REQUEST FOR APPLICATIONS

PHARYNGEAL GONORRHEA TEST OF CURE (TOC) PROJECT

National Association of County and City Health Officials (NACCHO)

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Due Date: February 26, 2021

For questions about the Request for Applications (RFA), contact Rebekah Horowitz, Senior Program Analyst, HIV, STI, & Viral Hepatitis, at rhorowitz@naccho.org.

I. Overview

The National Association of County and City Health Officials (NACCHO) represents the nation's nearly 3,000 local health departments (LHDs), which work to protect and improve the health of all people and all communities. NACCHO's HIV, STI, and Viral Hepatitis program aims to strengthen the capacity of LHDs to prevent, control, and manage HIV, STIs, and hepatitis in their communities. NACCHO supports these efforts by providing technical and capacity building assistance, developing and disseminating tools and resources, facilitating peer information exchange, and providing learning opportunities.

To galvanize local efforts to assess test of cure (TOC) for pharyngeal gonorrhea as a strategy to identify and prevent the spread of antimicrobial-resistant gonorrhea, NACCHO, with support from the Centers for Disease Control and Prevention (CDC) Division of STD Prevention (DSTDP), will fund four LHDs up to $100,000 to implement pharyngeal gonorrhea TOC. This implementation will provide essential information about the feasibility of implementing TOC for all pharyngeal gonorrhea cases in clinical practice. Findings will be shared broadly with STD programs across the country.

II. Problem Statement

Neisseria gonorrhoeae is the second most common notifiable disease in the United States with over 500,000 cases reported in 2018 and gonococcal infections in males and females continue to increase in the United States. Untreated gonococcal infection can lead to serious sequelae including pelvic inflammatory disease, ectopic pregnancy, infertility, epididymitis, and disseminated gonococcal infection and can facilitate HIV acquisition and transmission. Timely and effective treatment of gonococcal infections can prevent these adverse health outcomes and subsequent transmission in the community. However, the treatment and control of *N. gonorrhoeae* have been complicated by the organism's ability to acquire antimicrobial resistance. Starting in 2010, CDC recommended combined therapy with ceftriaxone 250mg intramuscularly and azithromycin 1g orally as first-line treatment for uncomplicated gonorrhea. Due to the development of antimicrobial resistance to multiple classes of antibiotics, including current first line therapies, gonorrhea was designated as one of five urgent antibiotic resistance threat level pathogens in the United States in 2019. Increasing concern for antimicrobial stewardship and the continued low incidence of ceftriaxone resistance in the United States has led to reevaluating the need for dual therapy. CDC has updated the 2015 gonococcal treatment recommendations and recommends a single dose of ceftriaxone 500mg intramuscularly as treatment for uncomplicated gonorrhea.[1]

Treatment failures with ceftriaxone, occurring primarily at the pharynx, have occurred outside of the U.S. with strains demonstrating ceftriaxone minimum inhibitory concentrations (MIC) of >0.25 µg/mL. Although the development of resistance in *N. gonorrhoeae* is not fully understood, the pharynx may serve as an incubator of resistance due to the lower drug concentrations at this anatomic site and increased opportunity to exchange genetic material with other bacteria. Therefore, the implementation of a test of cure (TOC), defined as performing *N. gonorrhoeae* culture or nucleic acid amplification testing (NAAT) 7–14 days after initial treatment for all cases of pharyngeal *N. gonorrhoeae* could

[1] St. Cyr S, Barbee L, Workowski KA, et al. Update to CDC's Treatment Guidelines for Gonococcal Infection, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1911–1916. DOI: http://dx.doi.org/10.15585/mmwr.mm6950a6external icon

potentially identify and prevent the spread of antimicrobial-resistant gonorrhea. CDC recommends a TOC for persons with pharyngeal gonorrhea by using either culture or NAAT 7–14 days after initial treatment, regardless of regimen, to ensure eradication or detection of a possible treatment failure.[1] The feasibility of implementing TOC for all pharyngeal *N. gonorrhoeae* cases in clinical practice has not been previously evaluated.

III. Objectives

This is a program evaluation project with the following objectives:

- **To assess feasibility of implementing TOC for all pharyngeal *N. gonorrhoeae* infections in routine clinical practice, which could include, but is not limited to:**
  - **TOC response rate** – defined as number of patients that had TOC performed within 7–30 days of treatment administration for pharyngeal *N. gonorrhoeae* over total number of patients treated for pharyngeal *N. gonorrhoeae*
  - **Impact on clinic capacity including time needed for TOC activities and lost opportunities for other clinical care (e.g., turn aways)**
  - **Staffing and supply requirements**
  - **Workflow challenges and solutions**

- **To understand the yield of TOC for all pharyngeal *N. gonorrhoeae* infections to detect treatment failures to CDC-recommended first-line gonorrhea treatment**

- **To identify models and best practices for monitoring and responding to potential *N. gonorrhoeae* treatment failures**

- **To explore relationships of gonococcal strains that fail CDC-recommended first-line treatment and to detect genetic markers associated with antimicrobial resistance**

IV. Intervention Guidance and Requirements

This funding is open to all jurisdictions with the organizational and project management capacity to support and operate a STD specialty clinic and public health laboratory over the course of the project period and at least one identified site that provides specialized STD services with the capacity to perform NAAT and cultures for *N. gonorrhoeae* at the pharyngeal site. The jurisdiction must also have the capacity to execute the program strategies and activities and demonstrate the ability to meet the project period outcomes.

Strategies to implement pharyngeal *N. gonorrhoeae* TOC can take many forms, and this project encourages areas to use these funds to pilot or scale-up promising and/or innovative approaches. Priority will go towards proposals for interventions that are:

Ready for implementation. Proposed pharyngeal *N. gonorrhoeae* TOC project needs to be ready for

implementation or should already be in the process of implementation. This project does not have the funding or timeframe to support a long period of time for start-up and building core infrastructure or partnerships for an intervention to occur. The interventions should be implemented over a time that guarantees sufficient programmatic experience with the pharyngeal *N. gonorrhoeae* TOC project such that the program can adequately describe outcomes.

Feasible. Proposed approach to integrating pharyngeal *N. gonorrhoeae* TOC into clinical practice needs to represent an approach that many other jurisdictions could implement if shown to be promising or effective. This project aims to help not only the funded jurisdiction address antimicrobial-resistant *N. gonorrhoeae*, but also to provide lessons to counterparts in other jurisdictions.

An appropriate local health department/project site should have, at minimum, the below features:

- Health department leadership committed to implementing program strategies outlined in this RFA;
- STD clinic staff with the capacity and commitment to follow project protocols related to effectively collecting, handling, and transporting *N. gonorrhoeae* culture specimens, in addition to shipping positive TOC *N. gonorrhoeae* pharyngeal isolates (i.e., concerning for possible treatment failure) to CDC for additional testing;
    - Antimicrobial susceptibility testing (AST) may be performed by project sites if the capacity to do so, with appropriate quality control measures in place, is available locally; if capacity to perform AST is not available, positive TOC *N. gonorrhoeae* pharyngeal isolates should be shipped to CDC for AST.
    - All project sites are required to ship positive TOC *N. gonorrhoeae* pharyngeal isolates to CDC for whole genome sequencing (WGS).
- Within the jurisdiction, a categorical STD clinic that diagnoses at least 150 cases of pharyngeal *N. gonorrhoeae* annually; jurisdictions must identify in writing, as part of the funding application, the burden of gonococcal infection in their proposed STD specialty clinic(s) by providing the number of pharyngeal infections seen in 2018 and 2019 for each clinic;
- Ability to enroll men and women, as indicated by local protocols, for the collection of pharyngeal *N. gonorrhoeae* TOC samples, including *N. gonorrhoeae* NAAT and *N. gonorrhoeae* culture per CDC STD Treatment Guidelines;
- Local laboratory capacity to perform *N. gonorrhoeae* identification and isolation, store duplicate *N. gonorrhoeae* isolates (for positive TOC cases), and to ship viable and non-contaminated isolates to CDC for additional testing (for positive TOC cases);
- Ability to collect, store, and electronically transmit requested demographic and clinical data elements to CDC.

V. Evaluation guidance and requirements

Each funded area will be expected to work with CDC/DSTDP and NACCHO to answer the following evaluation questions using scientific methods:

- How feasible was the pharyngeal *N. gonorrhoeae* TOC project to implement?
- What barriers and facilitators affected implementation?

- What is the impact of pharyngeal *N. gonorrhoeae* TOC implementation on other services offered by the clinic and on the staffing needs?
- To what extent did the pharyngeal *N. gonorrhoeae* TOC project reach the intended targets and outcomes?

Applicants should propose a basic evaluation design in their application. Funded projects should include both process and short-term outcomes related to the above evaluation questions. Funded projects are encouraged to include both quantitative and qualitative methods in the evaluation. Various types of data are needed to create a multi-dimensional description of feasibility, replicability, facilitators, and barriers. NACCHO and CDC are committed to working with funded jurisdictions to perform evaluations and support as otherwise needed. Applicants are encouraged to provide as much detail as possible in their applications to facilitate project timelines upon funding (e.g., attach a program implementation logic model, description of existing baseline data, draft data collection instruments, proposal of evaluation plan).

As part of their applications, jurisdictions should propose secondary outcomes of interest in addition to the primary outcome measure of interest, **TOC response rate**. Secondary measurable outcomes of interest and process measures for implementation of the pharyngeal *N. gonorrhoeae* TOC project will be determined by funded sites; exact specification of the outcome(s) selected can be determined in consultation with NACCHO and CDC/DSTDP. Examples could include but are not limited to the below examples.

Possible secondary outcome measures include:

- Predictors of pharyngeal *N. gonorrhoeae* TOC uptake
- Number/proportion of patients where follow-up outreach was made to encourage *N. gonorrhoeae* pharyngeal TOC visit
- Number of clinic patients that were turned away (i.e., turn aways) per month (compared to period before TOC implementation) including how this relates to staffing availability
- *Among those who return for TOC,*
    - Average time to TOC (from time of *N. gonorrhoeae* treatment)
    - Type of diagnostic test performed (e.g., % with both NAAT and culture performed vs. % NAAT only performed or % culture only performed)
    - Total number of pharyngeal *N. gonorrhoeae* cases with positive TOC (*N. gonorrhoeae* NAAT or culture)
    - Disposition of patients with positive pharyngeal *N. gonorrhoeae* TOC
        - Number of positive TOC likely due to re-infection
        - Number of positive TOC that are suspected to be due to delayed clearance (i.e., residual RNA post-treatment)
        - Number of positive TOC in which patient was initially treated with alternate regimen (i.e., <u>not</u> treated with CDC-recommended first-line therapy)

- Number of positive TOC with concerns for cephalosporin resistance (i.e., ceftriaxone MIC >0.25 µg/mL)
- Number of positive TOC with unknown reason for treatment failure (i.e., suspected pharmacokinetic/pharmacodynamic issues)
- Documentation of treatment regimen that cleared the infection

VI. Funding and timeframe

Selected LHDs will be awarded up to $100,000 to implement their approach and to evaluate and document lessons learned from implementing *N. gonorrhoeae* TOC performance for all pharyngeal *N. gonorrhoeae* cases at participating sites. Recipients will also participate in efforts to disseminate ongoing lessons learned. The selection of sites will be determined through demonstrated background need and site capacity as described in their application.

Funding should be used to support costs for personnel, training, laboratory supplies (i.e., pharyngeal TOC NAAT and culture supplies), and contractual support for surveillance or public health information systems enhancements. Funding can pay for up to a full FTE for clinic personnel responsible for active follow-up of every pharyngeal *N. gonorrhoeae* case. Funds may also be used to support a partial or full-time employee trained in epidemiology/data management since it is required that applicants demonstrate the capacity to review local data to inform public health action and prepare aggregate and deidentified line-listed data for transmission to CDC at least quarterly. All funding should support pharyngeal *N. gonorrhoeae* TOC activities.

KEY DATES

Event	Date
RFA Release	January 11, 2021
Informational Webinar for Potential Applicants	January 25, 2021
Application Submission Deadline	February 26, 2021
Telephone Interviews with Finalists (as needed)	Early March 2021
Anticipated Award Notification	Mid-March 2021
Anticipated Contract Execution	April 2021
Implementation and Evaluation Period	April 2021-April 2022
Submission of lessons learned to NACCHO	~3 months after the end of the implementation period

VII. Eligibility and Contract Terms

Eligible applicants include LHDs that are active NACCHO members, in addition to meeting criteria specified under Section VIII ("Intervention Guidance and Requirements"). To confirm membership status, or to become a dues-paying NACCHO member, visit http://www.naccho.org/membership. See the Requirements section on page 3 for additional information about eligibility.

Applicants should plan for approximately 12 months of project implementation. Projects will begin on the date of contract execution. Please note that NACCHO reserves the right to make changes to the project timeline and payment schedule if necessary.

VIII. Scope of Work and Project Requirements

During the project period, awardees will:

- Ensure that relevant local stakeholders (e.g., clinic staff) are aware of this project and are engaged and informed appropriately throughout the duration of the funding period.
- Finalize a plan to implement *N. gonorrhoeae* TOC performance for all pharyngeal *N. gonorrhoeae* cases at participating STD clinics.
- Finalize a plan to evaluate the implementation of the *N. gonorrhoeae* TOC project.
    - With process and outcome evaluation components, including at least the primary outcome measure described above
    - An evaluation plan that should be mixed methods, feasible, and outcome-oriented
- Implement the *N. gonorrhoeae* TOC project.
    - To such a scale that the evaluation can assess some short-term outcomes (e.g., TOC response rate)
    - Implementation should be completed by the end of April 2022 or planned and phased to demonstrate incremental, measurable achievement by end of April 2022, as NACCHO cannot presently guarantee additional time or funding to continue work beyond that date.
- Collaborate with NACCHO and CDC/DSTDP to collect, analyze, interpret, and synthesize evaluation findings. See "*Support and Technical Assistance*" section below for additional detail on the evaluation and analysis support that will be provided by NACCHO and CDC/DSTDP.
- Collaborate with NACCHO and CDC/DSTDP during and post-project period to share ongoing lessons learned and findings, through reports, webinars, and limited 1:1 technical assistance with other areas interested in learning more about implementation of *N. gonorrhoeae* TOC performance for all pharyngeal *N. gonorrhoeae* cases.
- Participate in regularly scheduled project conference calls, as well as site visit(s) and other potential project or dissemination meetings, as appropriate.
- Provide relevant staff and sufficient staff time to manage the project in collaboration with NACCHO and CDC/DSTDP.

<u>Summary of key project deliverables for funded jurisdiction:</u>

- Final pharyngeal *N. gonorrhoeae* TOC implementation plan
- Final evaluation plan
- Clean summaries of all data collected and analyzed under the site's evaluation plan and as required by CDC/DSTDP
    - E.g., Excel worksheets of aggregate clinic data, deidentified line-listed demographic and clinical data collected on pharyngeal gonorrhea cases, and summaries of any interviews or focus groups conducted

- Electronic copy of written protocols, procedures, tools, or job aids that were used to implement/guide the pharyngeal *N. gonorrhoeae* TOC implementation and which other jurisdictions might benefit from seeing
- Written summaries of results and lessons learned

IX. Support and Technical Assistance

NACCHO and CDC/DSTDP will provide ongoing support to awardees in the form of:

1) Technical assistance via conference call and webinar to facilitate project planning, implementation, data collection and analysis, and reporting
2) In-person site visits to observe the program model, review and discuss implementation plans and evaluation data, and provide technical assistance, as applicable
3) Analysis of reported data
4) Synthesis of evaluation findings across jurisdictions
5) Provision of templates for dissemination/summary products
6) Coordination of dissemination back to recipients and to the broader community of STD programs

X. Proposal Format

The application should be single-spaced and use Times New Roman 12-point font, not to exceed eight (8) pages in length, and should include the following sections:

A. Cover page

Provide a cover sheet that includes the applicant's contact information.

B. Background and Need (~2 pages)

a. Describe the problem statement including why you want to participate in this project and how your participation will address this public health issue. Describe your site population including an overview of your service area and community, number and socio-demographic description of clients seen/tested annually, socio-demographic description of STI positivity and rates, and trends over time.

b. Provide the total number of *N. gonorrhoeae* cases and the number of pharyngeal *N. gonorrhoeae* cases in 2018 and 2019 for each clinic; provide data on *N. gonorrhoeae* treatment completion and antimicrobial resistance for 2018 and 2019, if available.

C. Capacity to Implement and Evaluate Project (~ 3 pages)

a. Describe your clinical staffing and workflow. Do you actively follow up on pharyngeal *N. gonorrhoeae* cases and, if so, how?

b. Specifically, describe how you currently test patients for *N. gonorrhoeae* and who is tested for *N. gonorrhoeae*. Do you have the capacity to perform pharyngeal *N. gonorrhoeae* NAAT? What are the patient criteria for extragenital *N. gonorrhoeae* testing in your clinic? Do you currently perform *N. gonorrhoeae* culture and identification on pharyngeal specimens? Which type(s) of clinical staff currently collect pharyngeal specimens for *N. gonorrhoeae* NAAT and/or culture? Which laboratory receives specimens from the STD clinic? What is the nature of your relationship with your laboratory provider? How is the laboratory to be engaged in this project?

c. Please describe the project design and approach, including the model for how pharyngeal *N. gonorrhoeae* TOC will be implemented and evaluated. How will pharyngeal *N. gonorrhoeae* TOC be integrated into clinical care? How will patients be notified and/or reminded to have pharyngeal TOC performed? How will the STD clinic patient flow be modified and/or adjusted to account for TOC visits? How will the STD clinic track patient visits that are for pharyngeal *N. gonorrhoeae* TOC? What is the proposed evaluation design? What are the proposed process and outcome evaluation components of the evaluation plan? Will any components of the project require IRB review? If so, please describe how this may impact the project timeline.
d. What is your experience with managing and implementing special projects?
    i. Describe your experience with pilot projects and enhanced programmatic or surveillance projects, including experience modifying protocols and training staff to implement new initiatives or modifications to clinic processes.
    ii. Describe your experience and current capacity to follow project protocols related to effectively collecting, handling, performing *N. gonorrhoeae* identification, storing, and transporting of *N. gonorrhoeae* specimens and isolates.
    iii. Describe your experience and capacity to collect and electronically transmit requested demographic and clinical data elements to CDC for positive TOC cases (e.g., ability to extract clinical data from electronic medical record [EMR], capacity to add new data elements to EMR).

D. Key Staff and Partners (~2 pages)

a. Proposed key staff to manage the project overall, their role, and relevant experience
b. Proposed key staff to implement the TOC project, their role, and relevant experience
c. Proposed key staff to evaluate the TOC project (including data cleaning and analysis), their role, and relevant experience
d. Description and relationship to any partners critical to implementing the innovation or improvement
    i. Include letter(s) of support from critical partners (as an attachment, optional)
e. Description and relationship to any partners critical to evaluating the innovation or improvement

E. Attachments - Required

a. Proposed budget, with justification

F. Attachments – Optional

a. Resumes/CVs of Key Staff
b. Letters of support from any key partners critical to the project (including but not limited to the public health lab)

The cover page, budget and justification, resumes/CVs, and other optional attachments do not count against the total page limit. All pages, charts, figures, tables, and any additional information/attachments should be numbered.

XI. Selection Criteria

NACCHO and CDC/DSTDP will review and score applications for this RFA in accordance with the following criteria (out of 100 points):

- Evidence of *N. gonorrhoeae* burden (30 points)
- Jurisdictional Capacity (50 points) – This should include the project design/approach, promoting and tracking pharyngeal *N. gonorrhoeae* TOC visits, collection of additional data for primary and secondary outcomes and process measures, extraction and reporting of required data, clinical capacity for performing extragenital *N. gonorrhoeae* NAAT and *N. gonorrhoeae* culture specimen collection, laboratory capacity for processing *N. gonorrhoeae* cultures, and applicant's proposed evaluation design and capacity.
- Amount and relevant experience of key staff or partners responsible for carrying out project activities (20 points)

NACCHO and CDC reserves the right to award jurisdictions that do not have the highest raw score to account for factors such as geography or population size.

NACCHO and CDC/DSTDP may conduct telephone interviews with finalists. Interviews would be conducted in early March 2021, if necessary.

XII. Submission Instructions

The deadline to submit applications is **February 26, 2021** by 11:59 PM Pacific Daylight Time (PDT). Proposals should be submitted as a single PDF in an email to rhorowitz@naccho.org with subject line: "GC Test of Cure RFA."

XIII. Additional Information

An informational webinar will be hosted for potential applicants on **January 25, 2021** at 1-2PM ET. Please note that advanced registration is not required, simply click on the link below. Questions may be submitted in advance to rhorowitz@naccho.org, and will be accepted until 11:59PM Pacific Daylight Time (PDT) on January 24, 2021.

Webinar URL: https://naccho.zoom.us/j/2159647452.
Audio: +1 301 715 8592, Meeting ID: 2159647452

For questions, contact:
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