BOTH** the Clinical Criteria **AND** Laboratory Criteria)	Patient experienced STF including all the components below: Patient had laboratory-confirmed *N. gonorrhoeae* infection **AND** Patient received CDC-recommended ceftriaxone-based antimicrobial regimen **AND** Patient subsequently had a positive *N. gonorrhoeae* test result (positive culture 72 hours or more after treatment or positive nucleic acid amplification test (NAAT) at least 8 days after treatment) **AND** Patient had persistent symptoms 3-5 days after CDC recommended Rx **AND** Patient did not engage in sexual activity in the 3-5 days following treatment	Antimicrobial susceptibility testing (AST) of pre- or post-treatment isolate demonstrates ceftriaxone MIC greater than or equal to 0.125 µg/mL
Confirmed Case	Patient meets Clinical **AND** Laboratory criteria for a probable case*** AND** the Laboratory findings are confirmed by the CDC Wisconsin DHS will assist with consultation with CDC for treatment options of **Confirmed Cases**, which depend upon MIC results from culture specimens collected at TOC, and CDC discretion ***** Patient had persistent symptoms 3-5 days after CDC recommended Rx **AND** ***** Patient did not engage in sexual activity in the 3-5 days following treatment	

MICs by Antibiotic & Interpretation		
Cefixime	*Ceftriaxone*	*CLSI Interpretation*
Above 0.25	*Above 0.25*	*Reduced susceptible*
Greater or equal to 0.25	*Greater or equal to 0.125*	*Intermediate Resistance*
Greater or equal to 1	*Greater or equal to 1*	*Resistant*

Outbreak Definitions

Level of Outbreak	**Criteria**	**Actions**
Limited Outbreak	1 probable or suspect case identified in one jurisdiction	-Arrange for AST and treatment of cases -Enhanced investigation and partner identification -Define case by age, sex, gender, race/ethnicity, location -Alert local providers and advocate for enhanced monitoring within clinics or ERs and by jurisdictional LTHDs
Regional Outbreak	More than one probable or suspect case within a region	-Arrange for AST and treatment of cases -Enhanced investigation and partner identification -DHS to coordinate response across jurisdictions -Define case by age, sex, gender, race/ethnicity, location -Alert local providers and advocate for enhanced monitoring within clinics or ERs and by jurisdictional LTHDs -Perform social network analyses to further define the outbreak and identify other cases or contacts
Statewide Outbreak	More than one probable or suspect case spanning more than one region	-Arrange for AST and treatment of cases -Enhanced investigation and partner identification with DHS SURRG DIS coordinating statewide investigations -DHS to coordinate response across jurisdictions -Define case by age, sex, gender, race/ethnicity, location -Alert local providers and advocate for enhanced monitoring within clinics or ERs and by jurisdictional LTHDs -Perform social network analyses to further define the outbreak and identify other cases or contacts

		-Coordinate with bordering states to ensure testing and monitoring there.

Response Management Structure

- Response will be initiated and coordinated by the DHS STI Unit epidemiology coordinator, who will work alongside the reporting jurisdiction and the CDC to lead the response
- The data component of the outbreak response will be led by the DHS STI Unit data manager, with reports provided to partners.
- Laboratory leads from MHDL will offer consultation and support related to diagnoses, further assisting with arranging for sample delivery and testing if the reporting jurisdiction does not have access to culture and AST.
- Clinicians should follow guidance from the CDC for patient treatment and provide updates on the patient as available to the DHS, or directly to CDC when requested.
- Local and Tribal health departments with jurisdiction over the case(s) are asked to participate in response, assisting with local-level coordination, leading enhanced interviews and partner elicitation given local capacity, and helping to arrange for specimen collection and shipment when appropriate.

The ORP may be triggered via:

1. Direct provider report of STF

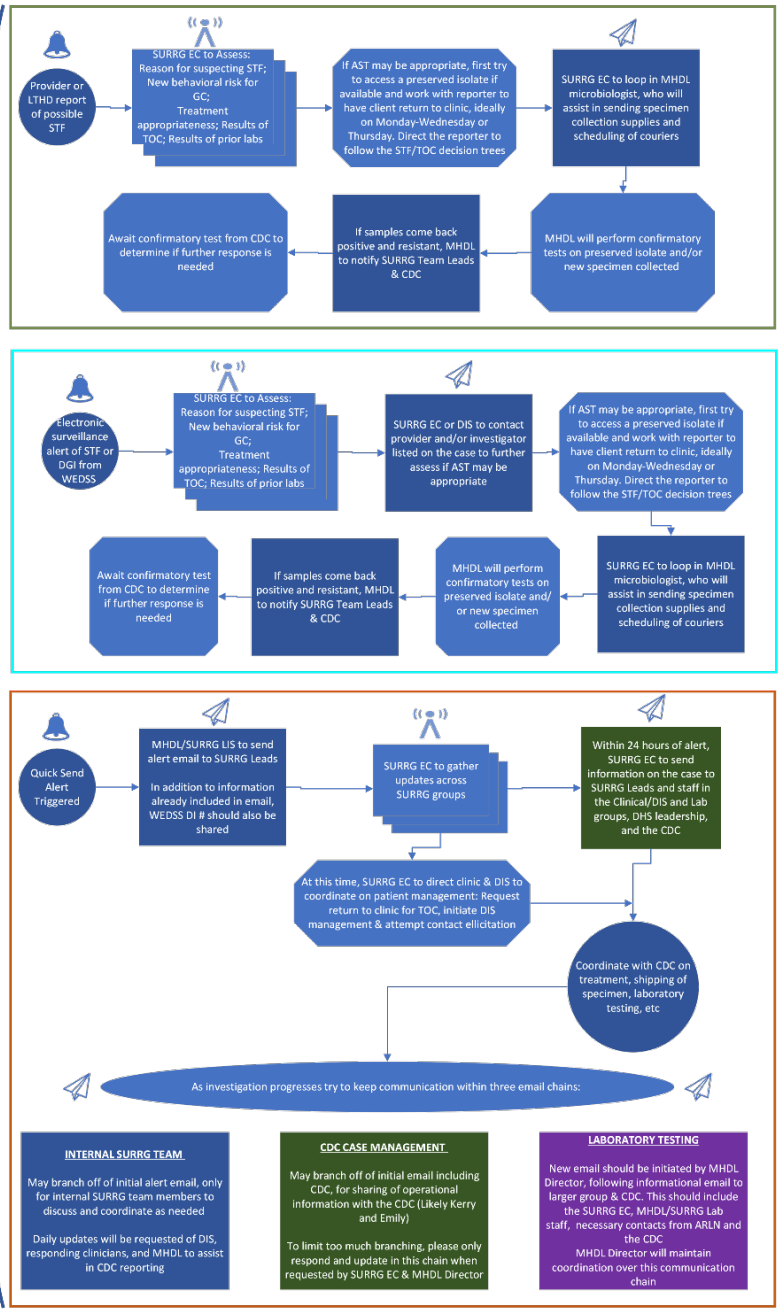
2. Electronic Case Surveillance, with an STF or DGI being detected, automatically alerting the SURRG EC & DM.

3. Laboratory based surveillance of SURRG Sites, with an alert or quick-send alert being sent if ETest of a sample yeilds MIC Values of:

*In all instances, response will be initiated if the patients' TOC is positive AND ETest results exhibit reduced susceptibility or resistance to cephalosporins, confirmed by the CDC via agar dillution

MICs by Antibiotic & Interpretation					
AZI	CFX	CRO	CIP	GEN	CLSI Interpretation
>1	> 0.25	> 0.25		N/A	Reduced susceptible
≥ 2	≥ 0.25	≥ 0.125	> 0.06	N/A	Intermediate Resistance
≥ 16	≥ 1	≥ 1	≥ 1	N/A	Resistant

Communications Cascade



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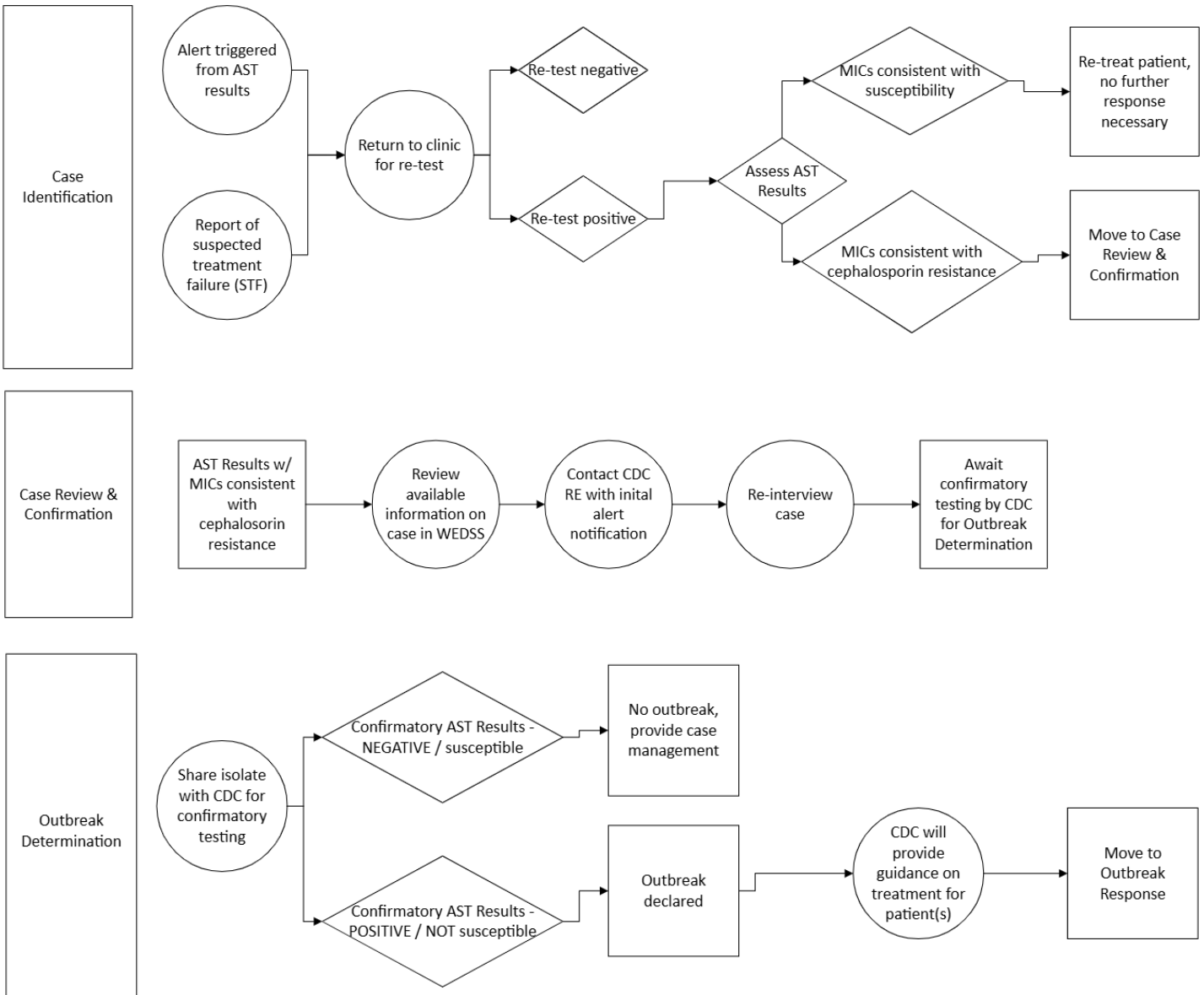
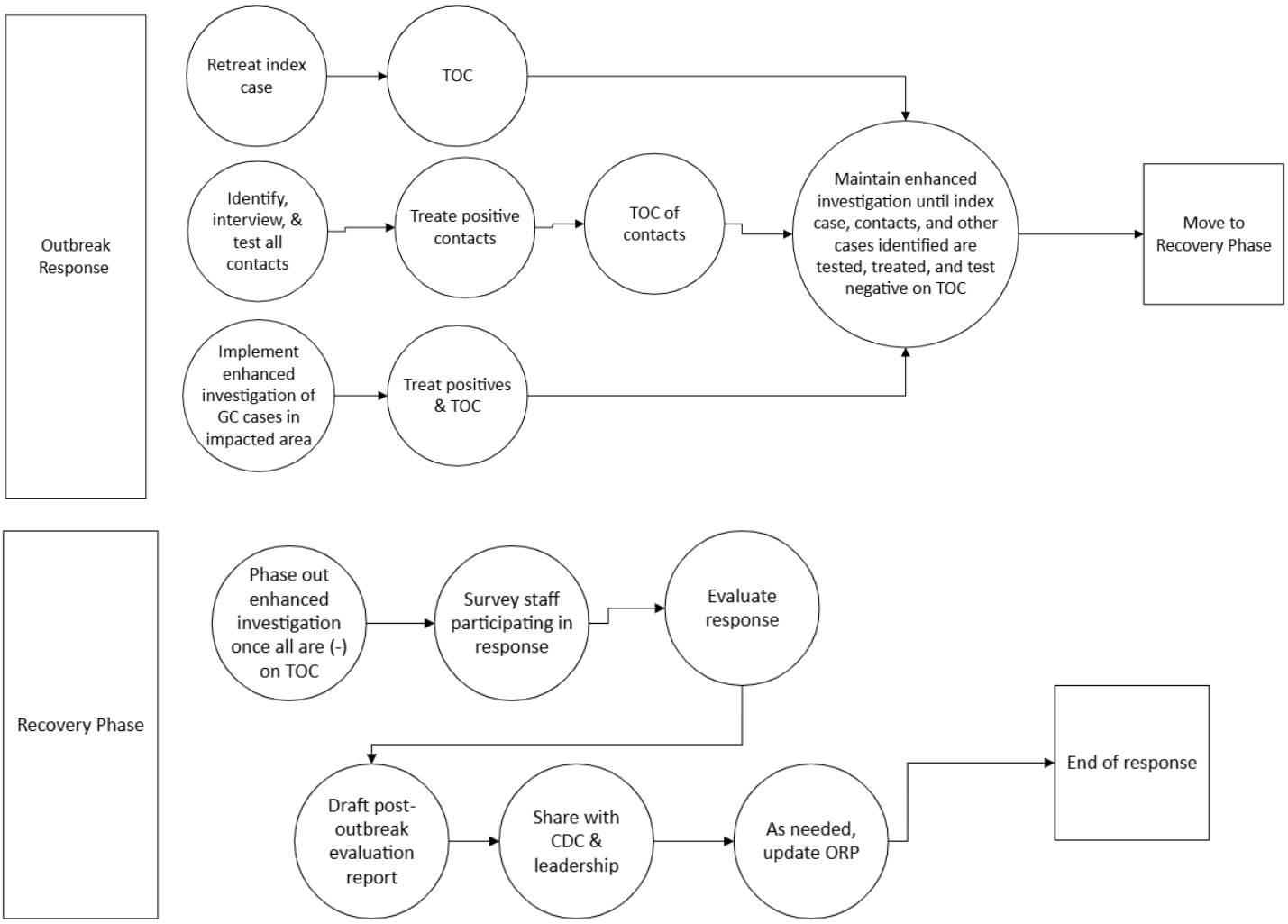

Case Identification
Alert triggered from AST results
Report of suspected treatment failure (STF)
Return to clinic for re-test
Re-test negative
Re-test positive
Assess AST Results
MICs consistent with susceptibility
Re-treat patient, no further response necessary
MICs consistent with cephalosporin resistance
Move to Case Review & Confirmation
Case Review & Confirmation
AST Results w/ MICs consistent with cephalosorin resistance
Review available information on case in WEDSS
Contact CDC RE with inital alert notification
Re-interview case
Await confirmatory testing by CDC for Outbreak Determination
Outbreak Determination
Share isolate with CDC for confirmatory testing
Confirmatory AST Results - NEGATIVE / susceptible
No outbreak, provide case management
Confirmatory AST Results - POSITIVE / NOT susceptible
Outbreak declared
CDC will provide guidance on treatment for patient(s)
Move to Outbreak Response


Outbreak Response
Retreat index case
TOC
Identify, interview, & test all contacts
Treate positive contacts
TOC of contacts
Maintain enhanced investigation until index case, contacts, and other cases identified are tested, treated, and test negative on TOC
Move to Recovery Phase
Implement enhanced investigation of GC cases in impacted area
Treat positives & TOC
Recovery Phase
Phase out enhanced investigation once all are (-) on TOC
Survey staff participating in response
Evaluate response
Draft post-outbreak evaluation report
Share with CDC & leadership
As needed, update ORP
End of response