CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 15-0090
Study Title:
Clinical Validation of a Molecular Test for Ciprofloxacin-Susceptibility in *Neisseria gonorrhoeae*

NCT02961751

Version 1.0

DATE: 08–April-2019

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 15-0090**
Development Phase:	Clinical Study
Products:	Ciprofloxacin
Form/Route:	Orally
Indication Studied:	Neisseria Gonorrhoeae
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	19OCT2016
Clinical Trial Completion Date:	TBD
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Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

ATC	Anatomical Therapeutic Chemical Classification System
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CRF	Case Report Form
DMID	Division of Microbiology and Infectious Diseases
DNA	Deoxyribonucleic Acid
eCRF	Electronic Case Report Form
FDA	The Food and Drug Administration
FP	False Positive
gyrA	Gyrase A Genotype
ICH	International Conference on Harmonization
ID	Identification
IRB	Institutional Review Board
ITT	Intention to Treat
MIC	Minimum Inhibitory Concentration
micro-ITT	Microbiological Intent-to-Treat
N	Number (typically refers to subjects)
NAAT	Nucleic Acid Amplification Test
NIH	National Institutes of Health
PCR	Polymerase Chain Reaction
PP	Per Protocol
PT	Preferred Term
SD	Standard Deviation
STD	Sexually Transmitted Disease
TP	True Positive
US	United States
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "Clinical Validation of a Molecular Test for Ciprofloxacin-Susceptibility *in Neisseria gonorrhoeae*" (DMID Protocol 15-0090) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use ICH Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA) and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains four sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for efficacy and safety outcomes, and (4) a list of proposed tables and figures. Any deviation from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

Genomic analyses are not described in this SAP; a separate SAP for the genomic analyses will be generated.

2. INTRODUCTION

Gonorrhea is the second most commonly reported notifiable disease in the United States with more than 330,000 cases reported in 2012, a rate of 107.5 per 100,000 population [reference 1 in protocol]. Over the past 75 years, *Neisseria gonorrhoeae (N. gonorrhoeae)* infections have become increasingly resistant to antimicrobial therapy, first to sulfa-based antibiotics, then penicillins, tetracyclines, fluoroquinolones, and now extended-spectrum cephalosporins [reference 2 in protocol]. Prior to the advent of ciprofloxacin-resistant *N. gonorrhoeae*, ciprofloxacin was the primary first-line recommended therapy for *N. gonorrhoeae* infections of the throat, rectum, urethra, and cervix. From 1998 to 2006, ciprofloxacin was the Centers for Disease Control and Prevention (CDC) recommended treatment for *N. gonorrhoeae* in all anatomic sites. Prior to widespread ciprofloxacin resistance, the efficacy of ciprofloxacin treatment in susceptible *N. gonorrhoeae* infections was estimated at more than 99% [reference 3-4 in protocol]. In 2007, due to high rates of ciprofloxacin resistance in *N. gonorrhoeae* nationally, the CDC recommended the discontinuation of ciprofloxacin treatment for gonorrhea, which was followed by a decline in ciprofloxacin *N. gonorrhoeae* resistance nationally [reference 5 in protocol]. At this time, the only recommended treatment for *N. gonorrhoeae* infection is dual antibiotic therapy with injectable ceftriaxone and oral azithromycin or doxycycline [reference 6 in protocol]. For decades, bacterial culture was the standard diagnostic modality for *N. gonorrhoeae* infections. Culture is specific, but studies have demonstrated that the molecular-based enzyme immunoassay or nucleic acid amplification test (NAAT) has a higher clinical sensitivity than culture [reference 7 in protocol]. However, there has not been a widely used and reliable technology that allows for antibiotic susceptibility testing from non-culture specimens.

It has been recently demonstrated that *N. gonorrhoeae*-deoxyribonucleic acid (DNA) mutations can be detected using modern molecular techniques and real-time polymerase chain reaction (PCR) assays can be used to detect reproducible, clinically significant resistance [reference 8-10 in protocol]. A protocol for the detection of alterations in the gyrase A gene (*gyrA*), the target of ciprofloxacin anti-gonococcal activity, has been validated [reference 8 in protocol]. While molecular markers of susceptibility have high concordance, sensitivity and a specificity of 93% and 100%, respectively, compared with standard antimicrobial susceptibility testing, the clinical performance of the test and the response to therapy based on a molecular susceptibility result in *N. gonorrhoeae* is unknown.

While molecular methods to diagnose *N. gonorrhoeae* have greatly improved the detection of infection [reference 14 in protocol], they have historically precluded the ability to perform antibiotic susceptibility testing. Although regional surveillance data critically inform treatment recommendations, those data cannot be used for real-time individualized clinical management. The clinical validation of an assay to determine the ciprofloxacin susceptibility of *N. gonorrhoeae* infections could result in increased use of ciprofloxacin for ciprofloxacin-susceptible *N. gonorrhoeae* infections and resultant decreased use of extended-spectrum cephalosporins, thereby reducing the selection pressure for cephalosporin resistance in *N. gonorrhoeae*. An immediate benefit to taking ciprofloxacin would be for those with cephalosporin allergies who would have to take combination therapy that is more difficult to administer. The study will help to assess the potential impact of a strategy to address the critical problem of emerging drug resistance in *N. gonorrhoeae*. Specifically, the information gained from this study can be used to influence national sexually transmitted disease (STD) treatment policies and, therefore, result in a marked decrease in extended-spectrum cephalosporin-resistant *N. gonorrhoeae* infection, improving the availability of treatment options for individuals infected with *N. gonorrhoeae*.

2.1. Purpose of the Analyses

These analyses will assess the efficacy of ciprofloxacin for treatment of uncomplicated *Neisseria gonorrhoeae* infections with *gyrA* serine 91 genotype and will be included in the clinical study report.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary Objectives

1. To determine the efficacy of ciprofloxacin for treatment of uncomplicated *Neisseria gonorrhoeae* infections with *gyrA* serine 91 genotype.

3.1.2. Secondary Objectives

1. To investigate efficacy of ciprofloxacin for treatment of uncomplicated *gyrA* serine 91 genotype *Neisseria gonorrhoeae* infection by anatomic site.
2. To determine the sensitivity of the *gyrA* assay for detection of ciprofloxacin-susceptible *Neisseria gonorrhoeae* infections.

3.1.3. Exploratory Objectives

1. To characterize *N. gonorrhoeae* isolates and non-*gyrA* gene-dependent mechanisms of ciprofloxacin resistance post-treatment of uncomplicated *N. gonorrhoeae* infection by anatomic site using traditional and molecular methods like genotyping and sequencing.
2. To investigate the efficacy of ciprofloxacin for treatment of uncomplicated serine 91 *gyrA N. gonorrhoeae* infections by demographic and clinical characteristics.

3.2. Endpoints

3.2.1. Primary Outcome Measure

1. The proportion of subjects infected with *gyrA* serine 91 genotype *N. gonorrhoeae* with microbiological cure at Visit 2 (Day 5-10)

3.2.2. Secondary Outcome Measure

1. The proportion of subjects infected with *gyrA* serine 91 genotype *N. gonorrhoeae* with microbiological cure at each anatomic site (throat, rectum, male or female urogenital tract) at Visit 2 (Day 5-10)
2. The proportion of subjects infected with *gyrA* serine 91 genotype *N. gonorrhoeae* identified by *gyrA* gene PCR who have ciprofloxacin-susceptible *N. gonorrhoeae* as identified by culture-based antimicrobial susceptibility testing at Visit 1 (Day 1)

3.2.3. Exploratory Outcome Measures

1. Identification and characterization of non-*gyrA* gene-dependent mechanisms of ciprofloxacin resistance by genotyping and whole genome sequencing (e.g., Illumina) of nucleic acid isolated from uncured subjects at Visit 2 (Day 5-10). Genotyping and sequencing may be performed on nucleic acid isolated from different anatomic sites.
2. The proportion of subjects infected with *gyrA* serine 91 genotype *N. gonorrhoeae* with microbiological cure at Visit 2 (Day 5-10) by demographic and clinical characteristics.

3.3. Study Definitions and Derived Variables

3.3.1. Baseline untreated serine 91 *gyrase* A genotype *N. gonorrhoeae* Diagnosis

For a particular anatomical site, a subject who has not been treated for *N. gonorrhoeae* prior to enrollment into the study will be identified as having untreated serine 91 *gyrA N. gonorrhoeae* if there is:

- Detectable *N. gonorrhoeae* at Visit 1 via culture, i.e. positive *N. gonorrhoeae* culture from the swab taken at Visit 1, and
- Detection of wild type *gyrA* by the real-time PCR analysis of the *gyrA* gene from the swab taken at Visit 1.

3.3.2. Microbiological Outcome Status

1 Microbiological outcome status for the primary analysis is evaluated at Visit 2 and is defined as follows:

- Microbiological Cure: *N. gonorrhoeae* not detectable by culture from all anatomical sites that had detectable *N. gonorrhoeae* at Visit 1.
- Microbiological Failure: *N. gonorrhoeae* detectable by culture from at least one anatomical site that had detectable *N. gonorrhoeae* at Visit 1.
- Non-evaluable: At least one of the following:
  - Subject did not return for Visit 2, or
  - Culture results at Visit 2 were not available for any reason, or
  - Subject could not be evaluated for microbiological outcome status for any other reason.

2 For the analysis of secondary objective 1, microbiological outcome status at each anatomical site is evaluated at Visit 2 and is defined for a particular anatomical site as follows:

- Microbiological Cure*: N. gonorrhoeae* not detectable by culture at the particular anatomical site that had detectable *N. gonorrhoeae* at Visit 1.
- Microbiological Failure: *N. gonorrhoeae* detectable by culture at the particular anatomical site that had detectable *N. gonorrhoeae* at Visit 1.
- Non-evaluable: At least one of the following:
  - Subject did not return for Visit 2, or
  - Culture results at Visit 2 were not available for any reason, or
  - Subject could not be evaluated for microbiological outcome status for any other reason.

3.3.3. Sensitivity of the *gyrA* assay

For the analysis of the sensitivity of the *gyrA* assay for the detection of ciprofloxacin-susceptible *N. gonorrhoeae* infections (secondary objective 2), two measures will be estimated. First, the sensitivity of the assay will be estimated using the following (overall and separately for each anatomical site):

True Positives (TP): the number wild type *gyrA* infections that are ciprofloxacin-susceptible *N. gonorrhoeae* as identified by culture-based antimicrobial susceptibility testing at Visit 1.

False Negatives (FN): the number of non-wild type *gyrA* infections that are ciprofloxacin-susceptible *N. gonorrhoeae* as identified by culture-based antimicrobial susceptibility testing at Visit 1.

Sensitivity = TP / (TP + FN)

Given the design of the study, the estimate of sensitivity may be biased because subjects with no wild type infections are not enrolled and thus their samples are not tested for culture-based susceptibility testing. To supplement the estimates of sensitivity, the assay's positive predictive value (PPV) will also be estimated. PPV is calculated using the following (overall and separately for each anatomical site):

True Positives (TP): the number wild type *gyrA* infections that are ciprofloxacin-susceptible *N. gonorrhoeae* as identified by culture-based antimicrobial susceptibility testing at Visit 1.

False Positives (FP): the number of wild type *gyrA* infections that are not ciprofloxacin-susceptible *N. gonorrhoeae* as identified by culture-based antimicrobial susceptibility testing at Visit 1.

PPV = TP / (TP + FP).

3.3.4. Baseline Value

The baseline value for all variables will be defined as the last value obtained prior to the dose of ciprofloxacin.

3.3.5. Within Window Test of Cure Visit

Version 6.0 of the protocol (03 July 2018) was updated to expand the visit window for Visit 2 from Day 5-9 to Day 5-10. For subjects enrolled under version 6.0 (or later) of the protocol, the Test of Cure visit will be considered within window if the visit occurred between Days 5 and 10 (inclusive). For subjects enrolled under a version prior to version 6.0, Test of Cure visit will be considered within window if the visit occurred between Days 5 and 9 (inclusive).

3.3.6. Treatment Compliance

A subject will be considered compliant with study treatment if the subject is able to swallow the pill and not vomit within 1 hour of administration. Otherwise, the subject will be considered non-compliant.

3.3.7. Symptomatic/Asymptomatic Status

For female subjects with baseline cervicovaginal infection, subjects will be classified as symptomatic if they report any of the following symptoms at baseline: abnormal vaginal discharge, abnormal vaginal bleeding, or pain during intercourse.

For male subjects with baseline urethral infection, subjects will be classified as symptomatic if they report any of the following symptoms at baseline: urethral discharge or pain with urination.

For subjects with baseline rectal infection, subjects will be classified as symptomatic if they report any of the following symptoms at baseline: anorectal pain, anorectal discharge, or anorectal bleeding.

For subjects with baseline pharyngeal infection, subjects will be classified as symptomatic if they report having a sore throat at baseline.

For all anatomic locations, baseline infections are those confirmed by culture. Subjects with baseline infections will be considered asymptomatic if they do not affirm these symptoms at baseline.

3.3.8. Ciprofloxacin Susceptible Infection

Ciprofloxacin susceptibility will be determined via culture-based antimicrobial susceptibility testing. An infection will be deemed susceptible to ciprofloxacin if the reported minimum inhibitory concentration for the isolate is < 1 mcg/ml.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This study is a multi-center, single-arm, open-label clinical study to assess the efficacy of one dose of ciprofloxacin given orally in subjects infected with untreated *gyrA* serine 91 genotype *N. gonorrhoeae* as determined by a real-time PCR assay. The study plans to enroll approximately 381 subjects to obtain a per protocol eligible target of 257 subjects age 18 years or older regardless of gender identification who are seeking care in STD clinics at participating sites in the United States. Subjects who have untreated *gyrA* serine 91 genotype *N. gonorrhoeae* of the rectum, or male or female urogenital tract identified by a positive culture or NAAT conducted at a prior visit are offered enrollment in the study. Subjects not consenting to participate in the study receive treatment per local standard of care.

At enrollment, Visit 1 (Day 1), a brief physical exam and medical and sexual history is performed. Subjects have samples collected for *N. gonorrhoeae* culture and *N. gonorrhoeae* NAAT (to include *gyrA* serine 91 genotype) from each infected anatomic site (throat, rectum, male or female urogenital tract) to verify infection status.

Subjects with *gyrA* serine 91 genotype rectal or urogenital *N. gonorrhoeae* receive one dose of directly observed ciprofloxacin 500 mg. Subjects are observed in the clinic for at least 5 minutes after receiving ciprofloxacin and are instructed to return to the clinic or to contact the study site coordinator immediately if they vomit within 1 hour of receiving ciprofloxacin. Subjects who vomit within 1 hour of study drug administration should be retreated for *N. gonorrhoeae* infection with an alternative recommended regimen per local standard of care.

Subjects return for clinical and laboratory assessments at Visit 2 (Day 5-10), the Test of Cure visit. Subjects have repeat samples collected for *N. gonorrhoeae* culture and *N. gonorrhoeae* NAAT from all anatomic sites swabbed at Visit 1 (Day 1).

For Visit 3 (Day 11-14), test results are provided to subjects by phone call. No further follow-up is required for subjects who test culture negative and NAAT negative. Subjects who test culture positive or NAAT positive are referred for standard of care treatment for *N. gonorrhoeae*.

The duration of the study for each subject is approximately 11-14 days. Table 1 provides the study schematic. Table 2 presents the schedule of events for each visit.

The study is monitored for futility. The number of treatment failures among subjects eligible for the Per Protocol (PP) analysis population is monitored by a statistician independent from the study team. If, at any point in the trail, 30 subjects eligible for the PP analysis population are classified as treatment failures, then the statistician will notify DMID to consider termination of the trial.

4.2. Discussion of Study Design, Including the Choice of Control Groups

This study is designed as a multi-center, single-arm, open-label clinical study to clinically validate a *gyrA* assay used to determine ciprofloxacin susceptibility in the treatment of uncomplicated gonococcal infection by assessing the efficacy of ciprofloxacin for treatment of uncomplicated *N. gonorrhoeae* infections with serine 91 *gyrA* genotype as identified by the *gyrA* assay.

As the study is designed to assess the ability of the *gyrA* assay to correctly detect subjects with ciprofloxacin-susceptible *N. gonorrhoeae* infections, only subjects with infections positively identified by the assay are enrolled and all subjects are treated with ciprofloxacin (i.e. there is no control group for this study).

4.3. Selection of Study Population

Subjects must meet all of the inclusion criteria in order to be eligible to participate in the study. Subjects who present with a new *N. gonorrhoeae* infection may be rescreened for eligibility. No exemptions are granted on Subject Inclusion/Exclusion Criteria in DMID-sponsored studies.

1. Willing and able to give voluntary written informed consent before any study related procedure is performed.
2. 18 years or older on the day of enrollment.
3. Untreated *gyrA* serine 91 genotype *N. gonorrhoeae* of the rectum, or male or female urogenital tract*, as determined by the *gyrA* test assay on a specimen collected within 30 days of enrollment.
   *Subjects must have *gyrA* serine 91 genotype detected for *N. gonorrhoeae* from at least one non-pharyngeal site.
4. Willing to abstain from sexual intercourse or use condoms during any sexual contact until the Test of Cure Visit (Visit 2, Day 5-10) is complete.
5. Women of childbearing potential* must have no vaginal intercourse 14 days before enrollment or use an effective birth control method ** for 30 days before enrollment and agree to continue through visit 2.
   *A woman is considered of childbearing potential unless post-menopausal (>2 years) or surgically sterilized (tubal ligation >1 year, bilateral oophorectomy, or hysterectomy).
   **Acceptable birth control methods for the purposes of this study may include abstinence from intercourse with a male partner, monogamous relationship with vasectomized partner, male condoms with the use of applied spermicide, intrauterine devices, and licensed hormonal methods. A highly effective method of contraception is defined as one that results in a low failure rate (i.e., less than 1% per year) when
   used consistently and correctly.
6. Able to swallow pills.
7. Willing to comply with protocol requirements, including availability for follow-up for the duration of the study.
8. Agree to avoid systemic or intravaginal antibiotics* with activity against *N. gonorrhoeae* from enrollment through Visit 2 (Day 5-10).
   *Topical and intravaginal antifungals are permitted.
9. Agree to avoid magnesium/aluminum antacids, sucralfate, didanosine, or highly buffered drugs, up to 2 hours after receipt of study drug.

Subjects meeting any of the following criteria at enrollment will be excluded from the study:

1. Known renal insufficiency from clinical history.
2. Use of systemic or intravaginal antibiotics* with potential activity against *N. gonorrhoeae* within 30 days prior to study drug administration.
   *Topical and intravaginal antifungals are permitted.
3. Use of systemic corticosteroid drugs or other immunosuppressive therapy within 30 days prior to enrollment.

4. Receipt or planned receipt of an investigational product in a clinical trial within 30 days prior to or 7 days after treatment administration.
5. Pregnant or breastfeeding.
6. Clinical diagnosis of pelvic inflammatory disease or genital ulcer.
7. Confirmed or suspected complicated or systemic gonococcal infection, such as abdominal pain, testicular pain, epididymitis, orchitis, arthritis, or endocarditis.
8. Receipt of magnesium/aluminum antacids, sucralfate, didanosine, or highly buffered drugs, within 6 hours before receipt of study drug.
9. Mutant *N. gonorrhoeae gyrA* serine 91 genotype from any anatomic site, as determined by the *gyrA* test assay on a specimen collected within 30 days of enrollment.
10. Known allergy or history of adverse reaction to ciprofloxacin.
11. Known allergy to quinolones.
12. Previous enrollment in this study.
13. Medical condition or other factor that in the judgment of the investigator might affect ability to comply with procedures.

Subjects may withdraw or be withdrawn from the study for any of the reasons given below. The reason for withdrawal is recorded in the data collection form.

- Subject vomits within 1 hour of study medication administration.
- Subject receives any systemic antibiotic other than the study medication prior to Visit 2 (Day 5-10).
- Subject is pregnant or breastfeeding.
- Discretionary decision by the site investigator.
- At the discretion of the Institutional Review Board (IRB), National Institutes of Health (NIH), or other government agency as part of their duties to ensure that research subjects are protected.

Subjects who withdraw voluntarily prior to receiving ciprofloxacin are offered local standard of care treatment for *N. gonorrhoeae* and followed per clinic guidelines.

Subjects who withdraw voluntarily or never return after receiving ciprofloxacin and tolerated medication without difficulty are not contacted for repeat gonorrhea testing or treatment.

Subjects who withdraw voluntarily or never return after being found to be positive for *N. gonorrhoeae* at Visit 2 (Day 5-10) are contacted by phone and by certified mail with instructions that they should follow-up for treatment per local standard of care and should be followed per clinic guidelines.

Although the study sponsor has every intention of completing the study, the sponsor reserves the right to terminate the study at any time for clinical or administrative reasons.

4.4. Treatments

4.4.1. Treatments Administered

Subjects with *gyrA* serine 91 genotype rectal or urogenital *N. gonorrhoeae* receive one directly observed dose of ciprofloxacin 500 mg. Subjects are observed in the clinic for at least 5 minutes after receiving ciprofloxacin and are instructed to return to the clinic or to contact the study site coordinator immediately if they vomit within 1 hour of receiving ciprofloxacin. Subjects who vomit within 1 hour of study drug administration should be retreated for *N. gonorrhoeae* infection with an alternative recommended regimen per local standard of care.

The dates of the treatment are presented for subjects in the Safety population by site in Table 3.

4.4.2. Identity of Study Product(s)

Ciprofloxacin is a quinolone medication approved by the FDA for the treatment of gonorrhea. Ciprofloxacin hydrochloride, USP, a fluoroquinolone, is the monohydrochloride monohydrate salt of 1- cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-7-(1piperazinyl)-3-quinolinecarboxylic acid. The molecular weight of the ciprofloxacin hydrochloride monohydrate is 385.82. It is a faintly yellowish to light yellow crystalline substance.

Ciprofloxacin will be supplied as 500 mg tablets.

4.4.3. Method of Assigning Subjects to Treatment Groups (Randomization)

Not applicable.

4.4.4. Selection and Timing of Dose for Each Subject

Subjects with *gyrA* serine 91 genotype rectal or urogenital *N. gonorrhoeae* receive one dose of ciprofloxacin 500 mg by mouth under direct observation with the date and time of administration documented.

4.4.5. Blinding

Not applicable. This is an unblinded study.

4.4.6. Prior and Concomitant Therapy

Medications history (concomitant medications contraindicated with ciprofloxacin) include a review of all current medications and medications taken 30 days prior to study enrollment. Assessment of eligibility also include a review of all permitted and prohibited medications per the Subject Inclusion and Exclusion Criteria (see Section 4.3).

Administration of any contraindicated medications or new antibiotics after enrollment are recorded on the appropriate data collection form.

Contraindicated medications include all medications contraindicated with ciprofloxacin (described in Section 4.3) taken 30 days prior to signing the informed consent form through Visit 2 or early termination, whichever occurs first.

Subjects who have received study medication and are subsequently diagnosed with a concomitant infection, which requires systemic antibiotics receive treatment according to the local clinic's standard of care.

Use of new medication should prompt evaluation for the presence of a new diagnosis of chronic medical disease or condition.

Oral contraceptives are allowed, as they do not alter the metabolism of ciprofloxacin.

4.4.7. Treatment Compliance

All subjects with *gyrA* serine 91 genotype rectal or urogenital *N. gonorrhoeae* will receive single dose of directly observed ciprofloxacin 500 mg in the clinic.

Subjects are observed for at least 5 minutes after administration of ciprofloxacin and are instructed to return to the clinic or to contact the study site coordinator immediately if they vomit within 1 hour of receiving study medication. Subjects who vomit within 1 hour of study drug administration are retreated for *N. gonorrhoeae* infection with an alternative recommended regimen per the local standard of care.

See Section 3.3.6 for the definition of treatment compliance.

4.5. Efficacy and Safety Variables

General principles for safety and efficacy analyses are to accept multiple observations within a specific visit period. In the case of multiple observations within a specific window, the assessment value that is closest to the scheduled visit window will be used in the analyses for the post-baseline records. The last observed values prior to administration of ciprofloxacin will be used as the baseline value. All the recorded data will be listed. If observations have the same distance to the scheduled assessment, the latest one will be used.

4.5.1. Safety Variables

Ciprofloxacin has a well-established safety profile and has been prescribed to several millions of people in the United States (US) and worldwide as it was the CDC's recommended treatment regimen for uncomplicated gonorrhea from 1993 to 2007. Therefore, adverse event assessment is not required for this study.

In order to address the FDA Drug Safety Communication dated May 12, 2016, regarding fluoroquinolone use for certain uncomplicated infections, subjects are asked at Visit 1, Visit 2, and any Unscheduled or Early Termination Visit if they have experienced any serious side effects related to fluoroquinolone use. These include tendon pain, joint pain, muscle pain, tingling or pricking sensation, confusion, and hallucinations. This information is recorded in the study source documents as a change in health status.

Any subject who experiences such an event is given instructions on how to submit a MedWatch Consumer Voluntary Reporting Form to the FDA if they desire.

Side effects of fluoroquinolone use will be summarized for all enrolled subjects (see Section 9).

4.5.2. Efficacy Variables

See Section 3.3 for efficacy variable definitions.

5. SAMPLE SIZE CONSIDERATIONS

The primary analysis will compute the proportion of ciprofloxacin-susceptible *N. gonorrhoeae*-infected subjects with microbiological cure 5-10 days after receiving ciprofloxacin in the per-protocol analysis population. The confidence interval for the microbiological cure proportion will be computed using a one-sided modified Jeffreys interval using a significance level of 0.05. Power calculations were performed via a simulation study based on 10,000 replications assuming a 98% microbiological cure rate.

Figure 1 presents the power available to test that the microbiological cure rate is at least 95% (i.e., lower bound of the one-sided confidence interval is at least 95%) across a range of evaluable sample sizes. Here, evaluable denotes eligible for the PP analysis population. The power reaches 80% at a sample size of 195 evaluable subjects; however, since the power curve is not monotonic, sample sizes directly on either side of 195 are below 80%. Since the exact number of evaluable subjects at the end of the study is difficult to predict, an evaluable target of 257 subjects is chosen to ensure at least 80% even if the exact number of evaluable subjects at the end of the study differs slightly from 257. With a target of 257, the power available is approximately 85% and we can fall at most 10 subjects short (sample size of 247 evaluable subjects) and still ensure 80% power. Any sample size greater than 257 will ensure at least 80% power.

To calculate the number of subjects required to enroll to reach 257 subjects in the PP analysis population, the following assumptions are made:

- 25% of enrolled subjects will be culture negative at baseline.
- 10% of subjects will be excluded from the PP analysis population (reasons for exclusion are stated in Section 6.3)

Under these assumptions, enrolling 381 subjects will provide 257 subjects in the PP analysis population. Since the proportion of subjects who will be culture negative at baseline can vary depending on a number of factors, 25% is a rough estimate. The exact number of subjects needed to provide 257 subjects in the PP analysis population may vary from 381, so 381 is an approximate enrollment target.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Tabulations will be used extensively to summarize the data. All continuous variables will be summarized using some or all of the following descriptive statistics: n (samples size), mean, standard deviation, median, maximum, and minimum. The frequency and percentages (based on the sample size) of observed levels will be reported for all categorical measures. Modified Jeffreys confidence intervals (CIs) for binomial proportions will be computed for efficacy variables [2]. A 5% one-sided significance level will be used; i.e. one-sided 95% confidence intervals will be generated. In general, all data will be listed, sorted by site and subject, and when appropriate by visit number within subject. All summary tables will be annotated with the total population size relevant to that table, including any missing observations.

Note that in the data listing, Subject ID is the unique subject identifier, not the Study ID used on study, and dates will not be included, only Study Day. Study Day 1 will be the day of the dose of treatment.

6.1.1. Pseudo Code

The following SAS® pseudo code will be used to calculate the following:

Lower bound of the one-sided 95% Jeffreys CI for proportions/percentages if the number of cures is less than the number of subjects included in the analysis:

```
proc freq;
   tables cure / alpha=0.1 binomial(jeffreys);
run;
```

Lower bound of the one-sided 95% Jeffreys CI for proportions/percentages if the number of cures is equal to the number of subjects (n) included in the analysis:

```
CILower = 0.05**(1/n);
```

95% Wilson CI for proportions/percentages:

```
proc freq;
      Table treatment*analysisvariable / alpha=0.1 binomial(wilson);
      ods output binomialcls=outputdsn;
run;
```

95% Exact Blaker CI for proportions/percentages:

```
proc freq;
      Table treatment*analysisvariable / alpha=0.1 binomial(blaker);
      ods output binomialcls=outputdsn;
run;
```

95% Agresti-Coull CI for proportions/percentages:

```
proc freq;
      Table treatment*analysisvariable / alpha=0.1 binomial(AC);
      ods output binomialcls=outputdsn;
run;
```

6.2. Timing of Analyses

The final analysis will be performed after database lock when all subjects have been followed through Visit 3, the final study visit.

6.3. Analysis Populations

6.3.1. Safety Analyses

There are no formal analyses of safety data (see Section 4.5.1 and Section 9).

6.3.2. Efficacy Analyses

All efficacy analyses will be performed in the Per Protocol (PP), microbiological Intent-to Treat (micro-ITT) and Intent-to-Treat (ITT) analyses populations.

6.3.2.1. Intent-to-Treat Analysis (ITT) Population

The ITT analysis population includes all enrolled subjects, regardless of whether they received study treatment or were compliant with the administration procedures or schedule.

Subjects with non-evaluable outcome status will be included in the ITT analysis population and classified as microbiological failures. Subjects who receive any treatment other than the study medication for their *N. gonorrhoeae* infection will be included in all efficacy analyses as treatment failures. Subjects who discontinued early from the study with lack of treatment effect being the documented reason for discontinuation will be included as microbiological failures. Subjects who vomited within 1 hour of administration will be included as microbiological failures.

6.3.2.2. Microbiological Intent-to-Treat (micro-ITT) Population

For the primary analysis, the micro-ITT population includes all enrolled subjects who have wild type *gyrA* serine 91 *N. gonorrhoeae* isolated from the rectum or urogenital site on Day 1 culture. Subjects with infections at multiple anatomic sites are included as long as one of the infected sites is the rectum or urogenital site. Subjects with infections at multiple anatomic sites must be wild- type at each culture-positive site to be included in the primary analysis.

Subjects with non-evaluable outcome status will be included in the micro-ITT population and classified as microbiological failures. Subjects who discontinued early from the study with lack of treatment effect being the documented reason for discontinuation will be included as microbiological failures. Subjects who vomited within 1 hour of administration will be included as microbiological failures.

For the analysis of secondary objective 1, subjects need to have wild type *gyrA* serine 91 *N. gonorrhoeae* isolated on Day 1 culture at the particular anatomical site being assessed. The results at the other anatomical sites will not be considered when determining a subject's eligibility into each of the site-specific populations.

There will be four micro-ITT populations identified:

- Primary micro-ITT population
- Rectal micro-ITT population
- Urogenital micro-ITT population
- Pharyngeal micro-ITT population

6.3.2.3. Per Protocol Population

For the primary outcome measure, the PP population includes enrolled subjects who met all inclusion/exclusion criteria, have wild type *gyrA* serine 91 *N. gonorrhoeae* isolated on Day 1 culture from the rectum or urogenital site, have an evaluable microbiological outcome status (see Section 3.3.2), complied with study treatment, did not receive any contraindicated medication or systemic antibiotic other than the study medication for any infection prior to Visit 2, and returned for their Visit 2 (Test of Cure) visit within window. Subjects with infections at multiple anatomic sites are included as long as one of the infected sites is the rectum or urogenital site.

In addition, subject who are infected at multiple anatomic sites must meet either of the two following criteria to be included in the PP population:

- wild-type at each culture positive site, or
- wild-type at the rectum/urogenital site and unknown *gyrA* status at the pharyngeal site (due to indeterminate or missing result).

For subjects who meet the second criteria above, the pharyngeal results will be ignored in the determination of cure status.

For the PP analysis population, subjects with non-evaluable outcome status will be excluded from the analysis. Subjects who discontinued early from the study with lack of treatment effect being the documented reason for discontinuation will be included as microbiological failures.

For the analysis of secondary objective 1, subjects need to have wild type *gyrA* serine 91 *N. gonorrhoeae* isolated on Day 1 culture at the particular anatomical site being assessed. In addition, alternate per-protocol analyses which exclude subjects with reported concomitant infection/disease/procedure that may interfere with study product, use of concomitant medications or products that may interfere with study product, significant protocol deviations, and other events that may impact study product effectiveness or study analyses will be explored. Exclusions from this alternate PP population will be determined on a case-by-case basis prior to database lock.

There will be four PP populations and identified based on wild type *gyrA* serine 91 *N. gonorrhoeae* isolation at Day 1 for a particular site. The results at the other anatomical sites will not be considered when determining a subject's eligibility into each of the site-specific populations.

- Primary PP population
- Rectal PP population
- Urogenital PP population
- Pharyngeal PP population

6.3.3. Considerations for all Analysis Populations

Table 4 summarizes the ITT, micro-ITT, and PP analysis population eligibilities for the analysis of the primary outcome measure and reasons excluded. Subjects will be included in the count for a particular reason for exclusion if they met that criterion. As subjects may meet more than one criterion for exclusion, the "Excluded from…" counts may be less than the sum of the individual reason counts. A listing of the subjects excluded from each of the analysis populations and the reasons for exclusion will be provided (Listing 1).

6.4. Covariates and Subgroups

The protocol does not define any formal subgroup analyses for the primary endpoint, and the study is not adequately powered to perform subgroup analyses. However, the secondary efficacy analyses will be performed within each anatomical site and the exploratory analyses will be performed within each demographic subgroup and clinical characteristics subgroup (see Section 8.3). In addition, enrollment summaries will be presented by clinical site (see Section 6.7).

6.5. Missing Data

For the primary analysis, subjects with non-evaluable outcome status will be included in the micro-ITT analysis population and classified as microbiological failures. Subjects who discontinued early from the study with lack of treatment effect being the documented reason for discontinuation will be included as microbiological failures.

For the PP analyses of the primary outcome measure, subjects who have a non-evaluable outcome status, including subjects who did not return for Visit 2, whose culture results at Visit 2 were not available for any reason, or could not be evaluated for microbiological outcome status for any other reason are excluded.

For the secondary analysis of microbiological cure at each anatomic site using site-specific micro-ITT analysis populations, subjects with non-evaluable outcome status at the particular anatomic site will be included in analyses and classified as microbiological failures.

Subjects who discontinued early from the study due to a lack of treatment effect are counted in all analysis populations as microbiological failures.

For secondary outcome of the sensitivity of the *gyrA* assay for detection of ciprofloxacin-susceptible N. *gonorrhoeae* infections, only specimens with determinate results for both the *gyrA* assay and the culture-based antimicrobial susceptibility test will be included. If either the *gyrA* assay or the culture-based antimicrobial susceptibility test results are indeterminate or missing, the specimen will be excluded from the analysis.

6.6. Interim Analyses and Data Monitoring

There are no planned interim analyses for this study. However, the study is monitored for futility. The number of treatment failures among subjects eligible for PP analysis population is monitored by a statistician independent from the study team. If, at any point in the trail, 30 subjects eligible for the PP analysis population are classified as microbiological failures, then the statistician will notify DMID to consider termination of the trail.

6.7. Multicenter Studies

Data will be pooled across all clinical sites. Center effects are not anticipated because the treatment is self-administered, the sites are using standardized procedures for assessment of serious side effects related to fluoroquinolone use and the collection and testing (via culture and NAAT) of specimens.

Screening, enrollment, subject demographics, baseline characteristics and disposition, and protocol deviations will be summarized by clinical site.

6.8. Multiple Comparisons/Multiplicity

No adjustments for multiple testing are planned.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

The disposition of subjects in the study will be tabulated by site and all subjects. Table 5 shows the number of subjects who are screen failures and number of subjects that met each inclusion/exclusion criterion. Table 6 shows the total number of subjects enrolled, treated, compliant with study treatment and completing each visit (Visit 1 through Visit 3). A listing of subjects who completed the study, terminated early from study and the reason for early termination is included in Listing 2.

Figure 2 is a flowchart showing the disposition of study subjects in the safety and efficacy analyses, adapted from the CONSORT statement [1]. It shows the number of subject eligible, enrolled and randomized, lost to follow-up, and analyzed for the safety and efficacy analyses.

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by the deviation category and the type of deviation for all enrolled subjects (Table 7). All subject-specific protocol deviations and non-subject-specific protocol deviations are provided in data listings (Listing 3 and Listing 4, respectively).

8. EFFICACY EVALUATION

8.1. Primary Efficacy Analyses

The primary analysis will test whether the microbiological cure rate of ciprofloxacin in subjects infected with *gyrA* serine 91 genotype *N. gonorrhoeae* at rectum or urogenital site is greater than or equal to 95%. The cure rate will be estimated by the proportion of subjects infected with *gyrA* serine 91 genotype *N. gonorrhoeae* with microbiological cure at Visit 2. The microbiological outcome status is defined in Section 3.3.2.

A formal hypothesis test will be performed with null hypothesis that the proportion of ciprofloxacin-susceptible (as identified by the *gyrA* assay) *N. gonorrhoeae*-infected subjects with microbiological cure 5-9 (or 10) days after receiving ciprofloxacin is less than 0.95 and alternative hypothesis that the proportion is at least 0.95. The test will be performed by calculating the one-sided 95% modified Jeffreys confidence interval and comparing it to the value 0.95.

The summary of microbiological cure number, microbiological cure rate, and one-sided 95% modified Jeffreys confidence interval by analysis population will be presented (Table 8). See Section 6.1.1 for pseudocode to fit the above analyses. Individual efficacy data is presented in Listing 7.

8.1.1. Sensitivity Analyses

A sensitivity analysis of the primary outcome will be performed to assess the impact of the choice of confidence interval. The primary analysis will be repeated using three different kinds of confidence intervals for binomial proportions: Wilson, Agresti-Coull, and Blaker intervals [2]. The summary of microbiological cure number, microbiological cure rate, and one-sided 95% confidence intervals by analysis population will be presented. See Table 9.

Additional sensitivity analyses of the primary outcome measure will be performed with modifications to the definition of the micro-ITT and PP populations. First, the micro-ITT and PP populations will be modified such that subjects with culture-positive but unknown (indeterminate or missing) *gyrA* results will be included as well as subjects with wild-type only infections. For each subject, all infected sites (whether the infection is wild-type or unknown) will be considered in determining the subject's cure status. Next, the primary analysis will be repeated in the alternate PP population described in Section 6.3.2.3. See Table 10 .

8.2. Secondary Efficacy Analyses

The analysis of the first secondary endpoint will proceed using the same methods as the primary efficacy analysis using the anatomical site-specific definition of microbiological outcome status (see Section 3.3.2). Summaries of the cure rate and associated confidence interval will be generated for each individual anatomical site and analysis population (Table 11).

For the analysis of the second secondary endpoint, the sensitivity and positive predictive value of the *gyrA* assay will be estimated as described in Section 3.3.3. This analysis will be performed by anatomic sites in the ITT analysis population. See Table 12.

The summaries of *N. gonorrhoeae* culture results, NAAT testing results and *gyrA* assay results will be presented by each anatomical site and visit (Table 13, Table 14, and Table 15**)**. Listing 5 and Listing 6 provide a complete listing of individual microbiological results.

8.2.1. Other Efficacy Analyses

An analysis of the *in vitro* minimum inhibitory concentrations against Ciprofloxacin of gonococcal isolates from cultures taken at Visit 1 and Visit 2 will be conducted. The number of urogenital, rectal and pharyngeal susceptible isolates for a number of antimicrobials, including Azithromycin, Cefixime, Ceftriaxon, Ciprofloxacin, Gentamicin, Penicillin, Tetracycline, and Spectinomycin will be summarized for each visit and subject's microbiological outcome status.

The Median (MIC50), minimum, maximum and 90th percentile (MIC90) MICs to each antimicrobial will also be reported at Visit 1 and Visit 2. Beta-lactamase results will be summarized, as well. See Table 16, Table 17, Table 18, Table 19, and Table 20. The distribution of MICs in histogram for each antimicrobial by Visit and specimen will be shown in Figure 3, Figure 4, Figure 5, Figure 6, Figure 7 and Figure 8. This analysis will be performed in the micro-ITT and PP populations.

8.3. Exploratory Efficacy Analyses

The proportion of subjects infected with *gyrA* serine 91 genotype *N. gonorrhoeae* with microbiological cure at Visit 2 will be summarized by demographic (sex, age, race, ethnicity) and clinical characteristics (symptomatic status and re-exposure status at follow up by anatomic sites). Age will be broken into two categories based on the median age: Age < median and Age >=median for each analysis population. The microbiological cure rate will be calculated separately for each category. See Table 21 and Table 26. The analyses by demographics will be repeated on the infection level, as well (see Table 22, Table 23, Table 24, and Table 25).

The genomic analyses of identification and characterization of non-*gyrA* gene-dependent mechanisms of ciprofloxacin resistance by genotyping and whole genome sequencing of nucleic acid isolated from uncured subjects at Visit 2 will be described in a separate statistical analysis plan.

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, ethnicity, and race will be presented by site for all enrolled subjects (ITT population) and PP population (Table 27, Table 28). Ethnicity is categorized as Hispanic or Latino, or not Hispanic and not Latino. Race is categorized as American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, Black or African American, White, Multi-Racial, or Unknown. In accordance with NIH reporting policy, subjects may self-designate as belonging to more than one race (Multi-Racial) or may refuse to identify a race (Unknown), the latter reflected in the electronic Case Report Form (eCRF) as "No" to each racial option. Age will be summarized by site for all enrolled subjects and PP population (Table 29, Table 30). A summary of signs and symptoms of *N. gonorrhoeae* will be presented by visit (Table 31).

Baseline and follow-up sexual history will be summarized for all enrolled subjects (ITT population) (Table 32, Table 33).

Individual subject listings (Appendix 3) will be presented for all demographics and baseline characteristics (Listing 8), sexual history (Listing 9, Listing 10, Listing 11), and *N. gonorrhoeae* symptomatology (Listing 12).

9.2. Measurements of Treatment Compliance

The number of subjects not compliant with study treatment will be presented as part of the subject disposition (Table 6). Individual subject listing will be presented for treatment compliance data (Listing 13).

9.3. Adverse Events

9.3.1. Side Effects Related to Fluoroquinolone use

Summary of side effects related to fluoroquinolone use will be presented by visits (Table 34). Individual subject listing will be presented for all side effects related to fluoroquinolone use (Listing 14).

9.4. Pregnancies

Female subjects who are pregnant at enrollment are excluded from the study. Urine pregnancy testing is conducted for females of childbearing potential. Urine collected at Visit 1 is analyzed for detecting pregnancies by use of a standard rapid urine βhCG assay (Listing 15).

9.5. Physical Evaluations

A targeted physical examination is performed at enrollment Visit 1 and Visit 2. The following body systems are assessed: Abdomen, Cardiovascular/heart, Extremities, General Appearance, Genitourinary, HEENT, Lymph nodes, Musculoskeletal, Neck, Neurological, Pulmonary/Chest, and Skin. Individual subject listings will be provided for physical exam findings (Listing 16).

9.6. Concomitant Medications

Summaries of concomitant medications contraindicated with ciprofloxacin that were taken 30 days prior to study enrollment and after enrollment will be presented by the World Health Organization (WHO), Anatomical Therapeutic Chemical Classification System (ATC) Level 1 and Level 2 for all enrolled subjects. (Table 35). Individual subject listing will be presented for concomitant medication (Listing 17).

10. PHARMACOKINETICS

Not applicable.

11. IMMUNOGENICITY

Not applicable.

12. OTHER ANALYSES

No other analyses are planned.

13. REPORTING CONVENTIONS

P-values ≥0.001 and ≤0.999 will be reported to three decimal places; p-values less than 0.001 will be reported as "<0.001"; p-values greater than 0.999 will be reported as ">0.999". The mean, median, standard deviation, and other statistics other than quantiles, will be reported to one decimal place greater than the original data. Quantiles other than the median will use the same number of decimal places as the original data. Proportions will be presented as two decimal places; values greater than zero but <0.01 will be presented as "<0.01". Percentages will be reported to the nearest whole number; values greater than zero but < 1% will be presented as "<1"; values greater than 99% but less than 100% will be reported as >99%. Estimated parameters, not on the same scale as raw observations (e.g. regression coefficients) will be reported to three significant figures.

14. TECHNICAL DETAILS

SAS version 9.4 or above will be used to generate all tables, figures, and listings.

15. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

There are no changes in the planned analyses.

16. REFERENCES

1. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. JAMA. 2001; 285(15):2006-2007.
2. Brown L, Cai T, DasGupta A. Interval estimation for a binomial proportion. Statistical Science 2001 16(2):101–33. doi:10.1214/ss/1009213286

17. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendices 1, 2, and 3, respectively.

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

Table 1: Study Design

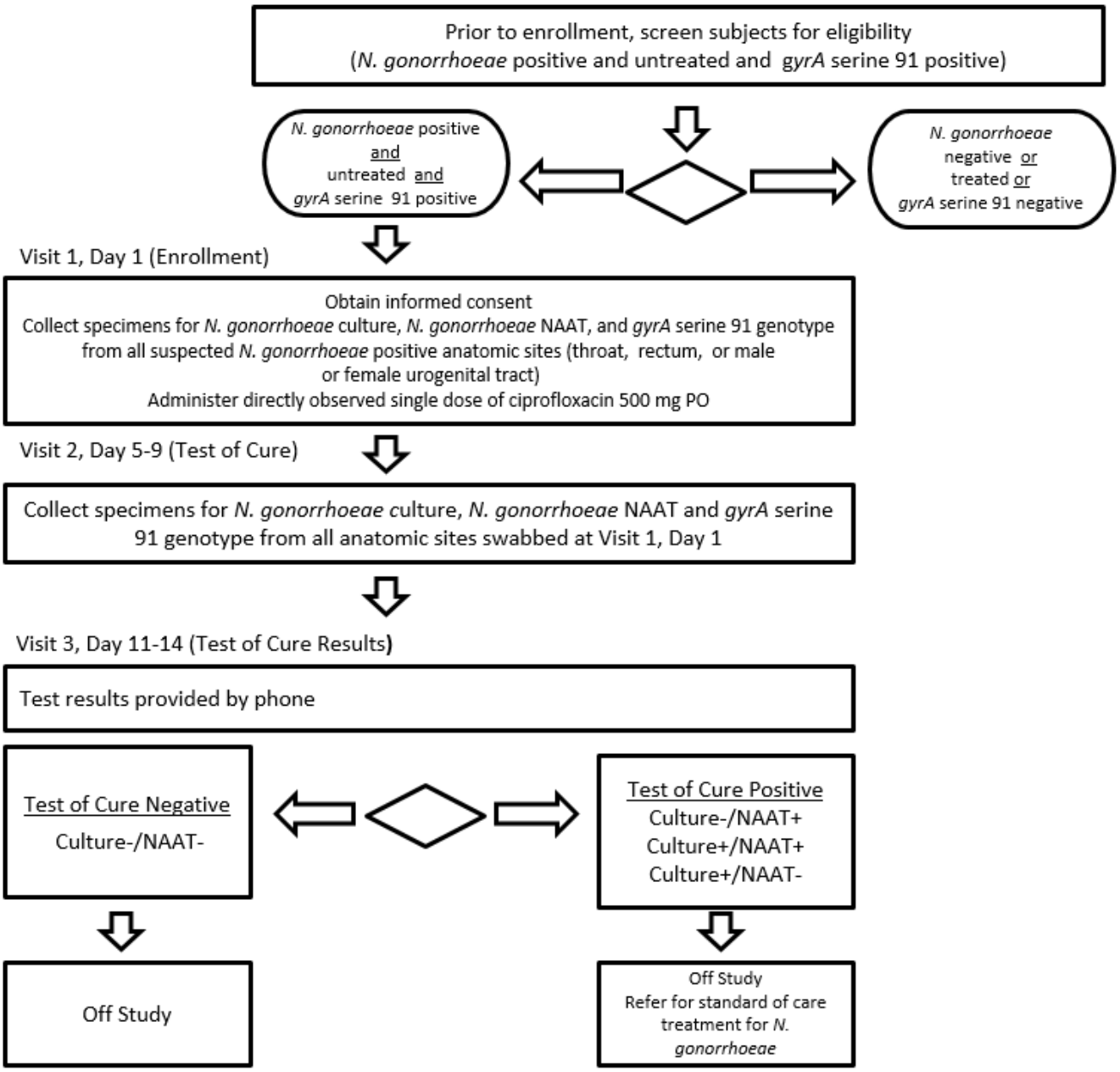


Table 2: Schedule of Study Procedures

Evaluation	Screening/ Enrollment Visit 1 Day 1	Visit 2 Day 5-10 (Test of Cure)	Visit 3 Day 11-14[3] (Test of Cure Results)	Unscheduled/ Early Termination Visit[5]
Signed consent form	X			
Confirmation of eligibility criteria	X			
Medical history for assessment of specific symptoms that are potentially related to fluoroquinolone use as described in section 9, Assessment of Safety	X	X		X
Signs/symptoms	X	X		X
Concomitant medications	X	X		X
Sexual history	X			
Interim sexual history		X		X
Targeted physical examination	X	X		X
Rapid urine βhCG pregnancy test (females)	X			
Speculum examination (females)	X			
Cervical swab for *N. gonorrhoeae* culture (females)	X[2]	X[2]		
Cervical or vaginal swab for NAAT and *gyrA* assay (females)[1]	X[2]	X[2]		
Urethral swab for *N. gonorrhoeae* culture (males)	X[2]	X[2]		
Urine specimen for NAAT and *gyrA* assay (males)[1]	X[2]	X[2]		
Throat swab for *N. gonorrhoeae* culture and NAAT and *gyrA* assay[1]	X[2]	X[2]		
Rectal swab for *N. gonorrhoeae* culture and NAAT and *gyrA* assay[1]	X[2]	X[2]		
Study intervention	X			
Reminder to abstain from sexual intercourse or use condoms	X			X[5]
Reminder to bring partners in for treatment	X	X	X	X
Follow-up for test of cure results			X[4]	

1. G*yrA* assay required only if NAAT is positive.
2. Collect specimen at anatomic site of *N. gonorrhoeae* infection.
3. Follow-up for test of cure results will be by phone call.
4. For subjects *N. gonorrhoeae* culture negative and NAAT negative, no further follow-up required. Subjects who are *N. gonorrhoeae* culture positive or NAAT positive will be referred for standard of care treatment for *N. gonorrhoeae*.
5. Not required at the Early Termination Visit.

Table 3: Dates of Treatment by Site

[Note: Dates will be categorized by breaking the calendar year into quarters.]

Dates of Dosing	AIDS Healthcare Foundation (N=X)		Los Angeles LGBT Center (N=X)		San Francisco Department of Public Health (N=X)		Philadelphia Department of Public Health (N=X)		University of Mississippi Medical Center (N=X)		Louisiana State University (N=X)		University of California, San Diego Antiviral Research Center (N=X)		Whitman-Walker Health (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total (Entire period of enrollment)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
DDMMMYYYY-DDMMMYYYY	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
DDMMMYYYY-DDMMMYYYY	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
DDMMMYYYY-DDMMMYYYY	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
DDMMMYYYY-DDMMMYYYY	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

N= Number of subjects enrolled at each site.

Table 4: Analysis Population Eligibilities for Primary Outcome Measure

Analysis Populations	Eligibility Category	Reason Subjects Excluded	All Subjects (N=X)	
			n	%
Intent-to-Treat (ITT) Population	Eligible for ITT		x	xx
Primary Microbiological Intent-to Treat (Micro-ITT) Population	Eligible for Primary Micro-ITT		x	xx
	Excluded from Primary Micro-ITT	Any Reason	x	xx
		Did not meet inclusion/exclusion criteria	x	xx
		Did not have rectum/urogenital *N. gonorrhoeae* on Day 1 culture	x	xx
Primary Per-Protocol (PP) Population	Eligible for Primary PP		x	xx
	Excluded from Primary PP	Any Reason	x	xx
		Did not meet inclusion/exclusion criteria	x	xx
		Did not have rectum/urogenital *N. gonorrhoeae* on Day 1 culture	x	xx
		Was not compliant with study product	x	xx
		Received other contraindicated medication or systemic antibiotic other than the study medication for any concomitant infection prior to Visit 2 (Day 5-10)	x	xx
		Did not complete Visit 2 (Test of Cure) visit within window	x	xx
		Did not have an evaluable microbiological outcome status	x	xx

Denominator of percentages is the number of all enrolled subjects (N).

Table 5: Ineligibility Summary of Screen Failures

		Screen Failures (N=xx)	
Inclusion/Exclusion Category	**Inclusion/Exclusion Criterion**	**n[a]**	**%[b]**
Inclusion and Exclusion	Number of subjects failing any eligibility criterion	x	100
Inclusion	Any inclusion criterion	x	xx
	[inclusion criterion 1]	x	xx
	[inclusion criterion 2]	x	xx
	[inclusion criterion 3]	x	xx
Exclusion	Any exclusion criterion	x	xx
	[exclusion criterion 1]	x	xx
	[exclusion criterion 2]	x	xx
	[exclusion criterion 3]	x	xx
Declined Enrollment	Any Reason	x	xx
	Time commitment	x	xx
	Concern of potential risks	x	xx
	Number of procedures	x	xx
	Unable to contact subject	x	xx
	Other	x	xx

[a] More than one criterion may be marked per subject.

[b] Denominator for percentages is the total number of screen failures.

Table 6: Subject Disposition – All Enrolled Subjects

Subject Disposition	All Subjects (N=X)	
	n	%
Screened	x	--
Enrolled	x	100
Enrolled with Positive Baseline rectum/urogenital *N. gonorrhoeae* culture result and with Wild type *gyrA* detected by *gyrA* assay	x	xx
Enrolled and Received Treatment	x	xx
Complied with Treatment	x	xx
Completed Visit 2, Day 5-10 (Test of Cure) [a]	x	xx
Completed Visit 3, Day 11-14 (Test of Cure Results)[a]	x	xx

N = Number of enrolled subjects.
[a] Refer to Listing 1 for reasons subjects terminated early.

Table 7: Distribution of Protocol Deviations by Category and Type

Category	Deviation Type	All Subjects (N=X)	
		No. of Subj.	No. of Dev.
Eligibility/enrollment	Any type	x	x
	Did not meet inclusion criterion	x	x
	Met exclusion criterion	x	x
	ICF not signed prior to study procedures	x	x
	Other	x	x
Treatment administration schedule	Any type	x	x
	Out of window visit	x	x
	Missed visit/visit not conducted	x	x
	Missed treatment administration	x	x
	Delayed treatment administration	x	x
	Other	x	x
Follow-up visit schedule	Any type	x	x
	Out of window visit	x	x
	Missed visit/visit not conducted	x	x
	Other	x	x
Protocol procedure/assessment	Any type	x	x
	Incorrect version of ICF signed	x	x
	Blood not collected	x	x
	swab not collected	x	x
	Urine not collected	x	x
	Other specimen not collected	x	x
	Too few aliquots obtained	x	x
	Specimen result not obtained	x	x
	Required procedure not conducted	x	x

Table 7: Distribution of Protocol Deviations by Category and Type (Continued)

Category	Deviation Type	All Subjects (N=X)	
		No. of Subj.	No. of Dev.
	Required procedure done incorrectly	x	x
	Study product temperature excursion	x	x
	Specimen temperature excursion	x	x
	Other	x	x
Treatment administration	Any type	x	x
	Required procedure done incorrectly	x	x
	Study product temperature excursion	x	x
	Other	x	x

Table 8: Microbiological Cure Rate by Analysis Population

Analysis Population	Statistic	All Subjects
Intent-to-Treat (ITT) Population	Number of Subjects with Microbiological Cure, n	x
	Number of Subjects, N	x
	Microbiological Cure Rate, %	xx.x
	95% CI, %	xx.x, 100
Microbiological Intent-to-Treat (micro-ITT) Population	Number of Subjects with Microbiological Cure, n	x
	Number of Subjects, N	x
	Microbiological Cure Rate, %	xx.x
	95% CI, %	xx.x, 100
Per Protocol (PP) Population	Number of Subjects with Microbiological Cure, n	x
	Number of Subjects, N	x
	Microbiological Cure Rate, %	xx.x
	95% CI, %	xx.x, 100

Table 9: Microbiological Cure Rate by Analysis Population and Alternate Confidence Interval

Analysis Population	Statistic	All Subjects
Intent-to-Treat (ITT) Population	Number of Subjects with Microbiological Cure. n	x
	Number of Subjects, N	x
	Microbiological Cure Rate, %	xx.x
	95% Jeffreys CI*, %	xx.x, 100
	95% Wilson CI, %	xx.x, 100
	95% Agresti-Coull CI, %	xx.x, 100
	95% Blaker CI, %	xx.x, 100
Microbiological Intent-to-Treat (micro-ITT) Population	Number of Subjects with Microbiological Cure, n	x
	Number of Subjects. N	x
	Microbiological Cure Rate, %	xx.x
	95% Jeffreys CI, %	xx.x, 100
	95% Wilson CI, %	xx.x, 100
	95% Agresti-Coull CI, %	xx.x, 100
	95% Blaker CI, %	xx.x, 100
Per-Protocol (PP) Population	Number of Subjects with Microbiological Cure, n	x
	Number of Subjects, N	x
	Microbiological Cure Rate, %	xx.x
	95% Jeffreys CI, %	xx.x, 100
	95% Wilson CI, %	xx.x, 100
	95% Agresti-Coull CI, %	xx.x, 100
	95% Blaker CI, %	xx.x, 100

*95% Modified Jeffrey CI is the primary confidence interval.

Table 10: Microbiological Cure Rate by Analysis Population (Alternate Definitions)

Analysis Population	Statistic	All Subjects
Modified micro-ITT Population	Number of Subjects with Microbiological Cure. n	x
	Number of Subjects, N	x
	Microbiological Cure Rate, %	xx.x
	95% Jeffreys CI*, %	xx.x, 100
Modified PP Population	Number of Subjects with Microbiological Cure, n	x
	Number of Subjects. N	x
	Microbiological Cure Rate, %	xx.x
	95% Jeffreys CI, %	xx.x, 100
Alternate PP Population	Number of Subjects with Microbiological Cure, n	x
	Number of Subjects. N	x
	Microbiological Cure Rate, %	xx.x
	95% Jeffreys CI, %	xx.x, 100

Table 11: Microbiological Cure Rate by Anatomical Site and Analysis Population

Analysis Population	Statistic	Urethral/Cervical	Rectal	Pharyngeal	All Anatomical Sites
Intent-to-Treat (ITT) Population	Number of Infections with Microbiological Cures, n	x	x	x	x
	Number of Infections, N	x	x	x	x
	Microbiological Cure Rate, %	xx.x	xx.x	xx.x	xx.x
	95% CI, %	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100
Microbiological Intent-to-Treat (micro-ITT) Population	Number of Infections with Microbiological Cure, n	x	x	x	x
	Number of Infections, N	x	x	x	x
	Microbiological Cure Rate, %	xx.x	xx.x	xx.x	xx.x
	95% CI, %	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100
Per-Protocol (PP) Population	Number of Infections with Microbiological Cure, n	x	x	x	x
	Number of Infections, N	x	x	x	x
	Microbiological Cure Rate, %	xx.x	xx.x	xx.x	xx.x
	95% CI, %	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100

Implementation Notes: The ITT Population, Micro-ITT Population and PP Population will be based on the anatomical site.

Table 12: Summary of *gyrA* Assay Results and Culture-Based Antimicrobial Susceptibility Testing at Visit 1—ITT population

			Culture-Based Antimicrobial Susceptibility Testing					
	Anatomic Site		Susceptible		Not Susceptible		Total	
			n	%	n	%	n	%
***gyrA* Assay**	**All Sites**	Wild Type *gyrA* detected	xx	xx	xx	xx	xx	xx
		Mutant *gyrA* detected	xx	xx	xx	xx	xx	xx
		Total	xx	xx	xx	xx	xx	100
	Urethral	Wild Type *gyrA* detected	xx	xx	xx	xx	xx	xx
		Mutant *gyrA* detected	xx	xx	xx	xx	xx	xx
		Total	xx	xx	xx	xx	xx	100
	Cervical	Wild Type *gyrA* detected	xx	xx	xx	xx	xx	xx
		Mutant *gyrA* detected	xx	xx	xx	xx	xx	xx
		Total	xx	xx	xx	xx	xx	100
	Rectal	Wild Type *gyrA* detected	xx	xx	xx	xx	xx	xx
		Mutant *gyrA* detected	xx	xx	xx	xx	xx	xx
		Total	xx	xx	xx	xx	xx	100
	Pharyngeal	Wild Type *gyrA* detected	xx	xx	xx	xx	xx	xx
		Mutant *gyrA* detected	xx	xx	xx	xx	xx	xx
		Total	xx	xx	xx	xx	xx	100

The denominator for percentages is based on the number of instances in which swabs taken from a subject at Visit 1 resulted in a determinate *gyrA* Assay result and a determinate culture-based antimicrobial susceptibility test result. If either *gyrA* Assay result or culture-based antimicrobial susceptibility test result is indeterminate or missing, both results will be excluded. Susceptible is defined as an MIC of < 1 ug/ml as reported by the antimicrobial susceptibility testing.

Implementation Notes: The ITT Population will be based on the anatomical site.

Table 13: Culture Results by Time Point and Anatomical Sites

Time Point	Result	Urethral (N=X)		Cervical (N=X)		Rectal (N=X)		Pharyngeal (N=X)	
		n	%	n	%	n	%	n	%
Visit 1 (Day 1)	Number of Subjects tested	x	-	x	-	x	-	x	-
	Positive	x	xx	x	xx	x	xx	x	xx
	Negative	x	xx	x	xx	x	xx	x	xx
	Indeterminate	x	xx	x	xx	x	xx	x	xx
Visit 2 (Day 5-10)	Number of Subjects tested	x	-	x	-	x	-	x	-
	Positive	x	xx	x	xx	x	xx	x	xx
	Negative	x	xx	x	xx	x	xx	x	xx
	Indeterminate	x	xx	x	xx	x	xx	x	xx

N=Number of subjects with culture results at the respective anatomical site.
The denominator of the percentages is the number of subjects tested at the specified anatomical site and visit.

Table 14: NAAT Results by Time Point and Anatomical Sites

Time Point	Result	Urethral (N=X)		Cervical (N=X)		Rectal (N=X)		Pharyngeal (N=X)	
		n	%	n	%	n	%	n	%
Visit 1 (Day 1)	Number of Subjects tested	x	-	x	-	x	-	x	-
	Positive	x	xx	x	xx	x	xx	x	xx
	Negative	x	xx	x	xx	x	xx	x	xx
	Indeterminate	x	xx	x	xx	x	xx	x	xx
Visit 2 (Day 5-10)	Number of Subjects tested	x	-	x	-	x	-	x	-
	Positive	x	xx	x	xx	x	xx	x	xx
	Negative	x	xx	x	xx	x	xx	x	xx
	Indeterminate	x	xx	x	xx	x	xx	x	xx

N=Number of subjects with NAAT results at the specified anatomical site.
The denominator of the percentages is the number of subjects tested at the specified anatomical site and visit.

Table 15: *gyrA* Assay Results by Time Point and Anatomical Sites

Time Point	Result	Urethral		Cervical		Rectal		Pharyngeal	
		n	%	n	%	n	%	n	%
Visit 1 (Day 1)	Number of Subjects tested	x	--	x	--	x	--	x	--
	Wild Type *gyrA* detected	x	xx	x	xx	x	xx	x	xx
	Mutant *gyrA* detected	x	xx	x	xx	x	xx	x	xx
	Indeterminate	x	xx	x	xx	x	xx	x	xx
Visit 2 (Day 5-10)	Number of Subjects tested	x	--	x	--	x	--	x	--
	Wild Type *gyrA* detected	x	xx	x	xx	x	xx	x	xx
	Mutant *gyrA* detected	x	xx	x	xx	x	xx	x	xx
	Indeterminate	x	xx	x	xx	x	xx	x	xx

N=Number of subjects with *gyrA* assay results at the specified anatomical site.
The denominator of the percentages is the number of subjects with a *gyrA* assay result at the specified anatomical site and visit.

Table 16: Antimicrobial Susceptibility of *N. Gonorrhoeae* Isolates by Specimen Type at Visit 1—Micro-ITT population

Specimen	Antimicrobial	Number of Subjects	MIC50 (µg/ml)	MIC90 (µg/ml)	Range (µg/ml)
Urethral/Cervical	Azithromycin	x	x	x	x.x, x.x
	Cefixime	x	x	x	x.x, x.x
	Ceftriaxone	x	x	x	x.x, x.x
	Ciprofloxacin	x	x	x	x.x, x.x
	Gentamicin	x	x	x	x.x, x.x
	Penicillin	x	x	x	x.x, x.x
	Tetracycline	x	x	x	x.x, x.x
	Spectinomycin	x	x	x	x.x, x.x
Rectal	Azithromycin	x	x	x	x.x, x.x
	Cefixime	x	x	x	x.x, x.x
	Ceftriaxone	x	x	x	x.x, x.x
	Ciprofloxacin	x	x	x	x.x, x.x
	Gentamicin	x	x	x	x.x, x.x
	Penicillin	x	x	x	x.x, x.x
	Tetracycline	x	x	x	x.x, x.x
	Spectinomycin	x	x	x	x.x, x.x
Pharyngeal	Azithromycin	x	x	x	x.x, x.x
	Cefixime	x	x	x	x.x, x.x
	Ceftriaxone	x	x	x	x.x, x.x
	Ciprofloxacin	x	x	x	x.x, x.x
	Gentamicin	x	x	x	x.x, x.x
	Penicillin	x	x	x	x.x, x.x
	Tetracycline	x	x	x	x.x, x.x
	Spectinomycin	x	x	x	x.x, x.x

Implementation Notes: The Micro-ITT Population will be based on the anatomical site.

Tables with similar format:

Table 17: Antimicrobial Susceptibility of *N. Gonorrhoeae* Isolates by Specimen Type at Visit 1—PP population

Implementation Notes: The PP Population will be based on the anatomical site.

Table 18: Beta-lactamase Susceptibility of *N. Gonorrhoeae* Isolates by Analysis Population, Specimen Type, and Visit 1

Analysis Population	Visit	Specimen	Number of Subjects	Positive		Negative	
				n	%	n	%
Micro-ITT	1	Urethral/Cervical	x	x	xx	x	xx
		Rectal	x	x	xx	x	xx
		Pharyngeal	x	x	xx	x	xx
	2	Urethral/Cervical	x	x	xx	x	xx
		Rectal	x	x	xx	x	xx
		Pharyngeal	x	x	xx	x	xx
Per-Protocol	1	Urethral/Cervical	x	x	xx	x	xx
		Rectal	x	x	xx	x	xx
		Pharyngeal	x	x	xx	x	xx
	2	Urethral/Cervical	x	x	xx	x	xx
		Rectal	x	x	xx	x	xx
		Pharyngeal	x	x	xx	x	xx

Implementation Notes: The Micro-ITT Population and PP Population will be based on the anatomical site.

Table 19: Antimicrobial Susceptibility of *N. Gonorrhoeae* Isolates by Specimen Type and Microbiological Outcome at Visit 2—Micro-ITT population

Specimen	Subject Microbiological Outcome	Antimicrobial	Number of Subjects	MIC50 (µg/ml)	MIC90 (µg/ml)	Range (µg/ml)
Urethral/Cervical	Microbiological Cure	Azithromycin	x	x	x	x.x, x.x
		Cefixime	x	x	x	x.x, x.x
		Ceftriaxone	x	x	x	x.x, x.x
		Ciprofloxacin	x	x	x	x.x, x.x
		Gentamicin	x	x	x	x.x, x.x
		Penicillin	x	x	x	x.x, x.x
		Tetracycline	x	x	x	x.x, x.x
		Spectinomycin	x	x	x	x.x, x.x
	Microbiological Failure	Azithromycin	x	x	x	x.x, x.x
		Cefixime	x	x	x	x.x, x.x
		Ceftriaxone	x	x	x	x.x, x.x
		Ciprofloxacin	x	x	x	x.x, x.x
		Gentamicin	x	x	x	x.x, x.x
		Penicillin	x	x	x	x.x, x.x
		Tetracycline	x	x	x	x.x, x.x
		Spectinomycin	x	x	x	x.x, x.x
	Overall	Azithromycin	x	x	x	x.x, x.x
		Cefixime	x	x	x	x.x, x.x
		Ceftriaxone	x	x	x	x.x, x.x
		Ciprofloxacin	x	x	x	x.x, x.x
		Gentamicin	x	x	x	x.x, x.x
		Penicillin	x	x	x	x.x, x.x
		Tetracycline	x	x	x	x.x, x.x
		Spectinomycin	x	x	x	x.x, x.x
Etc. for other sites (Rectal and Pharyngeal)						

The denominator for rate estimates is based on the number of subjects enrolled and eligible for the micro-ITT population for the particular anatomical site and microbiological outcome.

Implementation Notes: The Micro-ITT Population will be based on the anatomical site.

Tables with similar format:

Table 20: Antimicrobial Susceptibility of *N. Gonorrhoeae* Isolates by Specimen Type and Microbiological Outcome at Visit 2—PP population

Implementation Notes: The Micro-ITT Population will be based on the anatomical site.

Table 21: Microbiological Cure Rate by Demographic Characteristics and Analysis Population

Characteristic	Analysis Population											
	ITT Population				micro-ITT Population				PP Population			
	Number of Subjects with Microbiological Cure, n	Number of subjects, N	Cure Rate, %	Cure Rate 95% CI, %	Number of Subjects with Microbiological Cure. n	Number of subjects, N	Cure Rate, %	Cure Rate 95% CI, %	Number of Subjects with Microbiological Cure, n	Number of subjects, N	Cure Rate, %	Cure Rate 95% CI, %
Male	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
Female	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
Age < Median	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
Age >= median	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
American Indian/ Alaskan Native	x	x	xx.x	xx.x, 100	x	x	xx.	xx.x, 100	x	x	xx.x	xx.x, 100
Asian	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
Hawaiian/ Pacific Islander	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
White	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
Multi-Racial	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
Other/Unknown	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
Non-Hispanic	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
Hispanic	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100
Not Reported/ Unknown	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100	x	x	xx.x	xx.x, 100

Tables with similar format:

Table 22: Microbiological Cure Rate by Demographic Characteristics and Analysis Population — All Infections

Table 23: Microbiological Cure Rate by Demographic Characteristics and Analysis Population — Urethral Infections

Table 24: Microbiological Cure Rate by Demographic Characteristics and Analysis Population — Rectal Infections

Table 25: Microbiological Cure Rate by Demographic Characteristics and Analysis Population — Pharyngeal Infections

Implementation Notes: The analysis populations will be based on the anatomical site.

Table 26: Microbiological Cure Rate by Clinical Characteristics—Micro-ITT Population

Statistics	Cervical		Urethral		Rectal		Pharyngeal		All Anatomical Sites	
	Symptomatic Status		Symptomatic Status		Symptomatic Status		Symptomatic Status		Symptomatic Status	
	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic
Number of Infections with Microbiological Cure, n	x	x	x	x	x	x	x	x	x	x
Number of Infections, N	x	x	x	x	x	x	x	x	x	x
Microbiological Cure Rate	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Microbiological Cure Rate 95% CI, %	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100
	Re-exposure at Follow up		Re-exposure at Follow up		Re-exposure at Follow up		Re-exposure at Follow up		Re-exposure at Follow up	
	Sex with Protection	Sex without Protection	Sex without Protection	Sex without Protection	Sex without Protection	Sex without Protection	Sex without Protection	Sex without Protection	Sex without Protection	Sex without Protection
Number of Infections with Microbiological Cure, n	x	x	x	x	x	x	x	x	x	x
Number of Infections, N	x	x	x	x	x	x	x	x	x	x
Microbiological Cure Rate, %	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Microbiological Cure Rate 95% CI, %	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100	xx.x, 100

Implementation Notes: The Micro-ITT Population will be based on the anatomical site.

Table 27: Summary of Categorical Demographic and Baseline Characteristics by Site—All Enrolled Subjects

		AIDS Healthcare Foundation (N=X)		Los Angeles LGBT Center (N=X)		San Francisco Department of Public Health (N=X)		Philadelphia Department of Public Health (N=X)		University of Mississippi Medical Center (N=X)		Louisiana State University (N=X)		University of California, San Diego Antiviral Research Center (N=X)		Whitman-Walker Health (N=X)		All Subjects (N=X)	
Variable	**Characteristic**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Sex	Male	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Female	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Asian	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Native Hawaiian or Other Pacific Islander	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Black or African American	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	White	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Multi-Racial	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

N= Number of subjects enrolled at each site.

Tables with similar format:

Table 28: Summary of Categorical Demographic and Baseline Characteristics by Site—PP population

Table 29: Summary of Continuous Demographic and Baseline Characteristics by Site—All Enrolled Subjects

Variable	Statistic	AIDS Healthcare Foundation (N=X)	Los Angeles LGBT Center (N=X)	San Francisco Department of Public Health (N=X)	Philadelphia Department of Public Health (N=X)	University of Mississippi Medical Center (N=X)	Louisiana State University (N=X)	University of California, San Diego Antiviral Research Center (N=X)	Whitman-Walker Health (N=X)	All Subjects (N=X)
Age	Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Minimum	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x

N=Number of subjects enrolled at each site.

Tables with similar format:

Table 30: Summary of Continuous Demographic and Baseline Characteristics—PP Population

Table 31: Signs and Symptoms of *N. Gonorrhoeae* by Visit

Summary	Visit 1 (N = x)		Visit 2 (N = x)		Visit 3* (N=x)	
	n	%	n	%	n	%
Males assessed for signs/symptoms	x	-	x	-	x	-
Females assessed for signs/symptoms	x	-	x	-	x	-
Subjects with any symptoms of gonorrhea	x	xx	x	xx	x	xx
Signs/Symptoms for Males and Females						
Sore Throat[1]	x	xx	x	xx	x	xx
Anorectal Pain[1]	x	xx	x	xx	x	xx
Anorectal Discharge (subject-reported) [1]	x	xx	x	xx	x	xx
Anorectal Discharge (observed) [1]	x	xx	x	xx	x	xx
Anorectal Bleeding[1]	x	xx	x	xx	x	xx
Pharyngeal Erythema (observed) [1]	x	xx	x	xx	x	xx
Signs/Symptoms for Males Only						
Urethral Discharge (subject-reported)[2]	x	xx	x	xx	x	xx
Urethral Discharge (observed) [2]	x	xx	x	xx	x	xx
Pain with Urination[2]	x	xx	x	xx	x	xx
Signs/Symptoms for Females Only						
Abnormal Vaginal Discharge (subject-reported)[3]	x	xx	x	xx	x	xx
Abnormal Cervical Discharge (observed) [3]	x	xx	x	xx	x	xx
Abnormal Vaginal Bleeding[3]	x	xx	x	xx	x	xx
Pain during Intercourse[3]	x	xx	x	xx	x	xx

N is the number of subjects assessed for signs/symptoms at the particular visit.
'n' represents the number of subjects who reported each sign or symptom at the Visit(s) indicated.
The same subject may be counted at all visits;
*Only some subjects have data at Visit 3 due to the protocol amendment.
1 The denominator of the percentage is the number of subjects for each visit.
2 The denominator of the percentage is the number of males for each visit.
3 The denominator of the percentage is the number of females for each visit.

Table 32: Summary of Baseline Categorical Sexual History—ITT population

Sexual History Interview Question	Value	All Subjects (N=X)	
		n	%
1. What is your gender identity?	Man	x	xx
	Woman	x	xx
	Trans male/Trans man	x	xx
	Trans female/Trans woman	x	xx
	Genderqueer/Gender non-conforming	x	xx
	Multiple	x	xx
	Other	x	xx
	Refused to Answer	x	xx
2. What is your sexual orientation?	Heterosexual/Straight	x	xx
	Homosexual/gay/lesbian	x	xx
	Bisexual	x	xx
	Other	x	xx
	Refused to Answer	x	xx
3. Do you have sex with men, women, transgender men, transgender women, or multiple genders?	Men	x	xx
	Women	x	xx
	Trans male/Trans man	x	xx
	Trans female/Trans woman	x	xx
	Multiple	x	xx
	Refused to Answer	x	xx
4. Have you had sex (vaginal, anal, or oral) in the past 30 days?	Yes	x	xx
	No	x	xx
	Refuse to answer	x	xx

N=Number of all enrolled subjects

Table 33: Summary of Follow-up Categorical Sexual History—All Enrolled Subjects

Sexual History Interview Question	Value	Visit 2 (N=X)		Unscheduled Visit (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
1. Have you had sex (vaginal, anal, or oral) since the last visit?	Yes	x	xx	x	xx	x	xx
	No	x	xx	x	xx	x	xx
	Refuse to answer	x	xx	x	xx	x	xx
2. Have you had vaginal intercourse since the last visit?	Yes	x	xx	x	xx	x	xx
	No	x	xx	x	xx	x	xx
	Refuse to answer	x	xx	x	xx	x	xx
If Yes for question 2, did you use a condom with vaginal intercourse[1]	No	x	xx	x	xx	x	xx
	Always	x	xx	x	xx	x	xx
	Sometimes	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx
	Refuse to answer	x	xx	x	xx	x	xx
3. Have you given oral intercourse since the last visit?	Yes	x	xx	x	xx	x	xx
	No	x	xx	x	xx	x	xx
	Refuse to answer	x	xx	x	xx	x	xx
If Yes for question 3, did you use a condom or barrier with oral intercourse?[2]	No	x	xx	x	xx	x	xx
	Always	x	xx	x	xx	x	xx
	Sometimes	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx
	Refuse to answer	x	xx	x	xx	x	xx
4. Have you received oral intercourse since the last visit?	Yes	x	xx	x	xx	x	xx
	No	x	xx	x	xx	x	xx
	Refuse to answer	x	xx	x	xx	x	xx
If Yes for question 4, did you use a condom or barrier with oral intercourse?[3]	No	x	xx	x	xx	x	xx
	Always	x	xx	x	xx	x	xx
	Sometimes	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx
	Refuse to answer	x	xx	x	xx	x	xx
5. Have you had receptive 'bottom' anal intercourse since the last visit?	Yes	x	xx	x	xx	x	xx
	No	x	xx	x	xx	x	xx
	Refuse to answer	x	xx	x	xx	x	xx

Table 33: Summary of Follow-up Categorical Sexual History — All Enrolled Subjects (Continued)

Sexual History Interview Question	Value	Visit 2 (N=X)		Unscheduled Visit (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
If Yes for question 5, did you use a condom with receptive anal intercourse?[4]	No	x	xx	x	xx	x	xx
	Always	x	xx	x	xx	x	xx
	Sometimes	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx
	Refuse to answer	x	xx	x	xx	x	xx
6. Have you had insertive 'top' anal intercourse since the last visit? (Males only)[5]	No	x	xx	x	xx	x	xx
	Yes	x	xx	x	xx	x	xx
	Refused to answer	x	xx	x	xx	x	xx
	N/A (if female)	x	xx	x	xx	x	xx
If Yes for question 6, did you use a condom with insertive anal intercourse?[6]	No	x	xx	x	xx	x	xx
	Always	x	xx	x	xx	x	xx
	Sometimes	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx
	Refuse to answer	x	xx	x	xx	x	xx

N=Number of enrolled subjects at the specific visit.
[1] The denominator of the percentage for this question is the number of subjects answered "yes" for question 2 at each visit.
[2] The denominator of the percentage for this question is the number of subjects answered "yes" for question 3 at each visit.
[3] The denominator of the percentage for this question is the number of subjects answered "yes" for question 4 at each visit.
[4] The denominator of the percentage for this question is the number of subjects answered "yes" for question 5 at each visit.
[5] The denominator of the percentage for this question is the number of male subjects at each visit.
[6] The denominator of the percentage for this question is the number of male subjects answered "yes" for question 6 at each visit.

Table 34: Side Effects of Fluoroquinolone Use

Summary	Visit 1 (N = x)		Visit 2 (N = x)		Visit 3* (N = x)	
	n	%	n	%	n	%
Tendon Pain	x	xx	x	xx	x	xx
Joint Pain	x	xx	x	xx	x	xx
Muscle Pain	x	xx	x	xx	x	xx
Tingling or Pricking Sensation	x	xx	x	xx	x	xx
Confusion	x	xx	x	xx	x	xx
Hallucinations	x	xx	x	xx	x	xx

N is the number of subjects whose assessments were collected at the particular visit.
'n' represents the number of subjects who reported each sign or symptom at the Visit(s) indicated.
The denominator of the percentage is the number of subjects whose assessments were collected at the particular visit.
The same subject may be counted at all visits.
*Only some subjects have data at Visit 3 due to the protocol amendment.

Table 35: Number and Percentage of Subjects with Prior and Concomitant Medications Contraindicated with Ciprofloxacin or Systemic Antibiotics by WHO Drug Classification–All Enrolled Subjects

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	All Subjects (N=X)	
		n	%
Any Level 1 Codes	Any Level 2 Codes	x	x
[ATC Level 1 - 1]	Any	x	x
	[ATC 2 - 1]	x	x
	[ATC 2 - 2]	x	x
	[ATC 2 - 3]	x	x
[ATC Level 1 – 2]	Any	x	x
	[ATC 2 - 1]	x	x
	[ATC 2 - 2]	x	x
	[ATC 2 - 3]	x	x

N= Number of all enrolled subjects
n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.

APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

Figure 1: Sample Size/Probability Estimates

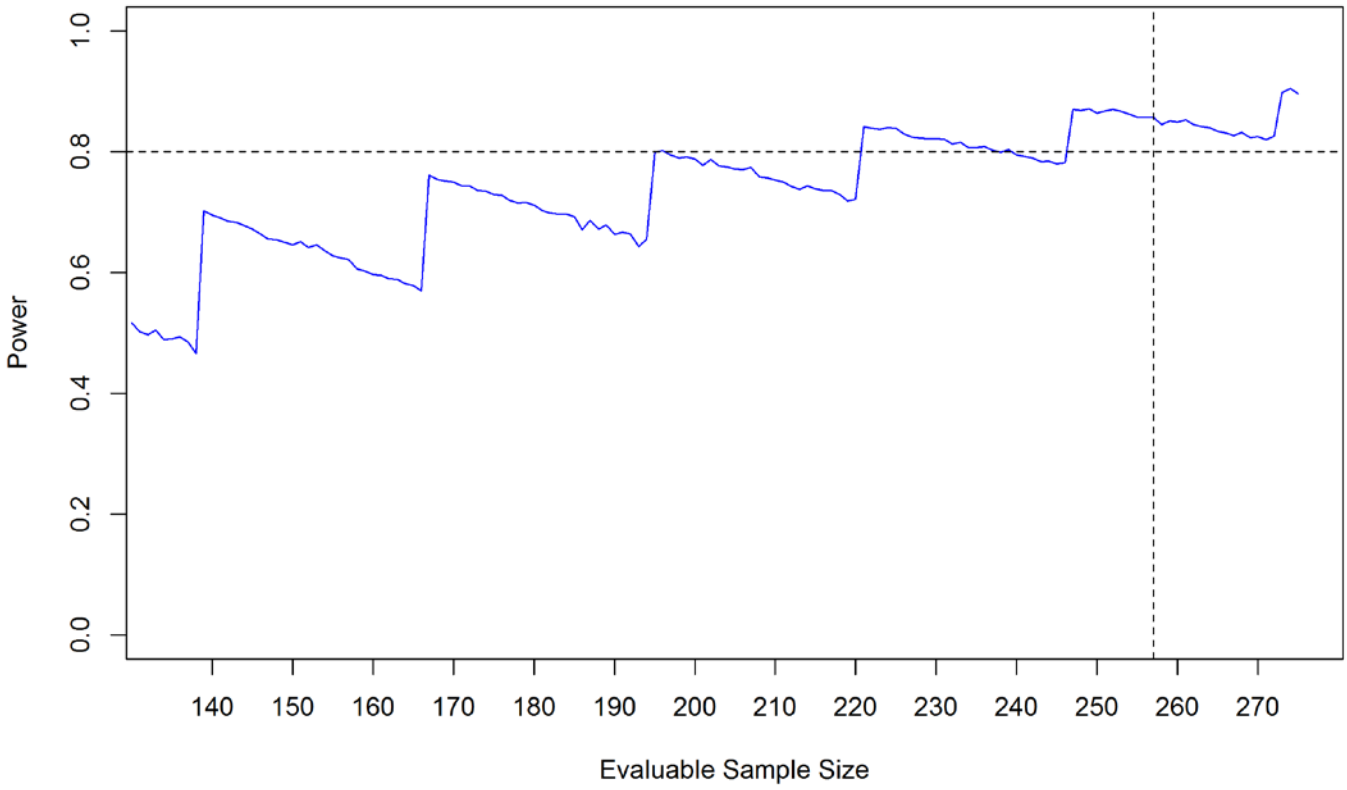


Figure 2: CONSORT Flow Diagram

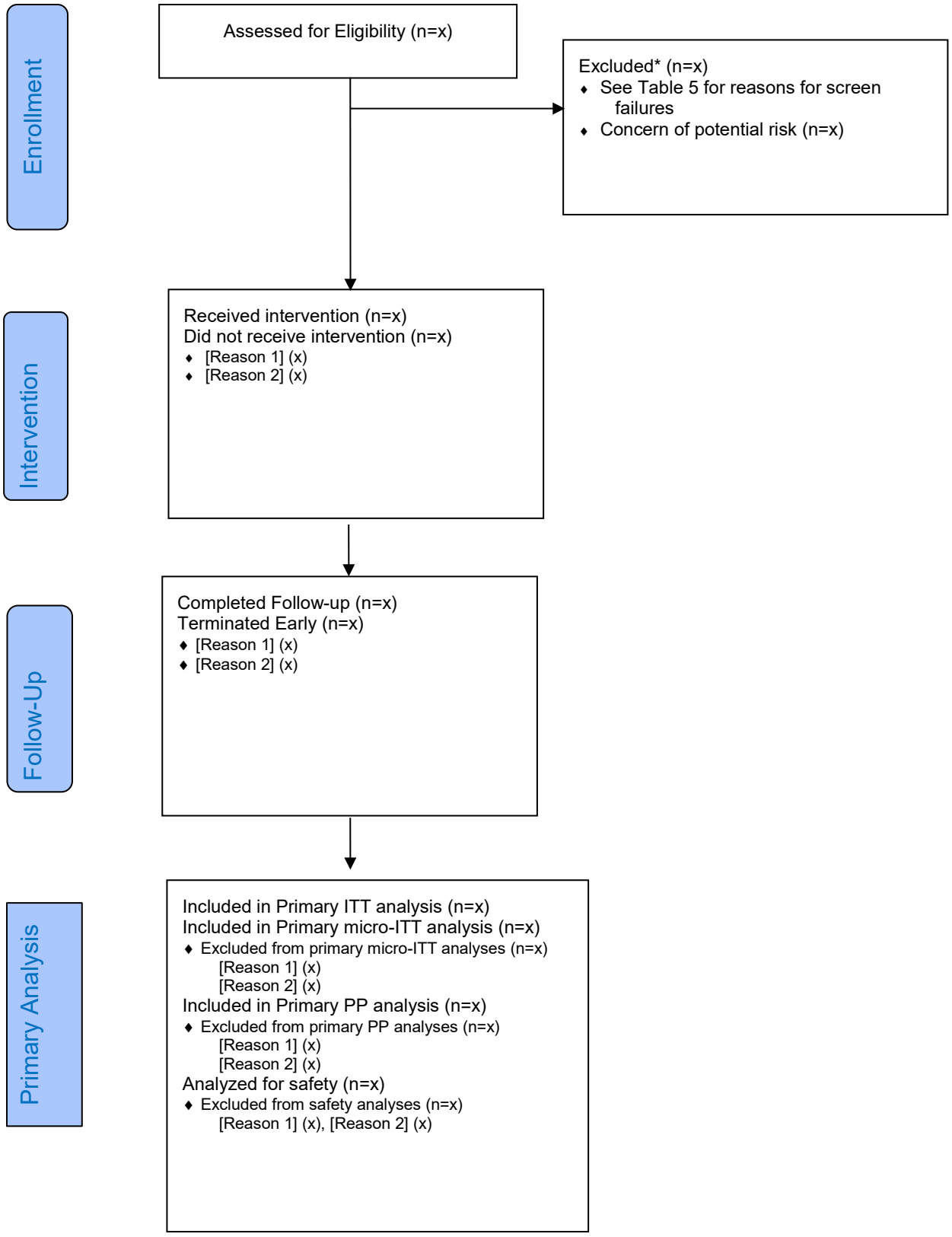
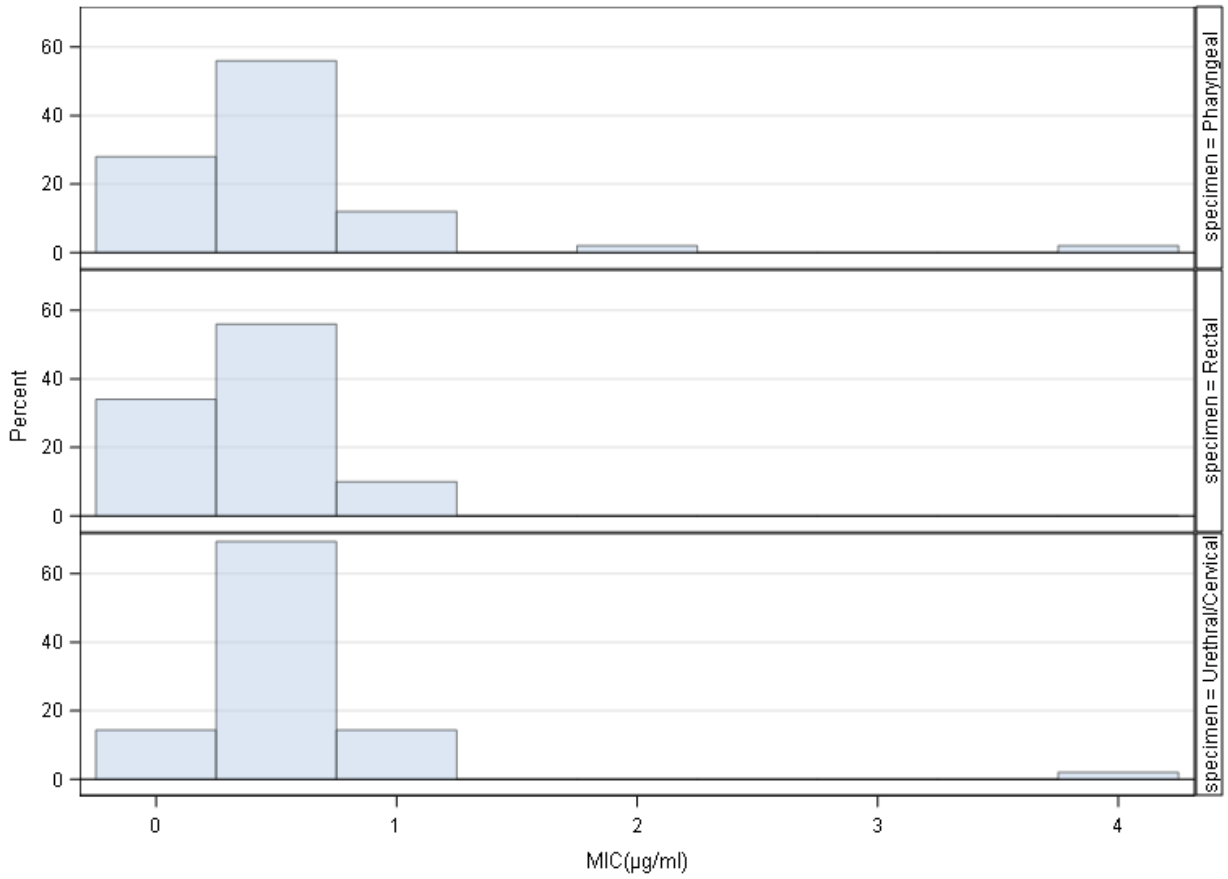


Figure 3: Histogram: MIC distribution for Antimicrobials by Visit— Urethral/Cervical— Micro-ITT population



Implementation notes:

The figure will be a paneled figure with specimen as columns and visits as rows.

Figures with similar format:

Figure 4: Histogram: MIC distribution for Antimicrobials by Visit— Rectal— Micro-ITT population

Figure 5: Histogram: MIC distribution for Antimicrobials by Visit— Pharyngeal — Micro-ITT population

Figure 6: Histogram: MIC distribution for Antimicrobials by Visit— Urethral/Cervical — PP population

Figure 7: Histogram: MIC distribution for Antimicrobials by Visit— Rectal— PP population

Figure 8: Histogram: MIC distribution for Antimicrobials by Visit— Pharyngeal — Micro-ITT population

APPENDIX 3. LISTINGS MOCK-UPS

LISTINGS

Listing 1: Subject Disposition

Subject ID	Category	Study Day Corresponding to Early Termination/Protocol Completion	Reason for Early Termination
xxxxxx	Protocol completed/ Early termination	x	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	Protocol completed/ Early termination	x	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
xxxxxx	Protocol completed/ Early termination	x	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Implementation Notes:

1. Sort order will be by Subject ID, Category.
2. Category will be “Early Termination” or “Protocol Completed”.
3. In the “Reason for Early Termination” column, concatenate any “specify” fields, including the DV number.

Listing 2: Subjects Excluded from Primary Analysis Populations

Subject ID	Analyses in which Subject is Included	Analyses from which Subject is Excluded	Results Available?	Reason Subject Excluded
xxxxxx	[e.g., ITT, micro-ITT, PP]	[e.g., ITT, micro-ITT, PP]	Yes/No	xxxxx
xxxxxx	[e.g., ITT, micro-ITT, PP]	[e.g., ITT, micro-ITT, PP]	Yes/No	xxxxx
xxxxxx	[e.g., ITT, micro-ITT, PP]	[e.g., ITT, micro-ITT, PP]	Yes/No	xxxxx
xxxxxx	[e.g., ITT, micro-ITT, PP]	[e.g., ITT, micro-ITT, PP]	Yes/No	xxxxx
xxxxxx	[e.g., ITT, micro-ITT, PP]	[e.g., ITT, micro-ITT, PP]	Yes/No	xxxxx

Note: "Yes" in the "Results available" column indicates that available data were removed from the primary analysis. "No" indicates that no data were available for inclusion in the analysis.

Implementation Notes:

1. Sort order will be Subject ID.
2. Reasons Subject excluded should match the same verbiage that is used on the analysis population tables.

Listing 3: Subject-Specific Protocol Deviations

DV Number	Study Day	Deviation	Deviation Category	Reason for Deviation	Deviation Resulted in Subject Termination?	Deviation Resolution	Comments
Subject ID:							
xx	x	xxxxxxxxxxx	xxxxxxxxxxxx	xxxxxxxxxxx	Yes/No	xxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxx
xx	x	xxxxxxxxxxx	xxxxxxxxxxxx	xxxxxxxxxxx	Yes/No	xxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxx

Implementation Notes:

1. Sort order will be by Subject ID, DV number.
2. In the "Deviation Category" column concatenate any specify fields.
3. In the "Reason for Deviation" column concatenate any "specify" fields.

Listing 4: Non-Subject-Specific Protocol Deviations

Site	Deviation	Start Date	End Date	Reason for Deviation	Deviation Resulted in Subject Termination?	Deviation Category	Deviation Resolution	Comments
xxxx	xxxxxxx	x	x	xxxxxxx	Yes/No	xxxx	xxxxxxxx	xxxxxxxxxxxxxxx
xxxx	xxxxxxx	x	x	xxxxxxx	Yes/No	xxxx	xxxxxxxx	xxxxxxxxxxxxxxx

Implementation Notes:

1. Sort order will be by Site Name, Start Date.
2. In the "Deviation Category" column concatenate any specify fields.
3. In the "Reason for Deviation" column concatenate any "specify" fields.

Listing 5: Microbiological Results

Study Visit	Actual Study Day	Sex	Age (years)	*N. gonorrhoeae* Culture Result	NAAT Testing Result	*gyrA* Assay Results	Culture-Based Antimicrobial Susceptibility Testing	Anatomical Site
Subject ID:								
Visit 1 (Day 1)	x	xxxxx	xx	Negative/ Positive/ Indeterminate/ Not Done	Negative/ Positive/ Indeterminate/ Not Done	Wild type *gyrA* detected/ Mutant *gyrA* detected/ Indeterminate/ Not Done	Susceptible/ Not susceptible	Urethral/Cervical/ Rectal/Pharyngeal
Visit 2 (Day 5-10)	x	xxxxxx	xx	Negative/ Positive/ Indeterminate/ Not Done	Negative/ Positive/ Indeterminate/ Not Done	Wild type *gyrA* detected/ Mutant *gyrA* detected/ Indeterminate/ Not Done	Susceptible/ Not susceptible	Urethral/Cervical/ Rectal/Pharyngeal

Implementation Notes:

1. Sort order will be Subject ID, Study Visit.
2. Subject may have multiple rows for different anatomical sites.

Listing 6: Clinical Laboratory Results – Urine Pregnancy Test

Subject ID	Study Day of Assessment	Collection Day	Was a Urine Pregnancy Test Performed?	Result
xxxxxx	x	x	Yes/No	Negative/ Positive
xxxxxx	x	x	Yes/No	Negative/ Positive
xxxxxx	x	x	Yes/No	Negative/ Positive
xxxxxx	x	x	Yes/No	Negative/ Positive

Implementation Notes:

1. Sort order will be Subject ID.

Listing 7: Individual Efficacy Data

Anatomical Site	*N. gonorrhoeae* Culture Result at Visit 1	*N. gonorrhoeae* Culture Result at Visit 2	Microbiological Outcome Status
Subject ID:			
Urethral/ Cervical/ Rectal/ Pharyngeal	Negative/ Positive/ Indeterminate/ Not Done	Negative/ Positive/ Indeterminate/ Not Done	Microbiological Cure/ Microbiological Failure/ Non-evaluable

Implementation Notes:

1. Sort order will be Subject ID.

Listing 8: Demographic and Baseline Characteristics Data—All Enrolled Subjects

Subject ID	Sex	Age at Enrollment (years)	Ethnicity	Race
xxxxxx	xxxxxx	xx	xxxxxxx	xxxxxxx
xxxxxx	xxxxxx	xx	xxxxxxx	xxxxxxx
xxxxxx	xxxxxx	xx	xxxxxxx	xxxxxxx
xxxxxx	xxxxxx	xx	xxxxxxx	xxxxxxx

Implementation Notes:

1. Sort order will be Subject ID.
2. For the "Race" column, if a subject is Multi-Racial, all races will be listed, separated by a comma.

Listing 9: Sexual History at Baseline Visit—All Enrolled Subjects

Subject ID	What is your gender identity?	What is your sexual orientation?	Do you have sex with men, women, transgender men, transgender women, or multiple genders?	Have you had sex (vaginal, anal, or oral) in the past 30 days?
xxxxxx	xxxxx	xxxxxx	xxxxxxx	Yes/No/Refused to answer
xxxxxx	xxxxx	xxxxxx	xxxxxxx	Yes/No/Refused to answer

Implementation Notes:

1. Sort order will be by Subject ID
2. Includes data from Visit 1
3. Note: Specify fields will be concatenated with a ":".

Listing 10: Sexual History at Follow-up Visit—All Enrolled Subjects

Subject ID	Study Day	1. Have you had sex (vaginal, anal, or oral) since the last visit	2. Have you had vaginal intercourse since the last visit	If Yes for question 2, did you use a condom with vaginal intercourse?	3.Have you given oral intercourse since the last visit	If Yes to question 3, did you use a condom or barrier with oral intercourse?
xxxxxx	xx	Yes/No/Refused to answer	Yes/No/Refused to answer	No/Always/Sometimes/Unknown/ Refused to answer	Yes/No/Refused to answer	No/Always/Sometimes/ Unknown/ Refused to answer
xxxxxx	xx	Yes/No/Refused to answer	Yes/No/Refused to answer	No/Always/Sometimes/Unknown/ Refused to answer	Yes/No/Refused to answer	No/Always/Sometimes/ Unknown/ Refused to answer

Implementation Notes:

1. Sort order will be by Subject ID, Study Day
2. For questions that are parented, if the parent question is "No" and the subsequent fields are not required, fill the cell with "—"

Listing 11: Sexual History at Follow-up Visit—All Enrolled Subjects

Subject ID	Study Day	4. Have you received oral intercourse since the last visit	If Yes to question 4, did you use a condom or barrier with oral intercourse?	5.Have you had receptive 'bottom' anal intercourse since the last visit	If Yes to question 5, did you use a condom with receptive anal intercourse	If Yes to question 5, did you use a condom with insertive anal intercourse	6. Have you had insertive 'top' anal intercourse since the last visit? (Males only)	If Yes to question 6, did you use a condom with insertive anal intercourse?
xxxxxx	xx	Yes/No/ Refused to answer	No/Always/Sometimes/ Unknown/ Refused to answer	Yes/No/ Refused to answer	No/Always/Sometimes/ Unknown/ Refused to answer	No/Always/Sometimes/ Unknown/ Refused to answer	No/Yes/ Refused to answer/ NA (if female)	No/Always/Sometimes/ Unknown/ Refused to answer
xxxxxx	xx	Yes/No /Refused to answer	No/Always/Sometimes/ Unknown/ Refused to answer	Yes/No/ Refused to answer	No/Always/Sometimes/ Unknown/ Refused to answer	No/Always/Sometimes/ Unknown/ Refused to answer	No/Yes/ Refused to answer/ NA (if female)	No/Always/Sometimes/ Unknown/ Refused to answer

Implementation Notes:

1. Sort order will be by Subject ID, Study Day
2. For questions that are parented, if the parent question is "No" and the subsequent fields are not required, fill the cell with "—"

Listing 12: *N. Gonorrhoeae* Symptomatology

Subject ID	Study Visit	Sex	Symptoms of Gonorrhea	Gender specific Symptoms of Gonorrhea	Signs of Gonorrhea	Gender specific Sign of Gonorrhea
xxxxxx	Visit 1 (Day 1)/ Visit 2 (Day 5-10)	xxxxxx	Sore throat/Anorectal pain/Anorectal discharge/Anorectal bleeding	Urethral discharge/Pain with urination (Males Only) Abnormal vaginal discharge/Abnormal vaginal bleeding/pain during intercourse (Female Only)	Pharyngeal erythema/Anorectal discharge	Urethral discharge (Males Only) Abnormal cervical discharge (Females Only)
xxxxxx	Visit 1 (Day 1)/ Visit 2 (Day 5-10)	xxxxxx	Sore throat/Anorectal pain/Anorectal discharge/Anorectal bleeding	Urethral discharge/Pain with urination (Males Only) Abnormal vaginal discharge/Abnormal vaginal bleeding/pain during intercourse (Female Only)	Pharyngeal erythema/Anorectal discharge	Urethral discharge (Males Only) Abnormal cervical discharge (Females Only)
xxxxxx	Visit 1 (Day 1)/ Visit 2 (Day 5-10)	xxxxxx	Sore throat/Anorectal pain/Anorectal discharge/Anorectal bleeding	Urethral discharge/Pain with urination (Males Only) Abnormal vaginal discharge/Abnormal vaginal bleeding/pain during intercourse (Female Only)	Pharyngeal erythema/Anorectal discharge	Urethral discharge (Males Only) Abnormal cervical discharge (Females Only)

Note: Only some subjects have data at Visit 3 due to the protocol amendment.

1. Implementation Notes:
2. Sort order will be Subject ID, Study Visit.

Listing 13: Compliance Data

Subject ID	Dose Taken?	Vomit Within 1 Hour of Study Drug Administration?	Compliance Status
xxxxxx	Yes/No	Yes/No	Compliant/Non-compliant
xxxxxx	Yes/No	Yes/No	Compliant/Non-compliant
xxxxxx	Yes/No	Yes/No	Compliant/Non-compliant
xxxxxx	Yes/No	Yes/No	Compliant/Non-compliant

Implementation Notes:

1. Sort order will be Subject ID.

Listing 14: Side Effects Related to Fluoroquinolone

Subject ID	Study Visit	Serious Side Effects Related to Fluoroquinolone
xxxxxx	Visit 1 (Day 1)/ Visit 2 (Day 5-10)	Tendon pain/Joint pain/Muscle pain/Tingling or pricking sensation/Confusion/Hallucinations
xxxxxx	Visit 1 (Day 1)/ Visit 2 (Day 5-10)	Tendon pain/Joint pain/Muscle pain/Tingling or pricking sensation/Confusion/Hallucinations
xxxxxx	Visit 1 (Day 1)/ Visit 2 (Day 5-10)	Tendon pain/Joint pain/Muscle pain/Tingling or pricking sensation/Confusion/Hallucinations

Note: Only some subjects have data at Visit 3 due to the protocol amendment.

Implementation Notes:

1. Sort order will be Subject ID, Study Visit.

Listing 15: Baseline Pregnancy Test Results

Subject ID	Was a urine pregnancy test performed?	Pregnancy Test Result
xxxxxxxx	Yes/No/NA	Negative/Positive
xxxxxxxx	Yes/No/NA	Negative/Positive

Implementation Notes:

1. Sort order is Subject ID

Listing 16: Physical Exam Findings

Study Visit	Actual Study Day	Body System	Abnormal Finding
Visit 1 (Day 1)	x	xxx	xxxxxxxxxxxxxxxxxxxx
Visit 2 (Day 5-10)	x	xxx	xxxxxxxxxxxxxxxxxxxx

Implementation Notes:

1. Sort order will be Subject ID, Study Visit.
2. Only abnormal findings will be presented.

Listing 17: Concomitant Medications

Subject ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	ATC 1/ ATC2
xxxxxx	xx	xxxxxxxx	xx	xx	xxxxxxxx	
xxxxxx	xx	xxxxxxxx	xx	xx	xxxxxxxx	
xxxxxx	xx	xxxxxxxx	xx	xx	xxxxxxxx	

Implementation Notes:

1. Sort order will be Subject ID, CM Number.