Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP): GENERAL PROTOCOL
Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP): GENERAL PROTOCOL
## CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acknowledgements</td>
<td>iv</td>
</tr>
<tr>
<td>Abbreviations and acronyms</td>
<td>v</td>
</tr>
<tr>
<td>1. Introduction</td>
<td>1</td>
</tr>
<tr>
<td>1.1 Objectives of EGASP</td>
<td>2</td>
</tr>
<tr>
<td>2. Methods</td>
<td>3</td>
</tr>
<tr>
<td>2.1 Surveillance setting</td>
<td>4</td>
</tr>
<tr>
<td>2.2 Inclusion criteria</td>
<td>4</td>
</tr>
<tr>
<td>2.2.1 Informed consent</td>
<td>5</td>
</tr>
<tr>
<td>2.3 Collection, handling and transporting specimens</td>
<td>5</td>
</tr>
<tr>
<td>2.4 Isolating and identifying <em>Neisseria gonorrhoeae</em></td>
<td>5</td>
</tr>
<tr>
<td>2.5 Preserving isolates</td>
<td>6</td>
</tr>
<tr>
<td>2.6 Antimicrobial susceptibility testing</td>
<td>6</td>
</tr>
<tr>
<td>2.7 External quality assessment</td>
<td>7</td>
</tr>
<tr>
<td>2.8 Treating and managing patients</td>
<td>8</td>
</tr>
<tr>
<td>2.9 EGASP data</td>
<td>8</td>
</tr>
<tr>
<td>2.9.1 Collecting, storing and reporting EGASP data</td>
<td>8</td>
</tr>
<tr>
<td>2.9.2 Data analysis</td>
<td>9</td>
</tr>
<tr>
<td>2.10 Monthly and annual process measure reporting</td>
<td>9</td>
</tr>
<tr>
<td>3. Data reporting to WHO, CDC/DSTDP/NCHHSTP and WHO collaborating centre</td>
<td>11</td>
</tr>
<tr>
<td>3.1 EGASP module in GLASS</td>
<td>12</td>
</tr>
<tr>
<td>4. Roles and responsibilities of institutions and partners implementing EGASP</td>
<td>13</td>
</tr>
<tr>
<td>4.1 Health Ministry (or other entity appointed by the Ministry)</td>
<td>14</td>
</tr>
<tr>
<td>4.2 Other national partners in the country</td>
<td>14</td>
</tr>
<tr>
<td>4.3 EGASP sentinel clinic(s)</td>
<td>14</td>
</tr>
<tr>
<td>4.4 EGASP reference laboratories</td>
<td>15</td>
</tr>
<tr>
<td>4.5 WHO</td>
<td>15</td>
</tr>
<tr>
<td>4.6 CDC/DSTDP/NCHHSTP and WHO collaborating centre</td>
<td>16</td>
</tr>
<tr>
<td>5. General issues</td>
<td>17</td>
</tr>
<tr>
<td>5.1 Timelines for EGASP implementation and communication</td>
<td>17</td>
</tr>
<tr>
<td>5.2 Disseminating and using EGASP data and specimens and isolates</td>
<td>18</td>
</tr>
<tr>
<td>5.3 Human subjects</td>
<td>19</td>
</tr>
<tr>
<td>5.4 Authorship of EGASP data</td>
<td>19</td>
</tr>
<tr>
<td>References</td>
<td>21</td>
</tr>
<tr>
<td>Annex 1 Participating EGASP institutions and partners</td>
<td>22</td>
</tr>
<tr>
<td>Annex 2 Methods for antimicrobial susceptibility testing</td>
<td>23</td>
</tr>
<tr>
<td>Annex 3 EGASP data elements</td>
<td>26</td>
</tr>
<tr>
<td>Annex 4 Monthly and annual process measure reporting</td>
<td>34</td>
</tr>
<tr>
<td>Annex 5 Summary of EGASP timelines for project participants</td>
<td>35</td>
</tr>
<tr>
<td>Annex 6 Use of EGASP data and specimens and isolates, including the EGASP concept proposal form for data and isolates, including requests for compiling an abstract or manuscript</td>
<td>37</td>
</tr>
</tbody>
</table>
ACKNOWLEDGEMENTS

WHO thanks the Member States, WHO Collaborating Centre for Gonorrhoea and other STIs, Örebro University, Sweden, WHO Collaborating Centre for Sexually Transmitted Infections and Antimicrobial Resistance, Prince of Wales University, Randwick, Australia and our technical partners who supported the development and pilot testing of the Enhanced Gonorrhoea Surveillance Programme (EGASP) protocol. The work of the dedicated health-care providers and partners at the local and national levels informed the development of this protocol.

WHO is grateful for the technical input of the following people: Hortense Faye-Kette (Institut Pasteur de Côte d’Ivoire), Eric Garges (STI Research Area, Infection Disease Clinical Research Program, Bethesda, MD, USA), Natnaree Girdthep, Rossaphorn Kittiyawamarn and Pachara Sirivongrangson (Department of Disease Control, Ministry of Public Health, Thailand), Ranmini Kularatne (National Institute of Communicable Diseases, South Africa), Monica Lahra (WHO Collaborating Centre for Sexually Transmitted Infections and Antimicrobial Resistance, Prince of Wales University, Australia), Noel Palaypayon (Epidemiology Bureau, Department of Health, Philippines), Genesis Samonte (public health specialist), Joseph Carlo Sangco (STD AIDS Cooperative Central Laboratory, San Lazaro Hospital, Philippines), Sonia Sia (Research Institute of Tropical Medicine, Philippines), Gianfranco Spiteri (European Centre for Disease Prevention and Control), Katy Town (Public Health England), Magnus Unemo (WHO Collaborating Centre for Gonorrhoea and other STIs, Örebro University, Sweden), Neirissa Dominguez (WHO Country Office in the Philippines), Naoko Ishikawa and Anne Brink (WHO Regional Office for the Western Pacific) and Mukta Sharma and Bharat Rewari (WHO Regional Office for South-East Asia). Additional input was provided by Barbara Tornimbene (Global Antimicrobial Resistance and Use Surveillance System (GLASS), WHO).

Teodora Wi (WHO Global HIV, Hepatitis and Sexually Transmitted Infections Programme) and Hillard Weinstock and Ellen Kersh (Division of STD Prevention, United States Centers for Disease Control and Prevention) led the development of this protocol. Cau Dinh Pham and Emily Weston (Division of STD Prevention, United States Centers for Disease Control and Prevention) and Martina Escher (WHO Global HIV, Hepatitis and Sexually Transmitted Infections Programme) compiled the protocol.

WHO is grateful for the technical review and comments provided by Jo-Anne Dillon (University of Saskatchewan, Canada) and Olusegun O. Soge (University of Washington, USA).

WHO thanks the United States Centers for Disease Control and Prevention for their financial support and for the technical contributions of other colleagues dedicated to strengthening the gonorrhoea antimicrobial resistance surveillance at the country, regional and global levels.

WHO thanks the Ministry of Public Health of Thailand and the Department of Health of the Philippines for the commitment to pilot EGASP in their countries and to the EGASP teams from both countries for the day-to-day work in implementing EGASP. WHO recognizes the ongoing efforts of Member States as they continue to work to improve sexually transmitted infection surveillance and service delivery at the national level.
### ABBREVIATIONS AND ACRONYMS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMR</td>
<td>Antimicrobial resistance</td>
</tr>
<tr>
<td>CDC/DSTDP/NCHHSTP</td>
<td>United States Centers for Disease Control and Prevention, Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STDs and TB Prevention</td>
</tr>
<tr>
<td>GASP</td>
<td>Gonococcal Antimicrobial Surveillance Programme</td>
</tr>
<tr>
<td>EGASP</td>
<td>Enhanced Gonococcal Antimicrobial Surveillance Programme</td>
</tr>
<tr>
<td>EUCAST</td>
<td>European Committee on Antimicrobial Susceptibility Testing</td>
</tr>
<tr>
<td>GAP-AMR</td>
<td>Global Action Plan on Antimicrobial Resistance</td>
</tr>
<tr>
<td>GLASS</td>
<td>Global Antimicrobial Resistance and Use Surveillance System (GLASS)</td>
</tr>
<tr>
<td>ISO</td>
<td>International Organization for Standardization</td>
</tr>
<tr>
<td>MIC</td>
<td>Minimum inhibitory concentration</td>
</tr>
</tbody>
</table>
1. INTRODUCTION

Widespread antimicrobial resistance (AMR) in highly variable strains of Neisseria gonorrhoeae has continually compromised the management and control of gonorrhoea. Because of widespread antimicrobial resistance, the persistence of resistant determinants in gonococci and the unavailability of diagnostic tests that provide antimicrobial resistance results at the time of treatment, clinicians resort to empirical treatment for gonorrhoea. Since the introduction of antimicrobial therapy, resistance has rapidly emerged to sulphonamides, penicillins, tetracyclines, macrolides, fluoroquinolones and early-generation cephalosporins. Currently, in most countries, the injectable extended-spectrum cephalosporin ceftriaxone is the only remaining empirical monotherapy for gonorrhoea. However, gonococcal in vitro resistance and/or treatment failures for the last-line oral extended-spectrum cephalosporin cefixime – and, more rarely, to ceftriaxone – have been observed in many countries (1). Consequently, dual antimicrobial therapy, mainly ceftriaxone plus azithromycin, is recommended (2).
The WHO Gonococcal Antimicrobial Surveillance Programme (GASP) is a worldwide surveillance laboratory network established in 1990 (3) that is coordinated by focal points and regional coordinating centres. GASP has been collecting data on gonococcal antimicrobial susceptibility since 1990. In GASP, each designated regional focal point, in partnership with its WHO regional office, collates data (isolate-based resistance data) submitted by participating countries. These data have provided evidence to inform national, regional and global treatment guidelines. However, several factors limit the data GASP collects. First, varied and changing sampling strategies, laboratory methods, standardized interpretative criteria and quality assurance procedures create difficulty in comparing data between countries and assessing trends over time. In addition, most countries do not routinely obtain demographic, behavioural or clinical data with the isolates, so the epidemiological factors associated with increased risk of resistance cannot be identified. Finally, there are frequently significant delays in testing and reporting critical alerts and significant trends within the GASP network, compromising global preparedness for emerging resistance.

In 2012, WHO published a global action plan to control the spread and impact of antimicrobial resistance in N. gonorrhoeae (4). This plan is linked to the WHO global action plan on antimicrobial resistance (5).

The Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP) aims to address the limitations of GASP and to strengthen sentinel surveillance for gonococcal antimicrobial resistance in selected countries. EGASP is a special project under the Global Antimicrobial Resistance Surveillance System (GLASS) umbrella.

EGASP is a collaboration between the WHO, the United States Centers for Disease Control and Prevention (CDC) and other WHO collaborating centres. EGASP monitors trends in antimicrobial susceptibility in N. gonorrhoeae by using standardized sampling and laboratory protocols in selected countries. This surveillance approach allows collaborators to improve the quality, comparability and timeliness of gonococcal antimicrobial resistance data across multiple countries. It also aims at enhancing the capacity of early detection and reporting of N. gonorrhoeae strains with elevated minimum inhibitory concentrations (MICs) to the internationally recommended treatment for gonorrhoea and emerging or novel mechanisms of resistance to new antibiotics for gonorrhoea at the national and global levels (6).

EGASP especially targets countries that have been able to document a substantial burden of gonococcal infection. Other factors considered when deciding to implement EGASP in a country are:
1. ease of access to health-care providers,
2. competent laboratory services,
3. government engagement and political will and
4. in-country partners to help champion the project.

This general EGASP protocol was developed based on the experience from EGASP implementation in the first two countries, the Philippines and Thailand (7), with the aim of supporting future countries implementing EGASP. The protocol describes the objectives and the methods of EGASP surveillance and guidance on how to implement and monitor the implementation of EGASP. This publication targets the national sexually transmitted infection and antimicrobial resistance programmes and other institutions with research capacity and good understanding of the epidemiological surveillance of sexually transmitted infections and/or antimicrobial resistance.

Standard operating procedures for clinical, laboratory and data management will be made available to countries when EGASP is implemented to be adapted to local needs.

1.1. OBJECTIVES OF EGASP

At the country level, the objectives of EGASP are:

- to monitor trends in antimicrobial susceptibility in N. gonorrhoeae using standardized protocols for systematic inclusion of patients and quality-assured laboratory testing; and
- to epidemiologically characterize men with gonorrhoea at selected sentinel sites, especially those with N. gonorrhoeae not susceptible to recommended antimicrobial agents.

In addition, implementing EGASP will strengthen:

- the capacity for improving the epidemiology and surveillance of sexually transmitted infections and antimicrobial resistance; and
- the clinical, epidemiological and laboratory understanding of the personnel of the participating clinics; and
- the epidemiological and laboratory capacity of the personnel of the participating laboratories.
2. METHODS

To ensure the operational feasibility, cost-effectiveness and optimal yield of *N. gonorrhoeae* isolated by culture, EGASP initially targets men seeking care because of suspected urogenital gonorrhoea (4).

EGASP proposes a sentinel surveillance approach to ensure that high-quality data are obtained. It deliberately involves a limited network of selected surveillance sites: sentinel clinics that have a high burden of gonococcal disease or men with urethral discharge and functioning reference laboratories that can perform culture, antimicrobial susceptibility testing and quality assurance measures.
2.1. SURVEILLANCE SETTING

EGASP sentinel clinics are selected health-care facilities with a known higher volume of gonorrhoea cases compared with other health-care facilities. These are usually outpatient facilities or clinics specialized in sexual health. Sentinel clinics should be able to collect culture specimens, store and transport specimens and maintain \( N. \text{gonorrhoeae} \) viability until the specimens are received at a designated reference laboratory (a laboratory that performs antimicrobial susceptibility testing), collect the core demographic, behavioural and clinical data elements and be able to maintain records and arrange for electronic data entry.

Each selected sentinel clinic should have a volume of gonorrhoea cases to ensure the collection of at least 100 gonococcal isolates (150–200 specimens from symptomatic men) per year (12-month period). One hundred gonococcal cases have been often considered the minimum sample size that would enable a level of 5% or more of resistance to the tested antibiotics to be detected (the critical level usually used to review and modify the national guidelines on sexually transmitted infection treatment) (4). Larger sample sizes will enable more precise estimates and analysis of the risk factors associated with harbouring antimicrobial-resistant gonococci.

EGASP sentinel clinics are supported by EGASP reference laboratories, which perform culture and antimicrobial susceptibility testing according to the EGASP protocol and laboratory standard operating procedures.

The health ministry or other entity appointed by the health ministry will coordinate and monitor overall EGASP activities at the country level. A designated EGASP national focal point and an EGASP coordinator will coordinate EGASP activities. The Division of Sexually Transmitted Disease Prevention of the National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention of the CDC (CDC/DSTDP/NCHHSTP) or other WHO collaborating centre or appointed international reference centres will supervise EGASP laboratory activities, coordinate the external quality assessment and perform confirmatory tests and additional isolate characterization (such as genetic characterization), as needed. WHO will provide overall support and coordination. Section 4 outlines the roles and responsibilities of each institution and partner. Further, the list of participating EGASP institutions and partners (Annex 1) will be completed as each EGASP country implements and establishes EGASP surveillance.

2.2. INCLUSION CRITERIA

EGASP does not imply active search of cases. To enable relatively unbiased results, EGASP systematically includes men attending participating clinics with a suspected urogenital gonorrhoea episode (such as the presence of urethral discharge). Men should be included only once for every urogenital gonorrhoea episode.

The eligibility criteria (inclusion and exclusion) should be specified so that only men meeting the inclusion criteria will be included in EGASP. Eligibility should be restricted to the following recommended criteria, with the EGASP coordinator clearly determining the eligibility criteria when EGASP implementation starts.

The proposed inclusion criteria for men presenting with urethral discharge are:

- attending a participating clinic for the first time for the current suspected urogenital gonorrhoea episode;
- older than the legal age of consent;
- able and willing to provide consent (if this applies (see subsection 4.2.1); and
- able and willing to provide a urethral specimen for testing.

The proposed exclusion criteria for men presenting with urethral discharge are:

- attending the clinic to follow up of a previously treated urogenital gonorrhoea episode (to avoid duplicate sampling for the same EGASP event); and
- do not give informed consent to participate in the study (if this applies (see subsection 2.2.1).

Each EGASP sentinel clinic receives people in accordance with local procedures. Eligible men will be identified during registration and informed about the surveillance by appointed personnel as detailed in subsection 4.2.1.

Clinical personnel (such as a clinic nurse) should be designated to collect demographic, clinical and behavioural information in accordance with local procedures. For the participants, a urethral specimen will be collected for culture and antimicrobial susceptibility testing as described in subsection 4.3.

According to the local standard of care, some clinics may choose to perform non-culture laboratory testing for \( N. \text{gonorrhoeae} \) in addition to culture testing (Gram stain).
2.2.1. INFORMED CONSENT

Depending on the national policies, requesting consent might be necessary before inclusion in the surveillance. If this is the case, the consent can be oral or written and should be obtained by someone who has no direct effect on care, because of power balances. For example, if the treating health professional requests consent, the person may feel obligated to accept. Further, this is not an intervention study, so no experimental changes will be made to the care or treatment regimen.

Potential participants should be provided with the following information:

- the purpose of the surveillance;
- the voluntary nature of participation;
- the procedures and protocols;
- the risks and benefits of participating;
- confidentiality elements; and
- how the results will be shared.

2.3. COLLECTING, HANDLING AND TRANSPORTING SPECIMENS

Clinical samples for *N. gonorrhoeae* culture should be collected using appropriate swabs such as plastic or wire shafts with rayon, polyethylene terephthalate (Dacron) or calcium alginate tips. Alternatively, a sterile wire loop may be used to collect samples from people with visible exudate. Other swab material such as wood shafts and cotton tips should be avoided because these materials might be inhibitory or toxic to the organism. For people with urethritis with visible exudate, collecting the exudate is enough for *N. gonorrhoeae* culture. However, when visible exudate is not observed or scant, the sample should be taken by inserting the swab 2–3 cm deep into the male urethra followed by 2–3 rotations.

The sample swab should be plated and streaked immediately onto growth medium that supports gonococcal (GC) growth such as non-selective GC agar base supplemented with IsoVitaleX™ and Chocolate II agar or a selective medium such as Thayer-Martin (TM) and modified Thayer-Martin (MTM) selective medium or gonococcal agar plate (GC agar base plus supplements). Using a selective medium is advised in case high contamination of the specimen is expected. Selective media contain antimicrobial agents (vancomycin, colistin, nystatin and trimethoprim or other antifungal agent) that inhibit the growth of other non-*Neisseria* bacteria species and fungi.

Within two hours from inoculation, gonococcal cultured plates should be placed at conditions conducive to promoting gonococcal growth: a humid atmosphere at 36 ± 1°C supplemented with 5% CO2. A candle-extinction jar using unscented candles (such as votive candles) or CO2-generating tablets could be used to establish a CO2-enriched (5%) environment if a CO2 incubator is not available. A water tray could be used to humidify the incubator, and a wet paper towel could be used in the candle jar.

The plate should be incubated at the above conditions for at least 18 hours to allow *N. gonorrhoeae* to grow and until transport to the appointed reference laboratory.

The inoculated plate should be transported within 18–24 hours of inoculation in a sealed biohazard bag (or similar) and inside a container that could maintain a constant temperature, around the optimal gonococcal growth temperature (such as 37°C). The transport time should not exceed two hours.

Standard operating procedures on specimen collection, inoculation, incubation and transport will be provided to countries when EGASP is implemented and adapted to the local needs. The EGASP sentinel clinic will be equipped adequately and supplied with swabs and growth media by the reference laboratories.

2.4. ISOLATING AND IDENTIFYING *N. GONORRHOEAE*

*N. gonorrhoeae* will be isolated and identified at reference laboratories on all gonococcal culture plates, and all laboratory outcomes should be recorded on appropriate laboratory tracking sheets. Any problems with the specimens such as improper transport, non-viability or contamination should be reported as soon as possible to the sentinel clinic.

When the *N. gonorrhoeae* culture plates are received from the sentinel sites, the reference laboratory should record all critical information pertaining to the inoculated plates. *N. gonorrhoeae* isolation starts by examining each plate for gonococcal growth.

1. If colonies that resemble *N. gonorrhoeae* in form and structure are visible, these should be transferred to a fresh chocolate II or GC base supplemented with 1% IsoVitaleX™ and incubate the plate at conditions conducive to promoting gonococcal growth (see subsection 2.3) for 18–24 hours.

2. If gonococcal growth is not visible and/or the plate is not covered with microorganisms, the plates should
be incubated at conditions conducive to promoting gonococcal growth (see subsection 2.3) for up to 48 hours and examine the plates every 18–24 hours for gonococcal growth. During this additional incubation period, when colonies that resemble *N. gonorrhoeae* in form and structure are visible on the plate, they should be transferred onto a new plate as described in point 1. If colonies similar to *N. gonorrhoeae* in form and structure are not visible within 48 hours after incubation, the plate should be discarded, and the specimen considered negative.

3. If the plate is completely covered with non-gonococcal microorganisms and no *N. gonorrhoeae* colonies are visible, the plate should be discarded, and the specimen should be reported as not acceptable or contaminated.

Once adequate growth is observed for the transferred colonies, *N. gonorrhoeae* should be identified within 24 hours after incubation. Otherwise frozen stock can be made for downstream identification and antimicrobial susceptibility testing (see subsection 2.5).

The criteria for presumptive *N. gonorrhoea* identification are:
1. growth of colonies with typical appearance on growth medium that supports gonococci at 36 ± 1°C in 5% CO2,
2. a positive oxidase test and
3. the observation of Gram-negative, oxidase-positive diplococci in stained smears.

In addition, reference laboratories are required to confirm the identity of all *N. gonorrhoeae* isolates by using a carbohydrate utilization test (such as rapid micro-carbohydrate test or API-NH test) before antimicrobial susceptibility testing (see below). Likewise, isolates with MICs meeting alert value MIC criteria (see below) must be reconfirmed both by identification and by antimicrobial susceptibility testing, in consultation with CDC/DSTDP/NCHHSTP or a WHO collaborating centre. For biosafety purposes, EGASP excludes the processing of suspected *Neisseria meningitidis* isolates. *N. gonorrhoeae* should be handled in accordance with Biosafety Level 2 practices described in the WHO Laboratory biosafety manual (8) and Biosafety in microbiological and biomedical laboratories (9).

Detailed guidelines on how to produce growth media and how to culture, isolate and identify *N. gonorrhoeae* are provided within the laboratory standard operating procedures.

### 2.5. PRESERVING ISOLATES

All EGASP isolates should be suspended in a suitable cryopreservation media (such as trypticase soy broth containing 20% (v/v) glycerol), frozen at −70°C in duplicate at the reference laboratory and transported to appointed locations for long-term storage. If isolates are transported to other laboratories for confirmation or other testing, duplicate copies of each isolate should be transported. Duplicate copies of each shipped isolate must be maintained at the original laboratory. In consultation with CDC/DSTDP/NCHHSTP or a WHO collaborating centre, reference laboratories may also consider storing isolates in a lyophilized state. See the standard operating procedure for sample retention and storage in Annex 2, Section H for more detail. Standard operating procedures describing methods for lyophilization will be made available to countries upon request.

### 2.6. ANTIBIOTIC SUSCEPTIBILITY TESTING

Antimicrobial susceptibility testing is required for cefixime, ceftriaxone and azithromycin, and MICs will be determined using ETEST® strips (bioMérieux, Marcy l’Etoile, France) on gonococcal (GC) medium base inoculated with 10⁸ colony-forming units/mL. Countries can choose up to two additional antibiotics to test (such as gentamicin and ciprofloxacin). Reference laboratories should apply internal quality control measures (see Annex 2). A laboratory standard operating procedure that describes the ETEST® procedure in more detail will be made available to countries. EGASP reference laboratories should include the following quality control strains with each test run: ATCC 49226, WHO L and WHO U. If the reference laboratory performs β-lactamase testing, the WHO M strain will be used on each run to determine β-lactamase positivity. The results from the quality control strains should be reported monthly to the health ministry.

Table 1 reports the MIC values considered epidemiologically relevant (alert value and high alert value). If a reference laboratory has an isolate with an MIC alert value, it should retest the isolate, using the same method, to confirm the MIC, ideally within five working days after the initial test result.
If the alert value MIC is confirmed, the EGASP national focal point, the EGASP coordinator and the concerned sentinel clinic should be notified by telephone or by e-mail within five working days of the retest date or on a mutually agreed schedule. The notification should include the EGASP-ID, the MIC values and the plan and timeline for any additional testing and confirmation of the alert MICs. Additional confirmation of the alert value MIC may be carried out by a second laboratory at the discretion of the health ministry, CDC/DSTDP/NCHHSTP or WHO collaborating centre and WHO.

If there are isolates with high alerts, retesting should occur immediately and the CDC/DSTDP/NCHHSTP and WHO collaborating centre colleagues should also be immediately notified (before retesting). This can also prompt conversation if the decision is made to send the isolate to the CDC/DSTDP/NCHHSTP and WHO collaborating centre (or appointed collaborating institution) laboratory.

### 2.7. EXTERNAL QUALITY ASSESSMENT

A single set of 15 coded cultures will be provided to the reference laboratories by CDC/DSTDP/NCHHSTP or the WHO collaborating centre for antimicrobial susceptibility testing twice a year in the first year of implementation and once a year in subsequent surveillance years (if suggested by the CDC/DSTDP/NCHHSTP or WHO collaborating centre laboratory based on previous external quality assessment performance). These cultures will include strains selected to represent susceptible and resistant isolates of *N. gonorrhoeae* and may include more than one copy of some strains. With the isolate shipment, CDC/DSTDP/NCHHSTP or the WHO collaborating centre will include the date by which results are requested to be returned by the reference laboratories to CDC/DSTDP/NCHHSTP or WHO collaborating centre. CDC/DSTDP/NCHHSTP or WHO collaborating centre will report back to each reference laboratory within 60 days of receiving the external quality assessment data from the laboratory. Some assessment of overall performance may be based on previously determined modal MICs for strains (such as modal MICs that were obtained when the strains were tested at Gonococcal Isolate Surveillance Project reference laboratories) or WHO collaborating centre laboratories. Each preliminary report will indicate individual MICs that are ≥2 doubling dilutions greater or less than the previously determined modal MIC for that strain and antimicrobial agent. If the external quality assessment results suggest problems in MIC testing (<80% agreement with the modal MIC ±1 dilution of each external quality assessment), CDC/DSTDP/NCHHSTP or the WHO collaborating centre will notify the reference laboratory. In case of two consecutive unsatisfactory external quality assessments, a higher level of oversight (the health ministry and WHO) will be involved to address the problems. The reference laboratory should identify and address these problems, and report to the health ministry, WHO and CDC/DSTDP/NCHHSTP or the WHO.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Requirement</th>
<th>Alert value</th>
<th>High alert value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>Must test for EGASP</td>
<td>≥0.125 µg/ml</td>
<td>≥0.5 µg/ml</td>
</tr>
<tr>
<td>Cefixime</td>
<td>Must test for EGASP</td>
<td>≥0.25 µg/ml</td>
<td>≥0.5 µg/ml</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Must test for EGASP</td>
<td>≥2.0 µg/ml</td>
<td>≥256 µg/ml</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Optional antibiotic</td>
<td>≥32.0 µg/ml</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

Table 1. MICs defined as alert and high alert values, with isolates requiring confirmation by retesting and prompt reporting

Ciprofloxacin does not have an alert value. It has an established MIC resistance breakpoint. If an isolate is found to be resistant to ciprofloxacin, isolates will not need to be retested as they are if there is an alert value.
collaborating centre on the corrections made. This report should be made within 30 days of notification that corrective actions are necessary. Depending on the extent of testing problems, a second set of external quality assessment cultures may then be provided for testing, with another 60 days for completion. A tailored troubleshooting approach may be used to address specific testing difficulties.

2.8. TREATING AND MANAGING PATIENTS

Participation in EGASP will not imply any difference in the care patients may receive. Regardless of participation in EGASP, all men with a complaint of urethral discharge should receive antimicrobial treatment and should be managed according to national sexually transmitted infection management guidelines and in accordance with WHO recommendations. All patients should be counselled that their recent sex partners should be evaluated and treated. The patients should also be advised to return to the clinic for follow-up if symptoms persist. If symptoms persist and patients return to the clinic for follow-up, the sentinel clinic should investigate for potential treatment failure: assess treatment compliance, assess whether the patient could possibly have been reinfected from re-exposure and collect a repeat specimen to perform the test of cure. Since persistent or recurrent genital discharge can also be caused by concurrent infections, it is important to ensure that chlamydial infection has either been adequately treated already or reliably excluded by appropriate laboratory tests. In addition, depending on the epidemiological importance of Trichomonas vaginalis and Mycoplasma genitalium in the causation of genital discharge within the specific setting, treatment for these infections should be given. The management of probable cases of treatment failure is outlined in the global action plan to control the spread and impact of antimicrobial resistance in N. gonorrhoeae (4).

2.9. EGASP DATA

EGASP collects patient-based surveillance data as part of routine clinical and laboratory activities. EGASP variables are categorized as core and optional. Core variables are required to be collected by each participating EGASP country; these data ensure that the objectives of surveillance can be met. If a country is able and has the resources to allow it, collecting optional variables, which provide additional information and are insightful in identifying risk behaviour and groups at the highest risk for antimicrobial-resistant gonorrhoea, is recommended. Unique codes will be assigned to each sentinel clinic and reference laboratory. A patient identifier (patient ID) will be assigned the first time a patient is included in EGASP and will be used for the same patient in case of multiple visits to the same clinic. The patient ID should not contain any directly identifiable information, such as name and/or date of birth; however, a registration number or patient record number consisting of numbers and letters can be used. The patient identifier and the key between the patient identifier and the patient code should be stored securely. In addition, an EGASP identifier (EGASP ID) is a unique code assigned at each EGASP visit and will be associated with each specimen collected. This code should not include any personal information and is unique for every specimen collected in EGASP.

EGASP data comprises demographic, clinical, behavioural and laboratory data. Annex 3 provides detailed information on all variables.

2.9.1. COLLECTING, STORING AND REPORTING EGASP DATA

Sentinel clinics will assign the patient ID and EGASP ID and will collect the demographic, behavioural and clinical data. All core data fields will be recorded on the standardized abstraction form (as developed by the EGASP country). These data will then be transmitted to the reference laboratory with the EGASP specimen(s).

---

1 Test-of-cure is the reculturing or isolation and identification of the pathogen, such as N. gonorrhoeae, from a site of initial infection to determine whether the patient has been cured following treatment. It should be realized that, for sexually transmitted infections, post-treatment infections result from reinfection caused by failure of sexual partners to receive treatment or a new infection due to initiation of sexual activity with a new infected partner. A careful history and a candid discussion with the patient are therefore essential to interpret a test-of-cure procedure.
The reference laboratory will complete all data fields related to laboratory data, including culture and antimicrobial susceptibility testing results. A copy of the antimicrobial susceptibility testing results should also be sent back to the respective sentinel sexually transmitted infection clinics for their records.

All patient and laboratory data should be sent to the EGASP coordinator no more than two months after the end of the month in which the corresponding isolates were collected (data collected and tested in January will be completed and sent by 31 March). All EGASP data should be thoroughly validated for duplication and consistency to ensure good data quality.

Data may be digitalized using information technology systems already adopted and implemented at the country level. Alternatively, an EGASP data entry form has been developed in the EGASP module of the GLASS IT Platform, where data can be entered, managed and validated in an anonymized and secured manner (more details in subsection 3.1).

Since collected surveillance data may contain sensitive information identifiable at the patient level, paper-based and electronic data must be stored safely with only authorized personnel able to obtain access to them. The means of storage may vary depending on the resources of the location, but the EGASP national focal point should ensure that safe storage is achieved, both at the national, reference laboratory and sentinel clinic level and that it is in accordance with the ethical and data safety regulations in that country. In addition, each country will receive support in developing a data management standard operating procedure for collecting, transmitting, collating and validating all EGASP data files.

2.9.2. DATA ANALYSIS

Analysis is based on (1) demographic, behavioural and clinical data from suspected and confirmed N. gonorrhoeae cases and (2) antimicrobial susceptibility data from N. gonorrhoeae cases. Depending on the aim of the analysis, aggregated data can be reported by sentinel clinic, laboratory or country and/or stratified by patients’ characteristics and risk factors (such as age, sex, comorbidities and sexual behaviour). Further, associations between epidemiological and behavioural data and the gonococcal antimicrobial susceptibility profiles can be evaluated using appropriate univariate and multivariate models to determine risk factors associated with harbouring antimicrobial-resistant gonococci.

2.10. MONTHLY AND ANNUAL PROCESS MEASURE REPORTING

Monitoring project implementation is an important element of all surveillance systems and is integral to ensure that surveillance objectives are being achieved and that planned activities are on track. This process should include reviewing implementation steps, data quality and laboratory procedures, adjusting the process as necessary, both at the sentinel clinic and reference laboratory. Monitoring should be performed at each EGASP sentinel site and reference laboratory monthly (both in a monthly and cumulative way) and yearly. Annex 4 lists the indicators to measure EGASP implementation. These indicators are not exhaustive and final – at the request of WHO, CDC, a WHO collaborating centre and the health ministry, additional indicators may be requested. A monthly summary, cumulative summary and MIC distribution graphs will be generated and shared by the 15th of each month with WHO and CDC/DSTDP/NCHHSTP and the WHO collaborating centre.

In addition, sentinel clinics and reference laboratories should work with the EGASP project coordinator to identify plans to address challenges faced in patient inclusion, specimen quality and viability, timeliness of specimen or data transmission and data completeness.
3. DATA REPORTING TO WHO, CDC/DSTDP/NCHHSTP AND THE WHO COLLABORATING CENTRE

Countries are expected to report anonymized and deidentified patient-based EGASP line-listed data monthly to WHO through the EGASP module of the GLASS IT Platform.

EGASP isolates with newly detected and emerging antimicrobial resistance (such as exceptional phenotypes that have not previously been reported or are very rare or novel resistance genotypes associated with mechanisms of resistance that may have a high public health impact) should be reported to WHO as defined by the International Health Regulations (10) and by the Emerging Antimicrobial Resistance Reporting component within GLASS (GLASS-EAR) (11).
3.1. EGASP MODULE IN GLASS

WHO and CDC have worked with the WHO GLASS team to develop the EGASP module in the GLASS IT Platform to support EGASP implementation in participating countries.

The EGASP module is a password-protected environment hosted on the WHO server, in which users nominated by the health ministry will be assigned to different roles and levels of access to the data. The module enables data entry for each EGASP visit. Otherwise participating countries can upload data each month. Patient IDs are stored in an encrypted manner and decode keys will only be available to appointed EGASP personnel at the country level.

This module, in the encrypted version, will also be accessible to appointed WHO, CDC/DSTDP/NCHHSTP and/or WHO collaborating centre officers, to provide support with data collection and data quality. The list of external users and their role will be agreed with the health ministry.

The main functionalities of the EGASP module include: data entry and/or data upload, data validation, data analysis and data extraction. Users will have access to all or part of these functions, according to the professional role within the surveillance.

The GLASS IT Platform is hosted on network servers that are physically located on the premises of WHO at its headquarters in Geneva. Information security at WHO is based on the ISO 27001 standard, and WHO has implemented many levels of security using industry best practices for the local WHO network and all databases maintained by WHO. Access to the web-based Internet GLASS platform requires an electronic identification comprising user name, password and potentially other security measures. WHO will provide users nominated by the health ministry a username and the needed security measures. Users are responsible for safekeeping this access information. By accessing the dedicated and protected Internet platform for GLASS, users accept the terms of use contained, which are in accordance with the WHO policy on the use and sharing of data collected by WHO in Member States outside the context of public health emergencies.
4. ROLE AND RESPONSIBILITIES OF INSTITUTIONS AND PARTNERS IMPLEMENTING EGASP

Successfully implementing EGASP begins with identifying national and international institutions, appropriate funding and partners and defined roles and responsibilities. A minimum set of responsibilities of each EGASP partner is detailed below. Additional activities and adaptations should be documented as EGASP is implemented in a country.
4.1. HEALTH MINISTRY (OR OTHER ENTITY APPOINTED BY THE HEALTH MINISTRY)

1. Seek human subjects review from the respective national ethical or legal review board or committees in accordance with national and institutional policies.

2. Serve as the primary point of contact for EGASP in country and as the main contact with the sentinel sites and reference laboratories when there are questions, problems, alert isolates in the laboratory or in general with protocol implementation.

3. Generate EGASP organizational structure, including determining EGASP sentinel clinics and reference laboratories and national focal point(s) and project coordinators.

4. Perform site visits to sentinel clinics and reference laboratories as needed.

5. Consult with WHO, CDC/DSTDP/NCHHSTP and the WHO collaborating centre to modify protocol and standard operating procedures as needed and manage isolates with alert values.

6. Ensure that EGASP data are received, collated, digitized monthly and validated for consistency and completeness.

7. Through the EGASP national focal point and project coordinators, report cumulative, deidentified line-listed EGASP data monthly to WHO, CDC/DSTDP/NCHHSTP and the WHO collaborating centre.

8. Generate monthly and annual reports from sentinel clinics and reference laboratories and transmit them to WHO, CDC/DSTDP/NCHHSTP and the WHO collaborating centre.

9. Review and provide input for any EGASP reports or publications.

At least one EGASP national focal point should be determined to serve as the central point of contact within the country and with collaboration between WHO, CDC/DSTDP/NCHHSTP and the WHO collaborating centre. An EGASP project coordinator should also be determined to coordinate all the above EGASP implementation activities and the day-to-day work among all partners.

4.2. OTHER NATIONAL PARTNERS IN THE COUNTRY

1. Serve as secondary point of contact for sentinel sites and reference laboratories when there is a problem with protocol implementation or when an isolate with an alert value or high alert value is identified (or other surveillance aspect, as needed).

2. Support the health ministry on activities as needed, including helping with study management, data entry, data quality checks, data management and data analysis.

3. Oversee project implementation at specific EGASP sentinel clinics and laboratories.

4. Upload site-specific EGASP data into the EGASP module of the GLASS database.

5. Together with the health ministry and in collaboration with WHO, CDC/DSTDP/NCHHSTP and WHO collaborating centre, review and analyse demographic, behavioural, clinical and antimicrobial susceptibility data.

4.3. EGASP SENTINEL CLINICS

1. Identify men attending the selected sentinel clinic with urethral discharge.

2. Collect, store and report demographic, behavioural and clinical data according to appropriate clinical procedures to ensure overall data quality and data security.

3. Collect urethral specimens and process, store and transport the specimens to the EGASP reference laboratory according to the procedures defined in the protocol and standard operating procedures.

4. Assist the EGASP project coordinator in monitoring EGASP implementation monthly and annually.

At each sentinel clinic, a team of individuals will be assigned to be responsible for EGASP activities.
**4.4. EGASP REFERENCE LABORATORIES**

1. Undergo initial (and as needed) laboratory training by CDC/DSTDP/NCHHSTP or WHO collaborating centre, which will review bacterial identification for gonococcal infection using culture and best practices for antimicrobial susceptibility testing.

2. Isolate *N. gonorrhoeae* and perform antimicrobial susceptibility testing according to standardized methods outlined in the protocol and laboratory standard operating procedures.

3. If an isolates has an alert or high alert value (elevated MIC above a previously determined threshold), inform the EGASP national coordination centre and national focal point and/or EGASP project coordinator.

4. Participate in routine internal quality control measures and external quality assessment activities.

5. Ensure proper recordkeeping; store data and report data according to appropriate procedures to ensure overall data quality and data security.

6. Ensure proper storage of gonococcal isolates so that viability is maintained.

7. Assist sentinel clinics as needed to facilitate appropriate specimen collection, handling, storage and transport of specimens to reference laboratories by sentinel clinic staff.

8. Ensure that the supply of laboratory equipment and supplies is sufficient and not expired and that enough supplies are on hand to match the number of specimens received.

9. Ensure safety and quality control (there should be a power back-up in case the electricity system fails).

At each EGASP reference laboratory, a team of individuals will be assigned to be responsible for EGASP activities.

**4.5. WHO**

1. Perform assessment site visits to investigate country structure and ability to implement EGASP activities.

2. Oversee country cooperative agreements and scopes of work.

3. Oversee the adaptation of EGASP protocol and standard operating procedures.

4. Perform routine site visits to health ministry partners, including visits to the sentinel clinics and reference laboratories as needed.

5. Provide epidemiological technical assistance and assist in training the EGASP national focal point and project coordinator when necessary.

6. Receive transmitted cumulative, deidentified line-listed EGASP data from the health ministry or national focal point each month and support data management activities to ensure data quality.

7. In collaboration with participating countries, analyse EGASP data to inform national and global treatment guidelines and public health policies and initiatives.

8. Maintain and manage the EGASP module of the GLASS database at WHO in collaboration with CDC/DSTDP/NCHHSTP or the WHO collaborating centre.

9. In collaboration with participating countries and CDC/DSTDP/NCHHSTP or the WHO collaborating centre, prepare and distribute an annual report summarizing project findings.

10. In collaboration with the health ministry and CDC/DSTDP/NCHHSTP or the WHO collaborating centre, evaluate annual progress reports and budget requests for each EGASP country.

11. In collaboration with the health ministry and CDC/DSTDP/NCHHSTP or the WHO collaborating centre, recruit new sentinel sites as needed.
12. Update WHO websites and other WHO documents as needed to include aggregated EGASP data.

13. Review and provide input for any EGASP reports or publications.

A WHO officer will be the overall WHO EGASP coordinator. If needed, a second WHO officer may be assigned to support EGASP activities in a specific country.

4.6. CDC/DSTDP/NCHHSTP OR WHO COLLABORATING CENTRE

1. Perform assessment site visits to investigate country structure and ability to implement EGASP activities.

2. Provide technical support in the adaptation of the EGASP protocol and standard operating procedures.

3. Perform routine site visits to health ministry partners, including visits to the sentinel clinics and reference laboratories as needed.

4. Provide epidemiological technical assistance and assist in training the EGASP national focal point and project coordinator when necessary.

5. Provide laboratory technical assistance and assist in training laboratory personnel when necessary.

6. Receive transmitted cumulative, deidentified line-listed EGASP data from the health ministry or national focal point each month and support data management activities to ensure data quality.

7. Maintain and manage the EGASP module of the GLASS database with assistance from WHO.

8. Work with WHO to prepare and distribute annual reports summarizing the project findings.

9. If requested by the health ministry, confirm antimicrobial susceptibility test results and further characterize isolates as needed and provide MICs to WHO, the health ministry and the submitting reference laboratory within four weeks after CDC/DSTDP/NCHHSTP or WHO collaborating centre receives the isolates.

10. Prepare and distribute external quality assessment cultures as described in the protocol.

11. Assist the health ministry (or other entity deemed), other in-country partners and WHO with analysis of demographic, behavioural, clinical and antimicrobial susceptibility data as needed.

12. Review and provide input for any EGASP reports or publications.

One or more contact points will be assigned to be responsible for EGASP activities. CDC/DSTDP/NCHHSTP and WHO collaborating centre partners will provide epidemiological and data management technical assistance as well as laboratory technical assistance and will work with WHO in the overall coordination and management of EGASP in a country.
5. GENERAL ISSUES

5.1. TIMELINES FOR EGASP IMPLEMENTATION AND COMMUNICATION

Before implementation, WHO and CDC/DSTDP/NCHHSTP or the WHO collaborating centre will make an introductory and assessment site visit. Countries are selected for EGASP implementation based on *N. gonorrhoeae* morbidity, geographical representativeness, ease of access to health-care providers and clinics, competent laboratory services, government engagement (health ministry willing to participate), and a partner in the country or in the region (such as a CDC or WHO in-country office) that will help champion the programme.
With WHO, CDC/DSTDP/NCHHSTP or the WHO collaborating centre works with the country to develop a strategy for implementing EGASP that will include the following steps:

- identifying the country’s coordinating institutions;
- nominating a national focal point and coordinator for EGASP;
- selecting sentinel surveillance sites or clinics and reference laboratories;
- clearly defining roles and responsibilities;
- adopting and adapting the EGASP protocol and standard operating procedures to the local needs;
- seeking human subjects review from the respective national ethical or legal review board or committees in accordance with national and institutional policies;
- developing the budget; and
- defining a training programme.

The training programme should include the EGASP protocol, clinical, laboratory and data management and ethical aspects of EGASP. It should be delivered by the national coordinator with the support of WHO and CDC/DSTDP/NCHHSTP or the WHO collaborating centre or other identified external partners. Participants at the training should include staff members nominated at the national level (health ministry and other national partners), reference laboratory and sentinel clinic staff.

Training should include reviewing the EGASP protocol standard operating procedures and surveillance tools. During the training sessions, surveillance staff should have the opportunity to discuss concerns and obtain further clarification on survey operations. Training sessions may be conducted either at the site or at a central location. Sessions that involve multiple staff members from each site would give staff members the opportunity to share experiences from their respective sites. Training should be offered on a regular basis to revise procedures, discuss difficulties and maintain motivation.

Sentinel clinics, reference laboratories, other in-country partners, the health ministry, WHO and CDC/DSTDP/NCHHSTP or the WHO collaborating centre (or other international institution) are expected to perform the tasks described in this protocol in a timely and efficient manner within the prescribed deadlines. Annex 5 summarizes the EGASP timelines for project participants. Difficulties in adhering to the protocol at sentinel clinic and reference laboratory level should be referred to the EGASP national focal point and/or project coordinator.

The duties listed in this protocol for the various EGASP participants may overlap in many areas. EGASP participants should communicate frequently to monitor the day-to-day activities of the project. During the first year of surveillance and as needed beyond the first year of surveillance, it is suggested that the national focal point and the EGASP project coordinator, WHO and CDC/DSTDP/NCHHSTP or WHO collaborating centre collaborators participate in quarterly conference calls to discuss issues related to the project. Additional meetings and site visits will be scheduled as required.

5.2. DISSEMINATION AND USE OF EGASP DATA AND SPECIMENS OR ISOLATES

At the country level, data should be analysed at each level – from the sentinel clinic to the national level – and the results included in local and national antimicrobial resistance surveillance reports or peer-reviewed articles. These results should be shared with all involved institutions and partners. Countries are encouraged to disseminate the EGASP data in a timely manner through annual reports, presentations in meetings and other forums and through peer-review publications.

To make EGASP data widely available, WHO, CDC/DSTDP/NCHHSTP or the WHO collaborating centre may publish aggregated EGASP data in an annual report, and EGASP data may be included in other GASP and GLASS reports. All partners involved will be acknowledged in these reports.

Although EGASP data and specimens or isolates are collected primarily to understand the antimicrobial susceptibility trends of N. gonorrhoeae, additional analyses using EGASP data and specimens or isolates not described in this protocol may be needed. Well-designed and thoughtful projects are valuable to disseminate important scientific and public health findings from EGASP surveillance.
EGASP data and specimens or isolates are owned by the country that generated them. To ensure adequate communication and address any human subject issues that may arise with the use of data or specimens or isolates collected for public health surveillance, each country should establish a systematic process to review concepts and ideas for the use of data and specimens or isolates for purposes not described in this protocol. This process should be in accordance with national rules for analysis, data sharing and publication and should include the approval process from key participants and collaborators as well as tracking and monitoring the data and/or specimens or isolates. Data from a special study outside of core surveillance should not be published before EGASP data are disseminated nationally.

Proposals for the use of EGASP data or specimens or isolates should be submitted to the EGASP national focal point and should include a brief (1–2 pages) written summary (Annex 6 provides an example). A designated EGASP core team comprising members from key institutions and partners participating in-country for EGASP (such as the health ministry, EGASP reference laboratories, WHO and CDC/DSTDP/NCHHSTP or the WHO collaborating centre) should be responsible for reviewing submitted proposals and report on updates of proposals and respective analyses during in-country EGASP meetings.

If necessary, the appropriate human subjects, ethics or institutional review board review should be determined based on additional analysis of EGASP data and specimens or isolates.

Publications based on EGASP surveillance data should reference the protocol and the version number. For proposals involving a WHO collaborating centre author, clearance may be needed. And for situations in which EGASP data are to be presented, the EGASP core team should be notified to have the opportunity to review the presentation.

Sentinel clinics and reference laboratories are also asked to notify the health ministry and WHO and the CDC/DSTDP/NCHHSTP or WHO collaborating centre collaborators of proposed local uses of specimens or isolates collected through EGASP.

5.3. HUMAN SUBJECTS

The WHO Research Ethics Review Committee has reviewed the protocol, which has been determined to be exempt from Committee review since the relevant activity is limited to public health surveillance. This approval allows this protocol to be available online for future use by countries interested in implementing EGASP.

To protect patient privacy and confidentiality, anonymized data will be transmitted to WHO or CDC/DSTDP/NCHHSTP or WHO collaborating centre. All records will contain a non-identifiable unique identification number (the EGASP number). Data collected and stored at the sentinel clinics and reference laboratories will be secured and kept confidential according to local standard operating procedures.

Before implementing EGASP, the EGASP national focal point and project coordinators must seek human subjects review from the respective national ethical or legal review board or committees in accordance with national and institutional policies. Review of the EGASP protocol should be sought, when possible, as public health surveillance rather than research. As part of this process, the fact that deidentified and line-listed data, collected for the purposes of surveillance, will be shared with WHO and CDC/DSTDP/NCHHSTP or the WHO collaborating centre should be made transparent.

5.4. AUTHORSHIP OF EGASP DATA

All authorship will be decided on a case-by-case basis but is ultimately the decision of the EGASP core team (Annex 6). Once authorship has been determined, all members of the author group should be indexed in MEDLINE as co-authors.
REFERENCES


ANNEX 1. PARTICIPATING EGASP INSTITUTIONS AND PARTNERS

HEALTH MINISTRY (AND/OR OTHER ENTITY AS DEEMED)
[insert the appointed institution(s)]
- EGASP national focal point: [insert name and degree(s), department, organization, location, email and telephone]
- EGASP coordinator [insert name and degree(s), department, organization, location, email and telephone]

OTHER NATIONAL ACTING PARTNERS (IF AVAILABLE)
[insert the appointed institution]
- Reference person: [insert name and degree(s), department, organization, location, email and telephone]
[insert the appointed institution]
- Reference person: [insert name and degree(s), department, organization, location, email and telephone]

EGASP SENTINEL CLINIC(S)
[insert the appointed EGASP sentinel clinic 1]
- Reference person: [insert name and degree(s), email and telephone]
[insert the appointed EGASP sentinel clinic 2]
- Reference person: [insert name and degree(s), email and telephone]

REFERENCE LABORATORIES
[insert the appointed EGASP reference laboratory 1]
- Reference person: [insert name and degree(s), email and telephone]
[insert the appointed EGASP reference laboratory 2]
- Reference person: [insert name and degree(s), email and telephone]

WHO
- WHO EGASP coordinator: [insert name and degree(s), department, location, email and telephone]
- WHO focal point (if different) [insert name and degree(s), department, location, email and telephone]

CDC/DSTDP/NCHHSTP OR WHO COLLABORATING CENTRE (OR OTHER APPOINTED INSTITUTION)
[insert the appointed institution]
- CDC/DSTDP/NCHHSTP or WHO collaborating centre EGASP coordinator: [insert name and degree(s), department, location, email and telephone]
- CDC/DSTDP/NCHHSTP or WHO collaborating centre EGASP laboratory coordinator: [insert name and degree(s), department, location, email and telephone]
ANNEX 2. METHODS FOR ANTIMICROBIAL SUSCEPTIBILITY TESTING

The laboratory standard operating procedures provide more detailed information. These will be made available when EGASP is implemented in a country.

A. REQUIRED EQUIPMENT AND SUPPLIES

EQUIPMENT

• Incubator 36 ± 1°C, 5 ± 1% CO2

REAGENTS AND MEDIA

• Chocolate agar (may be used for initial overnight growth or use GC II agar base plus IsoVitaleX™ plates)
• GC II agar base plus IsoVitaleX™ plates (used for ETEST®(bioMérieux, France); do not use chocolate agar plates for ETEST®)
• Mueller-Hinton broth
• ETEST® antibiotic strips
• Ceftriaxone
• Cefixime
• Azithromycin
• Gentamicin (optional)
• Ciprofloxacin (optional)
• McFarland standard, 0.5 on the scale

SUPPLIES, OTHER MATERIALS

• Forceps
• Cotton-tipped swabs with wooden handles (to be used for transferring isolates from broth to plate and not for collecting specimens from patients)
• Marking pen
• Sterile loops

B. SAFETY PRECAUTIONS

All specimens, microbial cultures and inoculated products should be considered infectious and handled appropriately. Aseptic techniques and usual precautions for handling the bacterial group studied should be observed throughout this procedure. See Protection of laboratory workers from occupationally acquired infections (1). For additional handling precautions, see Biosafety in microbiological and biomedical laboratories (2) or the regulations currently in use in each country.

Follow procedures for infectious or potentially infectious products for the disposal of all used materials.

C. SAMPLE INFORMATION AND PROCESSING

Use a pure culture of a confirmed N. gonorrhoeae grown on a nonselective medium (chocolate or IsoVitaleX™-supplemented GC base medium) and incubated for 18–24 hours at 36 ± 1°C in a 5 ± 1% CO2-enriched humid atmosphere.

D. QUALITY CONTROL

QUALITY CONTROL STRAINS

• Neisseria gonorrhoeae, strain WHO L
• Neisseria gonorrhoeae, strain WHO U
• Neisseria gonorrhoeae, strain WHO M (optional for β-lactamase test)
• ATCC 49226

Quality control strains are stored at −70°C in a suitable cryopreservation solution (such as tryptic soy broth containing 20% glycerol or brain heart infusion broth with 20% glycerol). Make sure that the antibiograms of quality control strains meet the specification at the time the frozen stocks are prepared. Quality control strains may be stored at −70°C for two years.

QUALITY CONTROL PROCEDURES

• Thaw vials of quality control strains stored at −70°C
• Streak inoculate strains onto plates of chocolate agar or supplemented GC agar medium for isolation and incubate plates at 36 ± 1°C in a 5 ± 1% CO2 incubator for 18–24 hours
• Perform tests as described in the section on examination (test) procedure below
• Read and record the results; compare the quality control results with the expected MICs to assess the accuracy of quality control testing

• Note: the MIC of an organism as determined by ETEST® may vary ±1 doubling dilution from the modal MIC. For highly reproducible testing, the range of MIC values for an individual isolate should not span more than 2 doubling dilutions.

QUALITY CONTROL SCHEDULE

• A quality control test is performed each time clinical isolates are tested
• Quality control results are recorded along with the test results
E. EXAMINATION (TEST) PROCEDURE

1. Warm, to room temperature, the appropriate number of GC agar plates for each strain to be tested.
   - The number of plates required per strain tested will depend on the size of the plates, 90 mm or 150 mm, and the number of antibiotic strips being used. It is recommended that a maximum number of one strip be used for a 90-mm plate, and a maximum number of four strips be used for a 150-mm plate.
   - The surface of the plates should be dry before the culture suspensions are inoculated. If moisture is visible on the surface of the plates, dry them (with lids ajar in a fume hood, laminar flow hood) in a 36 ± 1°C incubator just before inoculation. There should be no visible droplets of moisture on the surface of the agar or on the lids of the plates when they are inoculated. The surface of the dried medium should be smooth and should not show signs (webbed ribbing pattern on the agar surface) of desiccation.

2. Suspend isolated colonies from an overnight culture on supplemented chocolate agar medium in 1.0 to 2.0 ml of Mueller-Hinton broth. Mix the suspension thoroughly on a vortex mixer to break up clumps of growth.

3. Adjust the turbidity of the cell suspension by adding additional Mueller-Hinton broth or organisms, as required, until the turbidity of the suspension is equivalent to the turbidity of a 0.5 McFarland BaSO₄ standard. Discard this cell suspension if it is not used within 15–20 minutes after preparation and prepare a fresh suspension for testing.

4. Moisten a sterile applicator swab in the standardized cell suspension, and express excess moisture by rotating the swab against the glass above the liquid in the tube. Inoculate the entire surface of each plate, inoculating the surface completely in three different directions to ensure uniform, confluent growth.
   - It is recommended that cotton swabs with wooden handles be used for this procedure. Synthetic swabs do not soak up sufficient suspension to inoculate the entire surface of the plate.
   - It is recommended that swabs with plastic handles not be used to inoculate plates; the handles bend and may splatter liquid out of the tube when excess suspension is being expressed, creating a biohazard.

5. Repeat step 4, using a new sterile swab, to inoculate each additional plate as needed.

6. Allow the inoculated plates to sit at room temperature for 3–5 minutes to allow the moisture from the inoculum to absorb into the medium. Inspect the inoculated plates to ensure that there is no visible liquid on the surface of the medium; the surface of the medium must be dry before the ETEST® strips are applied.

7. Remove the ETEST® strips from the package using forceps and being careful to only touch the very top of the ETEST® strip.

8. When the surface of the medium is dry, apply the ETEST® strips of the selected antimicrobial agents to the surface of the medium and tamp them gently with forceps to ensure that they are in complete contact with the agar surface. All ETEST® strips should be applied with approximately the same distance from the edge of the plate and from each other.

9. Invert the inoculated plates (lid side down) and incubate the plates at 36 ± 1°C in 5 ± 1% CO₂ for 18–24 hours.

10. The plates should be read when there is sufficient growth and an elliptical zone of inhibition can be clearly seen.

11. The minimum inhibitory concentration (MIC) should be read at the point where the edge of the zone of inhibition intersects with the ETEST® strip. The MIC value should be reported using doubling-dilution units.

F. METHOD PERFORMANCE SPECIFICATIONS

The MIC of an organism as determined by ETEST® may vary by ±1 doubling dilution from the modal MIC. For highly reproducible testing, the range of MIC values for an individual isolate should not span more than 2 doubling dilutions.
ANNEX 2. METHODS FOR ANTIMICROBIAL SUSCEPTIBILITY TESTING

G. REFERENCE VALUES AND ALERT VALUES

*Neisseria gonorrhoeae* reference strains: expected MIC values (µg/ml)

<table>
<thead>
<tr>
<th>Antimicrobial agents</th>
<th>ATCC 49226</th>
<th>WHO L</th>
<th>WHO U</th>
<th>WHO M&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>0.004–0.016</td>
<td>0.125–0.5</td>
<td>0.001–0.004</td>
<td>0.008–0.03</td>
</tr>
<tr>
<td>Cefixime</td>
<td>0.004–0.03</td>
<td>0.064–0.25</td>
<td>&lt;0.016</td>
<td>&lt;0.016</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>0.25–1.0</td>
<td>0.25–1.0</td>
<td>2–8</td>
<td>0.125–0.5</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>ND</td>
<td>2–8</td>
<td>2–8</td>
<td>2–8</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>0.002–0.008</td>
<td>&gt;32</td>
<td>0.002–0.008</td>
<td>1–4</td>
</tr>
<tr>
<td>β-lactamase production</td>
<td>negative</td>
<td>negative</td>
<td>negative</td>
<td>positive</td>
</tr>
<tr>
<td>Penicillin&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.25–1</td>
<td>1–4</td>
<td>0.06–0.25</td>
<td>≥32</td>
</tr>
<tr>
<td>Tetracycline&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.25–1</td>
<td>1–4</td>
<td>0.5–2.0</td>
<td>1–4</td>
</tr>
</tbody>
</table>


<sup>a</sup> WHO M is only used for the β-lactamase assay as a positive control.

<sup>b</sup> Provided for reference only.

H. SAMPLE RETENTION AND STORAGE

Isolates are stored frozen at −70°C in a suitable cryopreservation solution (such as tryptic soy broth containing 20% glycerol or brain heart infusion broth with 20% glycerol) until no longer required.

**EQUIPMENT**
- Incubator (with 5% CO<sub>2</sub>)
- Freezer (−70°C to −80°C)
- Vortex
- Biosafety cabinet

**REAGENTS AND GROWTH MEDIA**
- Chocolate II plates or GC agar base plus 1% IsoVitale<sup>TM</sup> plate
- Trypticase soy broth with 20% glycerol or appropriate freezing medium

**SUPPLIES, OTHER MATERIALS**
- 2-ml cryovials or the equivalent
- Pipette aid
- 5-ml serological pipettes
- Inoculating swab
- Microcentrifuge tube rack or the equivalent
- Kimwipes® or equivalent low-lint disposable wipe

**PROCEDURE**

Day one: preparing the GC culture for frozen stock
- Perform the below steps inside a biosafety cabinet
  - Grow GC culture on Choc II or GC base supplemented with 1% IsoVitale<sup>TM</sup> plate with standard streaking techniques using an inoculating swab
  - Incubate the plates at 36 ± 1°C and 5% CO<sub>2</sub>
  - Incubate the plate for 16–18 hours
  - Do not allow the culture to grow longer than 24 hours

Day two: preparing the culture for freezing
- Label a sterile 2.0-ml cryovial
- Label a fresh, sterile tube of Trypticase soy broth with 20% glycerol
- Inside a biosafety cabinet, use an inoculating swab and scrape about one quarter to half of the 16- to 18-hour GC culture plate
- Completely resuspend the GC in Trypticase soy broth with 20% glycerol
- Pulse vortex to mix the solution
- Transfer 1 ml of the bacterial suspension into the labelled cryovial
- Transfer the cryovial to a −70°C to −80°C freezer

**REFERENCES**


### CORE AND OPTIONAL DEMOGRAPHIC, BEHAVIOURAL, CLINICAL AND LABORATORY DATA

<table>
<thead>
<tr>
<th>Variable name</th>
<th>Type and length</th>
<th>Description</th>
<th>Values</th>
<th>Core: must be collected for EGASP</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID_COUNTRY</td>
<td>[Character, 3]</td>
<td>Country submitting EGASP data</td>
<td>ISO International Organization for Standardization (ISO) ALPHA-3 Code</td>
<td></td>
</tr>
<tr>
<td>PT_ID</td>
<td>[Character, 15]</td>
<td>Patient number</td>
<td>PT_ID is unique to each EGASP patient; multiple specimens or isolates could be collected for one person</td>
<td></td>
</tr>
<tr>
<td>EGASP_ID</td>
<td>[Character, 10]</td>
<td>Specimen identification number</td>
<td>EGASP_ID is unique to each specimen collected</td>
<td></td>
</tr>
<tr>
<td>REPEAT</td>
<td>[Numeric, 1]</td>
<td>Multiple visits by one person to an EGASP clinic</td>
<td>1=yes, established EGASP patient If PT_ID&gt;1, then this variable will need to be set to “1”. If there is only one instance of PT_ID in the EGASP data, this variable would be set to “0”.</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>ID_SITE</td>
<td>[Character, 4]</td>
<td>Sentinel clinic code</td>
<td>1=CLIN1 2=CLIN2 3=CLIN3 4=CLIN4 n=CLINn A consecutive number will be assigned to each EGASP participating clinic. The number of participating clinics may vary from country to country.</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>DATE_C</td>
<td>[Date, 10]</td>
<td>Specimen collection date</td>
<td>DD-MM-YYYY MM-DD-YYYY YYYY-MM-DD Each of these three date formats can be accepted</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>SEX</td>
<td>[Numeric, 1]</td>
<td>Sex at birth</td>
<td>1=male For the current phase of EGASP implementation, all records should have SEX =1</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>GIDEN</td>
<td>[Numeric, 1]</td>
<td>Gender identity</td>
<td>1=male 2=female 3=transgender female 4=transgender male 9=unknown</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>ANAT</td>
<td>[Numeric, 1]</td>
<td>Anatomical site of specimen collection</td>
<td>1=male urethra For the current phase of EGASP implementation, all records should have ANAT=1</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>Variable name</td>
<td>Type and length</td>
<td>Description</td>
<td>Values</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------</td>
<td>-------------</td>
<td>--------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>AGE</td>
<td>[Numeric, 3]</td>
<td>Age in years</td>
<td>Enter 999 = unknown</td>
<td></td>
</tr>
<tr>
<td>ETHNIC</td>
<td>[Numeric, 1]</td>
<td>Place of birth of the EGASP patient</td>
<td>1=born in country 2=born in another country 9=unknown</td>
<td>Optional: include if EGASP country can collect</td>
</tr>
</tbody>
</table>
| DISUR, DISVG, DISAN, DISOR, DISNS, PAINSEX, PAINABD, PAINTEST, PAINUR, PAINREC, SYMPOTH, SYMPUNK | [Numeric, 1 for each] | Clinical signs and symptoms | Check all that apply  
For each: 1=yes; 0=no  
Discharge from urethra  
Discharge from vagina  
Discharge from anus  
Oral or pharyngeal discharge  
Discharge not specified  
Dyspareunia (painful intercourse)  
Lower abdominal pain  
Tenderness in testicles  
Painful urination  
Rectal pain  
Other symptoms  
Unknown symptoms  
For the current phase of EGASP implementation, all records should have DISUR=1 | Core must be collected for EGASP |
<p>| SYMP_SPC      | [Character, 25] | Specify other symptoms identified | Should only be completed if SYMPOTH=1 | Core: must be collected for EGASP |
| DIAG          | [Numeric, 1]    | Diagnosis at the time of current EGASP visit | 1=gonorrhoea 2=non-gonococcal urethritis or infection 3=other, specify 9=unknown | Core: must be collected for EGASP |
| OTHDIAG       | [Character, 25] | Specification of other diagnosis | Completed if DIAG=3 | Core: must be collected for EGASP |
| TRMT1         | [Numeric, 1]    | Primary treatment received for gonorrhoea | 0=None or not given 1=ceftriaxone 250 mg 2=ceftriaxone 500 mg 3=ceftriaxone 1 g 4=cefixime 400 mg 5=azithromycin 1 g 6=azithromycin 2 g 8=other (please indicate in other treatment 1, OTHTRMT1) 9=unknown or not documented | Core: must be collected for EGASP |</p>
<table>
<thead>
<tr>
<th>Variable name</th>
<th>Type and length</th>
<th>Description</th>
<th>Values</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRMT1_OTH</td>
<td>[Character, 25]</td>
<td>Other treatment not listed for TRMT1</td>
<td>Only complete if TRMT1=8. Enter the name and dosage of the other drug used for primary treatment of gonorrhoea</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>TRMT2</td>
<td>[Numeric, 1]</td>
<td>Second antibiotic received as part of dual therapy for gonorrhoea (and treatment of chlamydia or non-gonococcal urethritis)</td>
<td>0=None or not given 1=azithromycin 1 g 2=azithromycin 2 g 3=doxycycline 100 mg 4=tetracycline 8=other (please indicate in other treatment 2, OTHTRMT2) 9=unknown or not documented</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>TRMT2_OTH</td>
<td>[Character, 25]</td>
<td>Other treatment not listed for TRMT2</td>
<td>Only complete if TRMT2=8. Enter the name and dosage of the other drug used for secondary treatment of gonorrhoea, Chlamydia trachomatis or non-gonococcal infections</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>TRMTOUT</td>
<td>[Numeric, 1]</td>
<td>Outcome of treatment for patient</td>
<td>1=treatment completed 2=partial treatment completed 3=not treated – patient refused treatment 4=not treated – patient never came back for treatment</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>FUVIS</td>
<td>[Numeric, 1]</td>
<td>Outcome of follow-up visit</td>
<td>1=returned to clinic with symptoms 2=returned to clinic without symptoms 3=no follow-up visit</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>TOC</td>
<td>[Numeric, 1]</td>
<td>Result of test of cure</td>
<td>1=positive 2=negative 3=no test of cure performed</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>ANTIBIOT</td>
<td>[Numeric, 1]</td>
<td>Antibiotic use in the past two weeks</td>
<td>1=yes 2=no 9=unknown</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>ANTIBIOT_SPC</td>
<td>[Character, 25]</td>
<td>Name of antibiotic used in the past two weeks</td>
<td>Should only be completed if ANTIBIOT=1</td>
<td>Optional: include if EGASP country can collect</td>
</tr>
<tr>
<td>TRAVEL</td>
<td>[Numeric, 1]</td>
<td>History of travel within the last 30 days</td>
<td>1=within country (country TBD) 2=outside country (country TBD) 3=both 4=no travel history 9=unknown</td>
<td>Optional: include if EGASP country can collect</td>
</tr>
<tr>
<td>SEXWITH</td>
<td>[Numeric, 1]</td>
<td>History of sex with women, men or both in the past 30 days</td>
<td>1= sex with women only 2= sex with men only 3= sex with both (women and men) 9=unknown</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>Variable name</td>
<td>Type and length</td>
<td>Description</td>
<td>Values</td>
<td>Notes</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------</td>
<td>-------------</td>
<td>--------</td>
<td>-------</td>
</tr>
<tr>
<td>PART_N</td>
<td>[Numeric, 3]</td>
<td>Number of sexual partners in the past 30 days</td>
<td>Enter 999 = unknown</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>ETHNIC2</td>
<td>[Numeric, 1]</td>
<td>Nationality of sexual partner(s) in the past 30 days</td>
<td>1=born in country 2=born in another country 3=both (multiple partners) 9=unknown</td>
<td>Optional: include if EGASP country can collect</td>
</tr>
<tr>
<td>ETH2SPC</td>
<td>[Character, 25]</td>
<td>Specify nationality of sexual partner(s) in the past 30 days</td>
<td>Specify location (if possible) if ETHNIC2 = 2 or 3</td>
<td>Optional: include if EGASP country can collect</td>
</tr>
<tr>
<td>URET VAG ANAL1 ANAL2 ANAL3 ORAL1 ORAL2 ORAL3 UNKSEX</td>
<td>[Numeric, 1 for each]</td>
<td>Sexual behaviour characteristics (in the past 30 days)</td>
<td>Check all that apply. For each 1=yes; 0=no: Urethral Vaginal Anal receptive Anal insertive Anal not specified Oral receptive Oral insertive Oral not specified Unknown anatomical site</td>
<td>Optional: include if EGASP country can collect</td>
</tr>
<tr>
<td>STI</td>
<td>[Numeric, 1]</td>
<td>Presence of other sexually transmitted infections</td>
<td>1=yes 2=no 9=unknown</td>
<td>Optional: include if EGASP country can collect</td>
</tr>
<tr>
<td>GWAR CHANC CHLA HSV HBV HCV HIV LGV SYPH1 SYPH2 TRICH STIOTH STIUNK</td>
<td>[Numeric, 1 each]</td>
<td>Other sexually transmitted infections</td>
<td>Only specify if STI=1; check all that apply. For each: 1=yes; 0=no Anogenital warts Chancroid Chlamydia trachomatis Genital herpes simplex infection Hepatitis B infection Hepatitis C infection HIV infection Lymphogranuloma venereum Primary, secondary or early latent syphilis Latent (&gt;1 year) syphilis Trichomoniasis Other sexually transmitted infection Unknown sexually transmitted infection</td>
<td>Optional: include if EGASP country can collect</td>
</tr>
<tr>
<td>STIOOTH_SPC</td>
<td>[Character, 25]</td>
<td>Specify other sexually transmitted infection not listed</td>
<td>Only complete if STIOOTH=1</td>
<td>Optional: include if EGASP country can collect</td>
</tr>
</tbody>
</table>
### ENHANCED GONOCOCCAL ANTIMICROBIAL SURVEILLANCE PROGRAMME (EGASP): GENERAL PROTOCOL

The following are laboratory variables that should be merged with the epidemiological data:

<table>
<thead>
<tr>
<th>Variable name</th>
<th>Type and length</th>
<th>Description</th>
<th>Values</th>
<th>Core: must be collected for EGASP</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID_LABO</td>
<td>[Character, 4]</td>
<td>EGASP reference laboratory code</td>
<td>1=LAB1 2=LAB2 n=LABn</td>
<td>A consecutive number will be assigned to each EGASP reference laboratory. The number of participating EGASP reference laboratories may vary from country to country.</td>
</tr>
<tr>
<td>DATE_R</td>
<td>[Date, 10]</td>
<td>Date specimen received in the reference laboratory</td>
<td>DD-MM-YYYY MM-DD-YYYY YYYY-MM-DD</td>
<td>Each of these three date formats can be accepted</td>
</tr>
<tr>
<td>DATE_GRAM</td>
<td>[Date, 10]</td>
<td>Date Gram stain performed</td>
<td>DD-MM-YYYY MM-DD-YYYY YYYY-MM-DD</td>
<td>Each of these three date formats can be accepted</td>
</tr>
<tr>
<td>GRAM</td>
<td>[Numeric, 1]</td>
<td>Urethral Gram stain result</td>
<td>1=gram-negative diplococcus identified 2=no gram-negative diplococcus identified 3=not performed</td>
<td></td>
</tr>
<tr>
<td>SPECQUAL</td>
<td>[Numeric, 1]</td>
<td>Specimen quality before culture</td>
<td>1=acceptable 2=contaminated 3=non-viable 4=improperly transported</td>
<td></td>
</tr>
<tr>
<td>DATE_CULT</td>
<td>[Date, 10]</td>
<td>Date of culture result</td>
<td>DD-MM-YYYY MM-DD-YYYY YYYY-MM-DD</td>
<td>Each of these three date formats can be accepted To be reported if SPECQUAL is equal to “1=acceptable”</td>
</tr>
<tr>
<td>CULT</td>
<td>[Numeric, 1]</td>
<td>Culture result</td>
<td>1=Neisseria gonorrhoeae positive 2=Neisseria gonorrhoeae negative</td>
<td></td>
</tr>
<tr>
<td>SPECQUAL2</td>
<td>[Numeric, 1]</td>
<td>Specimen quality before susceptibility testing</td>
<td>1=acceptable 2=contaminated 3=non-viable</td>
<td>To be reported if SPECQUAL is equal to “1=acceptable”</td>
</tr>
<tr>
<td>Variable name</td>
<td>Type and length</td>
<td>Description</td>
<td>Values</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------</td>
<td>-------------</td>
<td>--------</td>
<td>----------------------------------</td>
</tr>
</tbody>
</table>
| DATE_AST      | [Date, 10]      | Date of susceptibility test result | DD-MM-YYYY  
                MM-DD-YYYY  
                YYYY-MM-DD  
Each of these three date formats can be accepted  
To be reported if SPECQUAL2 is equal to “1=acceptable” | |
| CFM           | [Numeric, 6]    | Cefixime MIC | Primary MIC result (via ETEST® alone)  
If not tested set it as 9999  
To be reported if SPECQUAL2 is equal to “1=acceptable”  
**Note: do NOT ever report disk diffusion results; EGSAP reports MIC results via ETEST® | Core: must be collected for EGASP |
| CRO           | [Numeric, 6]    | Ceftriaxone MIC | Primary MIC result (via ETEST® alone)  
If not tested set it as 9999  
To be reported if SPECQUAL2 is equal to “1=acceptable”  
Do not ever report disk diffusion results; EGSAP reports MIC results via ETEST® | Core: must be collected for EGASP |
| AZM           | [Numeric, 6]    | Azithromycin MIC | Primary MIC result (via ETEST® alone)  
If not tested, set it as 9999  
To be reported if SPECQUAL2 is equal to “1=acceptable”  
Do not ever report disk diffusion results; EGSAP reports MIC results via ETEST® | Core: must be collected for EGASP |
| GEN           | [Numeric, 6]    | Gentamicin MIC | Primary MIC result (via ETEST® alone)  
To be reported if SPECQUAL2 is equal to “1=acceptable”  
Do not ever report disk diffusion results; EGSAP reports MIC results via ETEST® | Optional: however, country must include if EGASP country decides to test |
| CIP           | [Numeric, 6]    | Ciprofloxacin MIC | Primary MIC result (via ETEST® alone)  
To be reported if SPECQUAL2 is equal to “1=acceptable”  
Do not ever report disk diffusion results; EGSAP reports MIC results via ETEST® | Optional: however, country must include if EGASP country decides to test |
| ATB_OTH       | [Character, 20] | Specify other antibiotic 1 tested | Specify the name of the other antibiotic tested  
To be reported if SPECQUAL2 is equal to “1=acceptable” | Optional |
<table>
<thead>
<tr>
<th>Variable name</th>
<th>Type and length</th>
<th>Description</th>
<th>Values</th>
<th>Core/Collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATB_OTH_MIC</td>
<td>[Numeric, 6]</td>
<td>Other antibiotic 1 MIC</td>
<td>Primary MIC result (via ETEST® alone) To be reported if SPECQUAL2 is equal to “1=acceptable”</td>
<td>Optional</td>
</tr>
<tr>
<td>ATB_OTH1</td>
<td>[Character, 20]</td>
<td>Specify other antibiotic 2 tested</td>
<td>Specify the name of the other antibiotic tested To be reported if SPECQUAL2 is equal to “1=acceptable”</td>
<td>Optional</td>
</tr>
<tr>
<td>ATB_OTH1_MIC</td>
<td>[Numeric, 6]</td>
<td>Other antibiotic 2 MIC</td>
<td>Primary MIC result (via ETEST® alone) To be reported if SPECQUAL2 is equal to “1=acceptable”</td>
<td>Optional</td>
</tr>
<tr>
<td>CFM_AL</td>
<td>[Numeric, 1 each]</td>
<td>Cefixime MIC alert MIC value</td>
<td>1=yes if MIC ≥0.25 µg/ml 2=no if MIC &lt;0.25 µg/ml There is no need to report this variable to the GLASS IT Platform since this is a calculated variable</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>CRO_AL</td>
<td>[Numeric, 1 each]</td>
<td>Ceftriaxone MIC alert value</td>
<td>1=yes if MIC ≥0.125 µg/ml 2=no if MIC &lt;0.125 µg/ml There is no need to report this variable to the GLASS IT Platform since this is a calculated variable</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>AZM_AL</td>
<td>[Numeric, 1 each]</td>
<td>Azithromycin MIC alert value</td>
<td>1=yes if MIC ≥2 µg/ml 2=no if MIC &lt;2 µg/ml There is no need to report this variable to the GLASS IT Platform since this is a calculated variable</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>GEN_AL</td>
<td>[Numeric, 1 each]</td>
<td>Gentamicin MIC alert value</td>
<td>1=yes if MIC ≥32 µg/ml 2=no if MIC &lt;32 µg/ml NB: there is no need to report this variable to the GLASS-IT platform since this is a calculated variable</td>
<td>Optional: however, country must include if EGASP country decides to test</td>
</tr>
<tr>
<td>RETEST</td>
<td>[Numeric, 1]</td>
<td>If the isolate was retested because of an alert value</td>
<td>1=retested 2=not retested Only if the isolate was retested because of an alert Only complete if SPECQUAL2 is equal to “1=acceptable”</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>DATE_CONF</td>
<td>[Date, 10]</td>
<td>Date of confirmation antimicrobial susceptibility test or retest result</td>
<td>DD-MM-YYYY MM-DD-YYYY YYYY-MM-DD Each of these three date formats can be accepted Only complete if RETEST=1</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td>Variable name</td>
<td>Type and length</td>
<td>Description</td>
<td>Values</td>
<td>Notes</td>
</tr>
<tr>
<td>-----------------</td>
<td>-----------------</td>
<td>----------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>CFM_1</td>
<td>[Numeric, 6]</td>
<td>Retested cefixime MIC</td>
<td>Confirmatory MIC result (via ETEST® alone)</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Only complete if CFM_AL=1</td>
<td></td>
</tr>
<tr>
<td>CRO_1</td>
<td>[Numeric, 6]</td>
<td>Retested ceftriaxone MIC</td>
<td>Confirmatory MIC result (via ETEST® alone)</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Only complete if CRO_AL=1</td>
<td></td>
</tr>
<tr>
<td>AZM_1</td>
<td>[Numeric, 6]</td>
<td>Retested azithromycin MIC</td>
<td>Confirmatory MIC result (via ETEST® alone)</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Only complete if AZM_AL=1</td>
<td></td>
</tr>
<tr>
<td>GEN_1</td>
<td>[Numeric, 6]</td>
<td>Retested gentamicin MIC</td>
<td>Confirmatory MIC result (via ETEST® alone)</td>
<td>Optional: however, country must include if EGASP country decides to test</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Only complete if RETEST=1 (i.e., isolate was retested because of an alert)</td>
<td></td>
</tr>
<tr>
<td>CFM_1_AL</td>
<td>[Numeric, 1 each]</td>
<td>Cefixime MIC alert value</td>
<td>1=yes if MIC ≥0.25 µg/ml</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2=no if MIC &lt;0.25 µg/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>There is no need to report this variable to the GLASS IT Platform since this is a calculated variable</td>
<td></td>
</tr>
<tr>
<td>CRO_1_AL</td>
<td>[Numeric, 1 each]</td>
<td>Ceftriaxone MIC alert value</td>
<td>1=yes if MIC ≥0.125 µg/ml</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2=no if MIC &lt;0.125 µg/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>There is no need to report this variable to the GLASS IT Platform since this is a calculated variable</td>
<td></td>
</tr>
<tr>
<td>AZM_1_AL</td>
<td>[Numeric, 1 each]</td>
<td>Azithromycin MIC alert value</td>
<td>1=yes if MIC ≥2 µg/ml</td>
<td>Core: must be collected for EGASP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2=no if MIC &lt;2 µg/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>There is no need to report this variable to the GLASS IT Platform since this is a calculated variable</td>
<td></td>
</tr>
<tr>
<td>GEN_1_AL</td>
<td>[Numeric, 1 each]</td>
<td>Gentamicin MIC alert value</td>
<td>1=yes if MIC ≥32 µg/ml</td>
<td>Optional: however, country must include if EGASP country decides to test</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2=no if MIC &lt;32 µg/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>There is no need to report this variable to the GLASS IT Platform since this is a calculated variable</td>
<td></td>
</tr>
</tbody>
</table>
ANNEX 4. MONTHLY AND ANNUAL PROCESS MEASURE REPORTING

Surveillance partners (such as sentinel clinics, reference laboratories and the health ministry) are requested to monitor and report on process measures to document progress towards achieving EGASP project outcomes. These measures should be compiled at the national level and submitted to WHO and CDC/DSTDP/NCHHSTP or the WHO collaborating centre monthly and then annually.

The following is a summary of indicators relevant at the sentinel and reference laboratory levels (should be monitored). However, per the request of WHO and CDC/DSTDP/NCHHSTP or the WHO collaborating centre and the health ministry, additional indicators may be requested.

INDICATORS TO BE MONITORED AT THE SENTINEL CLINIC LEVEL

- Number of EGASP patients
- Number (and percentage) of patients with repeat or multiple visits (several EGASP specimens and one patient ID)
- Median patient age (minimum and maximum)
- Number (and percentage) of patients by sex of the sex partner: history of sex with men, women or both
- Number (and percentage) of patients with antibiotic use in the past two weeks
- Number (and percentage) of patients who received primary treatment for gonorrhoea (by antibiotic categories)
- Number (and percentage) of patients who received second treatment for chlamydia or non-gonococcal urethritis
- Total number of EGASP specimens collected from each sentinel sexually transmitted infection clinic

In addition, sentinel clinics should describe their plans to address challenges faced in enrolment, specimen quality and viability, timeliness of specimen or data transmission and data completeness.

INDICATORS TO BE MONITORED BY THE REFERENCE LABORATORY

- Number (and percentage) of EGASP specimens received from each clinic that had no growth (non-viable)
- Number (and percentage) of EGASP specimens received from each clinic that were contaminated
- Number (and percentage) of submitted specimens that were found to be Gram stain positive (presence of diplococci)
- Number (and percentage) of isolates that were culture positive from each clinic
- Number (and percentage) of submitted specimens that were found to be Gram stain positive but culture negative
- Number (and percentage) of submitted specimens that were found to be culture positive but Gram stain negative
- Number (and percentage) of EGASP isolates that had no growth (non-viable) before antimicrobial susceptibility testing
- Number (and percentage) of EGASP isolates that were contaminated before antimicrobial susceptibility testing
- Number (and percentage) of EGASP isolates that had antimicrobial susceptibility testing
- Number (and percentage) of EGASP isolates that were tested for antimicrobial susceptibility within one month of receipt of isolates
- Number (and percentage) of EGASP isolates with initial alert MIC values
- Number of (and percentage) of EGASP isolates with final alert MIC values
- MIC distribution trend for each antibiotic – cumulative and for each clinic
- Record that each EGASP reference laboratory achieved a passing grade of ≥80% agreement with the modal MIC ±1 dilution of each external quality assessment for which results are available. Please note: this measure is for the annual report only.
ANNEX 5. SUMMARY OF EGASP TIMELINES FOR PROJECT PARTICIPANTS

SENTINEL CLINIC

1. **Demographic, behavioural and clinical data.** Should be merged with antimicrobial susceptibility data monthly, within one month of antimicrobial susceptibility testing, and received at the health ministry or equivalent no more than two months after the end of the month in which the corresponding isolates were collected.

2. **Specimens for gonococcal culture.** Up to the reference laboratory (may be daily, weekly or monthly depending on the determined clinical practices).

3. **Monthly and annual progress measure reports.** Due monthly and annually.

REFERENCE LABORATORY

1. **Testing of isolates.** Should be completed within one month of receiving isolates.

2. **Antimicrobial susceptibility test data.** Due monthly to the health ministry and to sentinel clinics, within one month of completion of testing.

3. **Control strain susceptibility test data.** Due monthly to the health ministry, within one month of completion of testing (together with the antimicrobial susceptibility data obtained from the same run).

4. **Notification of alert value MIC isolates.** Isolates with alert MIC values should be retested within five working days of the initial test. If the alert MIC value is confirmed on retesting, the principal investigators, co-investigators and sentinel clinics should be notified by telephone or by email within five working days of the retest date. Isolates with high alert MIC values should be retested immediately and communication should be made with the health ministry, WHO and CDC/DSTDP/NCHHSTP or the WHO collaborating centre.

5. **Monthly and annual progress measure reports.** Due monthly and annually.

HEALTH MINISTRY

1. **Ensure that data are merged (demographic, behavioural and clinical data and antimicrobial susceptibility data).** Merged cumulative, deidentified line-listed data should be updated and entered into the EGASP module of GLASS for WHO and CDC/DSTDP/NCHHSTP and/or the WHO collaborating centre each month.

2. **Annual progress reports from sentinel clinics and reference laboratory.** Should be reviewed and shared with WHO and CDC/DSTDP/NCHHSTP and/or the WHO collaborating centre annually.

WHO, CDC/DSTDP/NCHHSTP AND WHO COLLABORATING CENTRE

1. **Publish annual EGASP report with health ministry.** By autumn or winter of the year following a full year of isolate collection.
ANNEX 6. USE OF EGASP DATA AND SPECIMENS OR ISOLATES, INCLUDING THE EGASP CONCEPT PROPOSAL FORM

To encourage the sharing of the data and/or isolates or specimens, a systematic process to review the concepts and ideas for the use of data and specimens or isolates is required. This review will include the approval from key institutions and partners, referred to as the EGASP core team, and the tracking of the data and/or isolates. Sentinel clinics, reference laboratories, WHO, CDC DSTDP/NCHHSTP or the WHO collaborating centre and the health ministry can develop abstracts and manuscripts for peer-reviewed publications based on EGASP data, or participating institutions and partners can request specimens through this system.

To ensure adequate communication and to address any human subjects issues that may arise with the use of isolates or data collected for public health surveillance, proposals for the use of EGASP data or EGASP isolates (epidemiological and/or antimicrobial susceptibility data) should be initiated through the following process:

1. a brief (1–2 page) written proposal should be submitted to the country’s EGASP coordinator for the EGASP core team;
2. the country’s core EGASP team should review and approve the proposal, giving priority to such requests based on scientific merit and feasibility; and
3. the necessary human subjects, ethics, or institutional review board review should be sought as appropriate. For proposals involving a CDC author, CDC will clear this. For situations in which EGASP data are to be presented, the EGASP core team should be notified and have the opportunity to review the presentation or poster.

The country EGASP coordinator is also responsible for tracking submitted proposals and concepts and their disposition in a spreadsheet. Proposals should be shared and discussed during monthly in-country EGASP meetings.

The EGASP core team is a working group including the following members who are responsible for reviewing data and specimen or isolate requests:

[insert country-specific EGASP core team]

- country EGASP national focal point;
- country EGASP project coordinator;
- WHO EGASP coordinator/focal point; and
- CDC/DSTDP/NCHHSTP or WHO collaborating centre coordinator or focal point.
EGASP CONCEPT PROPOSAL FORM FOR DATA AND ISOLATES, INCLUDING REQUESTS FOR COMPILING AN ABSTRACT OR MANUSCRIPT

Date: 
Submitter name: 
Submitter institution: 

What is this proposal request for (check all that apply)?

- EGASP data (such as epidemiological and/or antimicrobial susceptibility data)
- EGASP specimens or isolates (such as isolates for molecular sequencing)
- Abstract
- Manuscript
- Presentation
- Other (please specify)

This proposal should be brief and include the following.

1. Proposed title of the project and names of the lead author and potential participating authors (if known).
2. Briefly describe the rationale for the proposed concept.
3. Describe the major goals of your proposal.
4. Provide details of the proposed outcomes and independent variables of primary interest (such as risk factors) that support the analysis.
5. List the study sites from which data will be used for the proposed analysis and data elements that will be summarized (such as the number of EGASP specimens, number of culture-positive gonococcal cases, epidemiological characteristics, antimicrobial susceptibility testing characteristics or whole-genome sequencing of isolates).
6. Proposed timeline for completing the analysis.
7. Specify the name of the meeting if it is a presentation or abstract submission (including the deadlines for submission) and/or the target journal for publication.

Send this proposal form to the EGASP core team for review via the EGASP coordinator: [insert name and contact information]
For more information, contact:
World Health Organization
Department of Global HIV, Hepatitis and STI Programme
20 Avenue Appia
1211 Geneva 27
Switzerland
E-mail: hiv-aids@who.int
www.who.int/hiv