Evaluation of the Australian Gonococcal Surveillance Programme

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Abstract

The Australian Gonococcal Surveillance Programme (AGSP) is a laboratory network that monitors the susceptibility of gonococcal isolates to antibiotics used in the treatment of infection. This report evaluates and reports on the simplicity, flexibility, sensitivity, representativeness, timeliness and acceptability of the AGSP. The World Health Organization's (WHO) Questionnaire for Assessment of Antimicrobial Resistance (AMR) National Networks was used in undertaking this evaluation and we report on the questionnaire's usefulness. The evaluation revealed that the AGSP was structurally simple, acceptable, timely and that the data were actively used by the stakeholders. However, the flexibility, representativeness and sensitivity of the AGSP are challenged by the increasing use of molecular based methods to diagnose gonococcal infections, as this is reducing the number of isolates available for testing. Despite this challenge, the AGSP has been able to identify differences in the antimicrobial susceptibility of gonococcal strains circulating in metropolitan and regional communities and the data generated are used to devise or modify standard treatment regimens for gonorrhoea. The functioning of the system can be improved by better availability of data through a dedicated website. Ideally, linkage of AGSP data to notification data would ensure that the AGSP is sensitive to and representative of the changes in gonococcal resistance amongst various sub-populations, although it will increase system complexity. The WHO questionnaire was found to be useful in undertaking the evaluation of the AGSP as it was simple and well-structured. However, the questionnaire needs to be expanded to include benchmarks that guide the assessment process. *Commun Dis Intell* 2005;29:142–148.

Keywords: antimicrobial resistance; disease surveillance; gonococcal infection; Neisseria gonorrhoeae

Introduction

Gonococcal infections are caused by the bacterium *Neisseria gonorrhoeae* and are almost always sexually transmitted. The disease is of public health importance as it impacts on sexual and reproductive health and amplifies the risk of HIV transmission by increasing the HIV viral load at the mucosa.[1]

Most effective treatments for gonococcal infections will eliminate the bacteria within 12 hours. The World Health Organization (WHO) recommends that an effective treatment should be a single dose of antibiotic that is prescribed on the patient's first presentation, where it should predictably cure at least 95 per cent of those treated.[2] To ensure that an antibiotic treatment is at least 95 per cent effective, public health practitioners need to monitor the rates of antibiotic resistance of the different gonococcal strains circulating in the community.

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A report released in 1999 by the Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) led to the development of an Australia-wide strategy for the surveillance and management of antimicrobial resistance (AMR).[3,4] In the consultation phase of the strategy, existing AMR surveillance systems were to be evaluated. The aim of the evaluations was to develop longer term mechanisms to acquire national data on AMR. One of the first systems to be evaluated was the Australian Gonococcal Surveillance Programme (AGSP).

The AGSP is a network of laboratories that, among other activities, aims to enhance laboratory contributions to control gonococcal disease and monitors the susceptibility of gonococcal isolates to antibiotics used in the treatment of infection. The AGSP is a collaborative program, with a reference laboratory in each state and territory and a coordinating unit in Sydney. The network was established in 1979 and has been reporting on gonococcal AMR trends in Australia since 1981. The reference laboratories analyse isolates for AMR testing from any private or public laboratory or patient clinic submitting samples. The results for individual patients are reported back to the referring service and after analysis and comment, consolidated data are also reported to state and territory and national public health officials to monitor changes in gonococcal resistance circulating in the community.

This article reviews the process of gonococcal AMR surveillance in Australia that is undertaken by the AGSP. An evaluation of the simplicity, flexibility, sensitivity, representativeness, timeliness and acceptability of the system is presented. The article also describes the utility of the WHO's 'Questionnaire for Assessment of AMR National Networks' in evaluating the AGSP.[5] This may guide practitioners in future evaluations of AMR surveillance systems.

Methods

The guidelines for the evaluation of surveillance systems developed by the United States Centers for Disease Control and Prevention (CDC) were used in this assessment.[6] The attributes of the surveillance system simplicity, flexibility, sensitivity, representativeness, timeliness and acceptability were evaluated because of their importance to national AMR surveillance.

Simplicity was determined by assessing the flow of data in the system (collection, transmission, analysis and reporting). This also provided information about the timeliness of the system. Representativeness was evaluated by comparing the number of isolates tested by the AGSP with the total number of gonococcal notifications between 1995 and 2003. Sensitivity was assessed by examining whether the AGSP tests enough isolates to detect changes in AMR and flexibility was evaluated by identifying examples of the system's ability to adapt to changes in testing methods. Acceptability was assessed through survey-based consultation with AGSP stakeholders. Stakeholders surveyed included the AGSP reference laboratories (n=8); private and public referral laboratories (n=33); sexual health clinics (n=28); public health officials at the state and territory, and national level (n=21); and international stakeholders (WHO and the International Collaboration on Gonorrhoea, n=30).

The WHO Questionnaire for Assessment of AMR National Networks contains two components: a component assessing individual laboratory status with respect to infrastructure and capacity, and a component evaluating the overall functioning of the surveillance network. In Australia, the first component is dealt with by an existing system of laboratory accreditation (National Association of Testing Authorities) and it was excluded from the evaluation. The second component was assessed in the current evaluation to evaluate its application to Australian systems.

Results

Description of the Australian Gonococcal Surveillance Programme

The AGSP reference laboratories receive isolates from various public and private laboratories in their respective state or territory. Even though the number of contributing laboratories varies over time due to laboratory mergers and takeovers, the AGSP central coordinating unit in Sydney estimates that 85 per cent of laboratories in New South Wales contribute data, including private laboratories. Some sexual health clinics send samples for diagnosis and AMR testing directly to the AGSP reference laboratories.

The reference laboratories use a standard agar plate dilution methodology in AMR testing.[7] This was developed about 25 years ago and has been the basis for national studies on gonococcal AMR. An AGSP-specific quality assurance program which uses internationally validated reference cultures, is used to validate results.[8] Most isolates are tested and stored in the jurisdiction's reference laboratory.

The AGSP reference laboratories collect identifying information about the patient (name, date of birth, gender) and site of sample isolation. The AGSP also attempts to collect clinical notes and data on geographic acquisition, but these are rarely provided by the referring practitioner or laboratory. At a national level, the AGSP collects de-identified data including gender, state or territory for each isolate tested and site of sample isolation. There is good completion of the data fields collected at the national level, where

between 1996 and 2003 an average of only 0.5 per cent of isolates were missing these data (range 0.2% to 0.8%).

The state and territory AGSP reference laboratories maintain databases that have identifying information on each case in line-listing format. Each reference laboratory uses a different information technology system, depending on what is utilised by their hosting organisation. One concern with the current data flow is that there is duplication of data entry for the isolates received from the initial diagnostic laboratories, decreasing simplicity, acceptability and timeliness.

For the national data, the state and territory reference laboratories send aggregated data to the AGSP coordinating unit in a standard summary aggregated format, quarterly. The coordinating unit then collates and maintains the information in a Microsoft Access database. The states and territories sometimes delay sending the summary information due to the need to complete laboratory analyses of late-arriving referred isolates and to revise and clean their data e.g. of duplicate samples. Despite this, the national network has consistently reported on a quarterly and annual basis to the various stakeholders within six months of the end of the time period.

The AGSP disseminates information to a variety of stakeholders. At a local level, the reference laboratories circulate information to clinicians about recommended standard treatments through emails or by responding to queries. At a state and territory level, the AGSP produces updates on gonococcal AMR trends to public health units; sexually transmissible infections (STI) clinics; divisions of general practice; and laboratories through state and territory health bulletins. At the national and international levels, the AGSP produce quarterly and annual reports that are published in *Communicable Diseases Intelligence* (*CDI*). *CDI* is distributed to government agencies, public health practitioners, general practice and laboratories.

Usefulness of the Australian Gonococcal Surveillance Programme

The surveillance of gonococcal resistance patterns is essential for the establishment and modification of standardised treatment regimens for gonorrhoea and enables the economic and acceptable use of antimicrobials in this disease. One example of where the AGSP data were useful is in Western Australia, where regional and rural areas have different standard treatment regimens to those recommended in metropolitan areas. Despite widespread resistance to penicillins in many parts of Australia, the AGSP has demonstrated that most strains circulating in the regional and rural communities remain sensitive to penicillins. The penicillins (usually given orally as amoxycillin, often combined with clavulanic acid) are both cheaper and easier to administer than intramuscular ceftriaxone, which is the recommended treatment in metropolitan settings because of AMR. The Table shows cost comparisons of the two formulations based on standard purchasing procedures for individual patients. Although these costs would differ with bulk purchasing arrangements, they are indicative of the substantial price differentials between the two treatments.

In Western Australia, approximately 580 gonococcal infections per year are locally acquired and non-metropolitan (based on data from the last four years). Since the treatment regimen in Western Australia for this category of patients is penicillin, then the overall cost savings are substantial. There are also benefits at the patient level, where penicillin is a more acceptable drug than ceftriaxone since it is easy and pain-free to administer.

Evaluation

The evaluation of the system attributes and findings from the stakeholder surveys are presented below. The stakeholder survey was distributed to 90 national stakeholders and 30 international stakeholders. The response rate for the national stakeholders was 57 per cent (n=51) and 27 per cent (n=8) for the international stakeholders. One

Table. Comparison of drugs used in the treatment of gonococcal infections

Attribute	Penicillin (amoxycillin)	Ceftriaxone
Administration	Oral	Intramuscular
Cost*	$7.86 per course	$56.30 per course
Acceptability for patient	Few side effects, no associated administration equipment or expertise required	Very painful, additional cost of equipment and expertise needed to administer
Pharmaceutical Benefit Scheme*	Yes – easily accessible to clinicians	Restricted benefit

* Data obtained from MIMS Online, 2004[9]

potential reason for the low response rate was that questionnaires were sent to various individuals in most organisations, where co-workers may have collated their views and returned a single response or assigned a single person to respond on behalf of the group. The low response rate could also be attributed to the fact that email surveys are easily forgotten or ignored, although a reminder was sent after two weeks. The low response rate for the international stakeholders, most of whom were in the WHO system, may reflect the high turnover of technical staff in that organisation.

Simplicity

The AGSP is a relatively simple system as all the reference laboratories use standardised testing methods and the common Public Health Laboratory Network case definition. As Figure 1 shows, there are clear mechanisms for data flow through the system. The AGSP keeps the database fields to a minimum to help reduce the complexity of data collection and analysis.

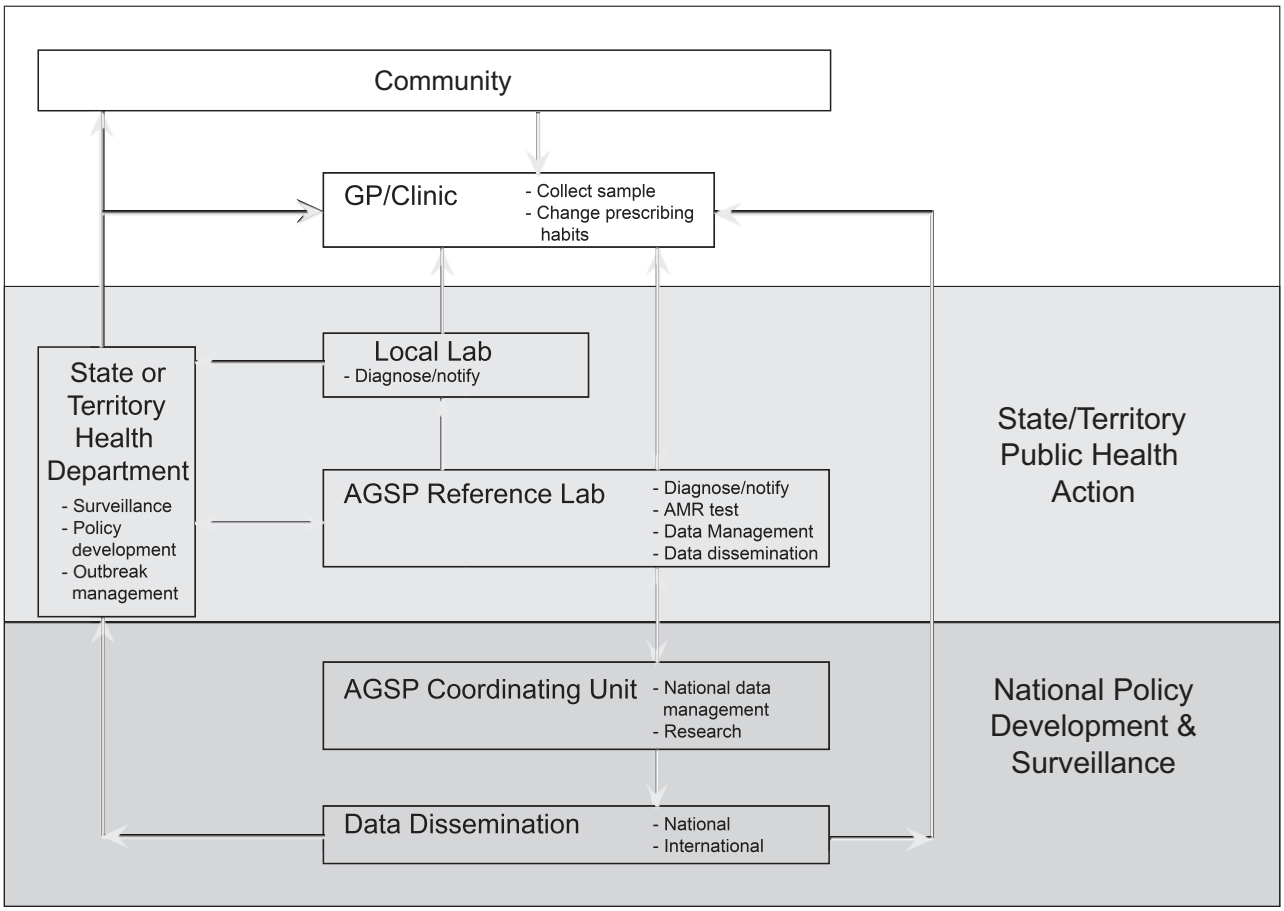
The majority (88%) of stakeholders responding to the survey thought that the AGSP was a simple system. Of those who disagreed, issues such as poorly defined jargon in annual reports and an ambiguous network structure were identified as concerns. One respondent noted, however, that the outputs of the system are too simple and that more detail in the annual reports is needed.

Flexibility

The network has had to adapt to some challenges. Since isolates currently need to be cultured for AMR testing, the introduction of molecular based methods to diagnose gonococcal infections has challenged the flexibility of the AGSP. Molecular based methods are cheaper and faster to use and have been eligible for rebates from Medicare since 1999. This is problematic for gonococcal AMR surveillance as it can decrease the number of isolates available for testing. To adapt to this advance in technology, the AGSP is in regular communication with public and private laboratories to remind them to forward any available isolates.

As more antimicrobials have been introduced for the treatment of gonococcal infections, the AGSP has adapted by introducing new controls and modifying quality assurance to include new resistance testing.

Figure 1. Flow chart of the Australian Gonococcal Surveillance Programme



Sensitivity

Sensitivity is an important attribute since the AGSP aims to detect changes in AMR over time so that public health action can be taken if resistance to a particular antimicrobial exceeds five per cent. Currently, the AGSP tests over 3,000 isolates each year nationally because the system is comprehensive and continuous. Even though this is a large number of isolates, it is difficult to assess whether this number is sufficient to detect significant changes in gonococcal AMR rates in sub-populations, such as men who have sex with men or rural populations. Detecting changes in sub-populations is only possible if clinical and risk factor information is made available to the AGSP laboratories, but this occurs infrequently and is beyond the capacity of laboratory-based systems to obtain, so little is known about these groups.

One measure of the system's sensitivity and usefulness is its ability to detect outbreaks of particular types of gonococcal infections distinct from issues of AMR. In 2002, the New South Wales reference laboratory noticed an increase in the number of disseminated gonococcal infections. The laboratory typed the isolates and found that they were identical. The reference laboratory informed the public health units, sexual health clinics and NSW Department of Health. The outbreak came to an end one year later. The AGSP also gave advice on patient treatment and follow-up in this outbreak, which may have reduced the infectivity period of cases.

Representativeness

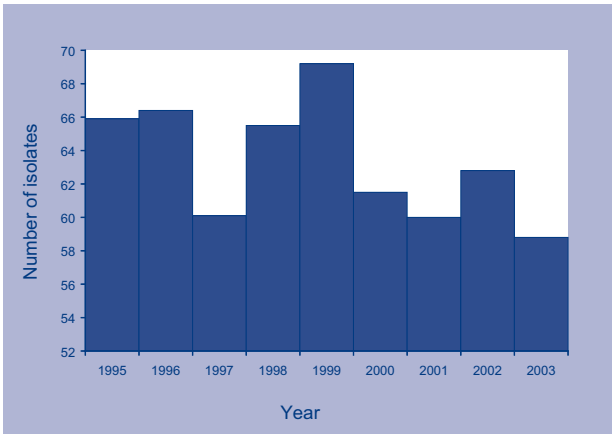
Between 1995 and 2003, the total isolates tested annually by AGSP averaged 63.1 per cent of the total gonococcal notifications in Australia (Figure 2). The representativeness of the system is affected by the increasing reliance on molecular based methods to diagnose gonococcal infections, which has decreased the number of isolates available for AMR testing. This is especially problematic in remote settings where the reliance on molecular based methods is increasing due to its cost efficiency. In addition, due to logistic issues of specimen collection and transport, molecular based testing is the only practical test method in remote communities. In time, this may compromise the ability to detect AMR patterns in these communities, and other ways of assessing the effectiveness of treatment regimens will need to be found.

Despite these challenges to representativeness, the AGSP has been able to show that a large proportion of the gonococcal infections contracted in larger cities is in homosexually active men where antibiotic resistant gonococci are observed, whilst gonococcal infections in rural settings are mostly transmitted heterosexually and gonococci are less antibiotic resistant.[11] To increase confidence in the inferences made about the patterns of resistance in specific sub-populations, some jurisdictions such as Western Australia attempt to integrate AMR data with clinical information. This includes anatomical site of infection (with rectal/pharyngeal gonorrhoea a surrogate for homosexual acquisition), overseas travel history and Indigenous status. The findings of these state health systems support the findings of the AGSP that gonococcal strains circulating in regional communities are less resistant than those circulating in metropolitan communities.

Timeliness

The timeliness of the national AGSP system is dependent not only on the efficiency of all the state and territory reference laboratories, but also on the timeliness of laboratories referring isolates for testing. Despite these constraints, the AGSP have continuously reported on a quarterly and annual basis in *CDI* within six months of the end of the reporting period. This is adequate for reporting on AMR trends.[2] Furthermore, the majority of stakeholders (78%) thought that the AGSP was a timely system.

Figure 2. Gonococcal isolates tested for antimicrobial resistance proportional to the annual notifications, 1995 to 2003



Acceptability

The acceptability of the system is high for the contributors to the system, where all reference laboratories have participated continually over the last 25 years. This is a very positive finding in the evaluation as it highlights the dedication of the individual laboratories to gonococcal AMR surveillance.

Ninety-two per cent of surveyed stakeholders believe that the AGSP contributes to the public health control of gonococcal infections. Of the 59 stakeholders responding to the evaluation survey, a large proportion used the AGSP data for patient treatment (n=30), treatment regimen change (n=28), outbreak detection and control (n=20), research (n=23) and disease prevention (n=17). The majority (83%) of stakeholders also noted that the outputs are well presented. Remarks made by the respondents included:

> 'I think the AGSP has functioned very well to date and has amassed a dataset that is the envy of the Western World because all contributors use a standard methodology to generate the data'.

On the other hand, users of the system noted the breakdown in the feedback of surveillance data as an issue:

> 'It would be nice to nominate a Public Health position in each region where the reports are routinely sent. It took me a year to get the first report and prior to that I would access the yearly reports from *CDI* which do not include as much details as I need' (State department public health officer).

This is currently a major concern in the surveillance activities of the AGSP. Even though report dissemination is timely for public health action, the evaluation found that some important public health stakeholders did not have access to the information. One potential mechanism of reaching this audience is through a website, where users of the system can access up-to-date reports, enhancing the accessibility and usefulness of the data. Forty-three (73%) respondents thought that a website would be a good idea. Respondents proposed that the website should contain the following information:

- network organisational chart and contact details of the reference laboratories;
- Public Health Laboratory Network case definition;
- protocols and surveillance data (e.g. local information on case clusters of disseminated gonococcal infections);
- mapping geographic distribution of AMR;
- risk factor data by geographic distribution (e.g. gender, sexual preference, travel, age, site of infection, Indigenous status);
- past reports and a general list of relevant articles, PowerPoint presentations produced by the reference laboratories and resources for medical students; and
- links to national and international websites relevant to the field.

The World Health Organization guidelines

The WHO's Questionnaire for Assessment of AMR National Networks was useful in evaluating the AGSP. The questionnaire recommended the collection of general information including population served by the network, years in operation and frequency of national data collation. However, the questionnaire did not provide quantitative or qualitative benchmarks to judge the adequacy of the network's activity levels on these attributes. One example was the question 'does the network receive regular and complete AMR data reports from all participating laboratories'? For this question, the evaluator does not have an estimate of acceptable levels of 'regular' and 'complete'.

The next section of the WHO questionnaire assessed quality control. This section was very useful for conducting the evaluation from a public health perspective as opposed to a laboratory perspective where it succinctly examined aspects of laboratory quality control that are relevant to AMR testing. Examples of this include whether the network has an external quality assurance program and whether the methodologies used at each laboratory enable comparability. For future evaluations of AMR systems, this section will be valuable for evaluators with little laboratory quality assurance knowledge.

The last section of the questionnaire considered the network's dissemination of information. Even though the questions were relevant, they were too general. For example, the question 'are the results of the AMR surveillance network regularly and effectively communicated to decision-makers in the Ministry of Health or other governing bodies?' needs clearer definitions of 'regular' and 'effective' to provide useful information.

Based on the current evaluation experience, it would have been useful if the questionnaire explored the integration of AMR networks with other public health surveillance systems or a national AMR strategy. Overall, until the questionnaire is expanded and benchmarks are provided to guide the assessment process, it is advisable to use the questionnaire in

conjunction with other tools such as WHO's surveillance standards for AMR or the CDC guidelines for the evaluation of surveillance systems.[2,6]

Conclusions and recommendations

The AGSP is a clearly defined laboratory based AMR surveillance system with stated objectives. It has been operating for many years using standardised methodologies including rigorous quality control components and has been meeting its goals. The system is connected with international programs such as the International Collaboration on Gonorrhoea and is regarded by many stakeholders as a model for good practice.

The strengths of the system are the quality of the methods used to generate the data, its high acceptability and its usefulness. The stakeholders currently utilise the outputs for a variety of purposes, including treatment of patients, control and research.

The major weaknesses of the system are the poor accessibility of the outputs to stakeholders and the technological challenges to its flexibility and representativeness. Information needs to be disseminated quickly and effectively to clinicians and public health practitioners in the states and territories to respond to the rapidly changing epidemiology of the disease. The increasing use of molecular methods for diagnosis may in time challenge the ability of the system to adequately monitor AMR and the ongoing representativeness of the system must be carefully monitored.

The problems identified by the evaluation would be improved by:

- reviewing the AGSP stakeholders in the states/territories and having points of contact within the health departments for communication of AGSP data; and
- establishing a website to enable ready access to AGSP data and information.

The dataset would undoubtedly be improved if state and territory health departments were able to enhance the dataset for gonococcal infections and to enable greater data linkage. This would be useful to allow reporting on the number of isolates by population density (rural/metropolitan) and age and gender and enable targeted health campaigns and to monitor gonococcal resistance in various subpopulations. However, these expanded objectives would increase the complexity of a currently simple and well functioning laboratory system which is currently meeting its remit under JETACAR recommendations for AMR surveillance.[3,4]

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References

1. Chin J, editor. *Control of Communicable Diseases Manual*. 7th edn. Washington: American Public Health Association; 2000.

2. World Health Organization. Surveillance standards for antimicrobial resistance. 2001. Available from: http://www.who.int/emc/pdfs/CDSsurveillance1.pdf Accessed on 14 July 2004.

3. Joint Expert Advisory Committee on Antibiotic Resistance (JETACAR). The use of antibiotics in food-producing animals: antibiotic-resistant bacteria in animals and humans. Canberra: Australian Department of Health and Ageing, Australian Department of Agriculture, Fisheries and Forestry, 1999.

4. Hundy R. Editorial: A strategy for the surveillance of antimicrobial resistance in Australia. *Commun Dis Intell* 2003;27:433–434.

5. World Health Organization. Antimicrobial Resistance Surveillance. Questionnaire for Assessment of National Networks. 2003. Available from: http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_RMD_2003_1/en/ Accessed on 14 July 2004.

6. Updated Guidelines for Evaluating Public Health Surveillance Systems. *MMWR CDC Surveill Summ* 2001;50.

7. Australian Gonococcal Surveillance Programme. Penicillin sensitivity of gonococci in Australia: the development of an Australian gonococcal surveillance programme. *Br J Vener Dis* 1984;60:226–230.

8. Tapsall JW. Use of a quality assurance scheme in a long-term multicentric study of antibiotic susceptibility of *Neisseria gonorrhoeae*. *Genitourin Med* 1990;66:8–13.

9. Health Communication Network. MIMS online. 2004. Available from: http://www.mims.hcn.net.au/ifmx-nsapi/mims-data/?MIval=2MIMS_ssearch Accessed on 4 March 2005.