CAPTURA Test practices and quality report

World Health Organization

WHO Test Laboratory

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Test practices and quality report

This report addresses the issue of "quality" from several perspectives. The analyses include a number of indicator metrics that be used to identify priority areas for improvement, to monitor improvement over time, and to compare results from different laboratories.

- Data entry and data management: Completeness and accuracy of data entry, antibiotic configuration, use of recommended WHONET codes
- Laboratory results: Organism identification, antimicrobial susceptibility test practices, quality control results

1. Data entry and management

1.1 Data volume

The below table and figure present the number of isolates records (including negative results) and the number of patients by laboratory over time. These results are also included in the Epidemiology Report.

Time period	2000
Data file	WHO-TST-2000-01.sqlite

From a data quality perspective, some of the main considerations include the below:

- Are there any results from outside of the expected date ranges? This may suggest an error in data entry.
- Are there time periods where there are number of records are lower or higher than expectations? This may suggest incomplete data entry or double data entry. Data entry practices may change over time. For example, some laboratories only enter positive results when they begin to use WHONET, but over time they may expand to include both positive and negative results.
- What is the average number of isolate records per patient? In low-resource settings, there are typically between 1.1 and 1.5 isolate records per patient on average. If the value is below this, it is possible that the laboratory does not have meaningful patient identification numbers that can be used to track patients over time. If the number is above this, there may be a problem in the data: 1) perhaps patient numbers are not unique, and they are used to represent different people over time; and 2) perhaps there is a mistake in data capture and BacLink configuration.

Laboratory	Number of isolates	Number of patients	Isolates per patient	2000
TST	622	277	2.2	277

Table 1: The table presents the distribution isolate records and patients over time.
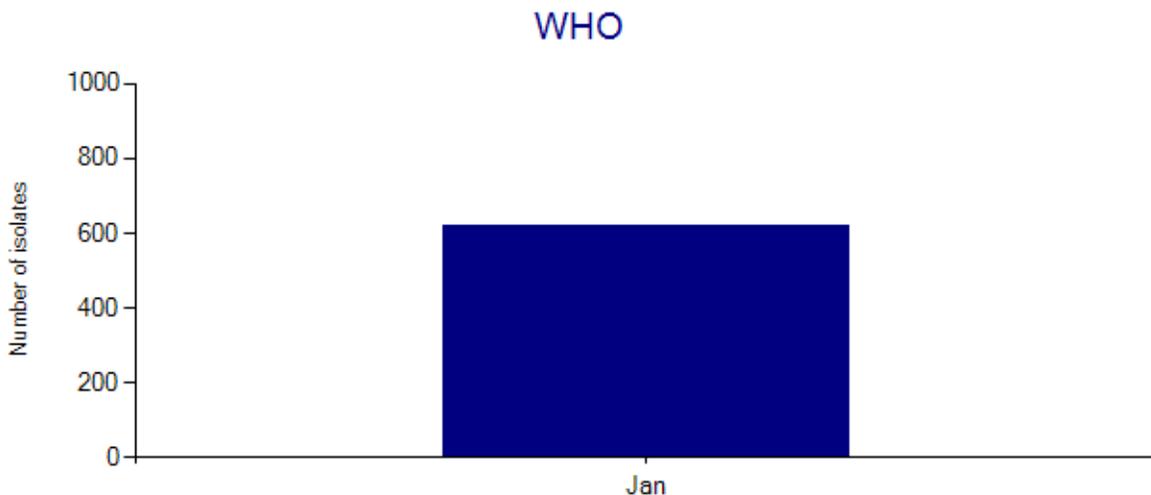

Figure 1: The distribution of isolates over time.

1.2 Completeness and validity of data entry

The below table presents statistics for the completeness of data entry for some high priority data fields. The table also presents statistics for the use of valid WHONET codes. WHONET users are not required to use WHONET codes, but it is recommended to facilitate data sharing and standardized public health reporting.

Data Field	% Completed	% Use of standard codes
Total	100%	99%
Age	100%	
Organism	100%	100%
Identification number	100%	
Sex	100%	100%
Specimen type (Numeric)	100%	96%
Specimen date	100%	
Location	100%	
Location type	100%	100%

Table 2: Data entry completeness and quality metrics

2. Quality control testing

The regular testing of standard quality control strains such as ATCC 25922 Escherichia coli and ATCC 25923 Staphylococcus aureus is highly recommended to ensure the reliability of test results. The user can enter the results of these standard strains into WHONET.

No quality control results found.

3. Organism results

A review of the organism results provides valuable insights into a laboratory's capacity for isolating and identifying organism.

- Does the laboratory identify organisms using general terms such as "Gram negative enteric organism" or can the laboratory identify organisms to the genus, species, subspecies, or serotype level such as "Klebsiella sp." or "Klebsiella pneumoniae"?
- Can the laboratory isolate fastidious organisms such as Haemophilus influenzae, Campylobacter sp., or anaerobic organisms?

3.1 Capacity for organism identification

There are many important microbes that are usually identified to the species level, for example Escherichia coli and Staphylococcus aureus. For other microbes, it depends on the resources, capacity, expertise, and practices of the laboratory, especially for laboratories using manual identification methods. The below table presents indicators of laboratory capacity for bacterial isolation and identification.

Organism	% Speciated
Enterococcus sp.	1 / 82 (1%)
Klebsiella sp.	35 / 35 (100%)
Pseudomonas sp.	37 / 38 (97%)
Overall	73 / 155 (47%)

Table 3: Level of organism identification for aerobic bacteria. Staphylococcus aureus and Escherichia coli have been excluded from the calculations because most laboratories routinely identify these organisms to the species level.

3.2 Capacity for the isolate of fastidious organisms

Some bacteria are difficult for laboratories to isolate or identify for several reasons.

- Organisms may not be viable when the specimen arrives in the laboratory
- Special medium required for the organism to grow
- Special incubation conditions
- Special reagents required for organism identification
- Advanced knowledge and experience required by laboratory staff

Examples include Haemophilus sp., Campylobacter sp., Helicobacter sp., Streptococcus pneumoniae, Neisseria sp., Mycobacteria sp., and anaerobic organisms.

The below table presents results for several fastidious organisms.

Organism	Number of isolates	(%)	Number of patients	Isolates per patient
Bordetella bronchiseptica	4	8	4	1
Moraxella (Branh.) catarrhalis	14	28	14	1
Haemophilus influenzae	24	48	24	1
Neisseria meningitidis	2	4	2	1
Streptococcus pneumoniae	6	12	6	1

Table 4: Results for fastidious organisms

3.3 Blood culture results

Blood cultures are an important for the diagnosis and management of many serious illnesses. Typically, the majority of blood cultures taken have no microbial growth. For blood cultures with microbial growth, many will represent true pathogens causing disease, such as Staphylococcus aureus. Unfortunately, blood cultures can also be contaminated at the time the sample is collected with skin commensal organisms or later in the laboratory. Common contaminants include Staphylococcus epidermidis and diphtheroids. It is important to remember that these commensal organisms can also cause severe disease, especially in vulnerable hospitalized patients.

The below table shows the distribution of findings among positive blood cultures.

Organism type	Organism	Number of isolates (%)	Number of patients	Isolates per patient
Aerobic Gram-positive bacteria	Enterococcus faecalis	1 (1.2%)	1	1
	Enterococcus sp.	2 (2.4%)	2	1
	Staphylococcus aureus	12 (14.1%)	11	1.1
	Staphylococcus, coagulase negative	41 (48.2%)	33	1.2
	Streptococcus pneumoniae	5 (5.9%)	5	1
	Streptococcus viridans, alpha-hem.	7 (8.2%)	6	1.2
Aerobic Gram-negative bacteria	Escherichia coli	7 (8.2%)	6	1.2
	Klebsiella pneumoniae	2 (2.4%)	2	1
	Proteus mirabilis	7 (8.2%)	4	1.8
Other results	Other	1 (1.2%)	1	1

Table 5: Distribution of organism types in positive blood cultures

4. Antimicrobial susceptibility test practices

Clinicians and public health authorities depend on microbiology laboratories to provide reliable antimicrobial susceptibility test results. To this end, laboratories must decide which antimicrobials to test for different organism groups and by which test method. For disk diffusion tests, the laboratory must also select an appropriate disk potency. These decisions should be based primarily in recommendations from CLSI or EUCAST guidelines.

It is important to explore two aspects of antimicrobial susceptibility test practices.

- Appropriateness of antimicrobial selected: Many laboratories test antimicrobials that have no validated CLSI or EUCAST breakpoints. For example, there are no breakpoints for cephradine and there are no breakpoints for imipenem and Staphylococcus aureus.
- Regularity of testing: Laboratories often test antimicrobials inconsistently for reasons such as stock outages of required disks or changes in purchases over time. There is often insufficient appreciation of the importance of consistent testing for clinical reporting and antimicrobial resistance surveillance.

4.1 Antibiotic Configuration

The below table displayed the antimicrobials defined in the WHONET laboratory configuration. Antimicrobials with no results in the data files analyzed are also indicated. If there are no plans to enter and analyze results from these antimicrobials, they could be removed from the laboratory configuration.

Guidelines	Test method	Number of antibiotics	Antibiotics
CLSI	Disk diffusion	47	Amikacin, Amoxicillin/Clavulanic acid, Ampicillin, Aztreonam, Carbenicillin, Cefamandole, Cefepime, Cefotaxime, Cefotaxime/Clavulanic acid, Cefoxitin, Ceftazidime, Ceftazidime/Clavulanic acid, Ceftiofur, Ceftizoxime, Ceftriaxone, Cefuroxime, Cephalothin, Chloramphenicol, Ciprofloxacin, Clindamycin, Doxycycline, Erythromycin, Gentamicin, Imipenem, Kanamycin, Meropenem, Mezlocillin, Minocycline, Nalidixic acid, Nitrofurantoin, Norfloxacin, Novobiocin, Ofloxacin, Oxacillin, Penicillin G, Piperacillin, Piperacillin/Tazobactam, Rifampin, Streptomycin, Sulfonamides, Teicoplanin, Tetracycline, Ticarcillin, Ticarcillin/Clavulanic acid, Tobramycin, Trimethoprim/Sulfamethoxazole, Vancomycin
CLSI	MIC	10	Cefotaxime, Ceftriaxone, Ciprofloxacin, Colistin, Erythromycin, Gentamicin, Nalidixic acid, Penicillin G, Tetracycline, Vancomycin
CLSI	Etest	3	Cefotaxime, Penicillin G, Vancomycin

Table 6: Antibiotics defined by the laboratory

4.2 Antibiotic tests without validated breakpoints

The following antibiotics have no breakpoints for any organism.

Cefotaxime/Clavulanic acid_CLSI_Disk_30/10µg, Ceftazidime/Clavulanic acid_CLSI_Disk_30/4µg, Novobiocin_CLSI_Disk_5µg

The following antibiotics were tested for Staphylococcus aureus and Escherichia coli, but they do not have breakpoints for these organisms.

Test method	Antibiotic	Number tested
Disk diffusion	Vancomycin	76

Table 7: Invalid tests performed for Staphylococcus aureus

No results found

Table 8: Invalid tests performed for Escherichia coli

The two most common reasons for invalid antibiotic tests include:

- The laboratory is testing incorrect antimicrobials (e.g. cephalexin), and they should be encouraged to switch to a similar antimicrobial with validated breakpoints (e.g. cephalothin).
- There is a mistake in the WHONET laboratory configuration, for example, choosing the wrong antimicrobial agent or choosing an incorrect disk potency. This would likely be the case above for SXT with a disk potency of 5.2μg TMP/240μg SMX. The correct potency is 1.25μg TMP/8.75μg SMX.

In both circumstances, corrective action is indicated. If there is a mistake in the WHONET or BacLink configuration, this should be corrected. If the laboratory is performing incorrect testing, then education and review of purchasing and test practices would be indicated.

There are a few circumstances in which antimicrobials without validated clinical breakpoints would not be considered to be a testing mistake.

- The laboratory may be aware of published acceptable vendor-specific breakpoints which have not been evaluated by CLSI or EUCAST. In these cases, the user should manually enter the vendor-specific breakpoints into WHONET.
- The antimicrobial is tested for reasons that do not require clinical breakpoints, for example novobiocin or optochin are used for species identification, while ceftriaxone/clavulanic acid is used for ESBL confirmation.
- The laboratory may test an appropriate antibiotic, such as cefoxitin with Staphylococcus aureus, to predict the findings of another antibiotic that may be used in clinical therapy, such as methicillin or nafcillin. This has been described as proxy testing or surrogate testing.
- The laboratory is working collaboratively with CLSI or EUCAST to develop new breakpoints.
- The laboratory may not have sufficient resources to perform MIC testing when it is recommended, so the disk diffusion method is used instead to screen for resistance, for example Staphylococcus aureus and the vancomycin disk test. However, such results should not be considered reliable.

4.3 Regularity of antimicrobial testing

The below figure displays the number of isolates tested for each antimicrobial against Staphylococcus aureus and Escherichia coli. The figure permits the reader to see which antimicrobials are tested as well as the frequency of testing.
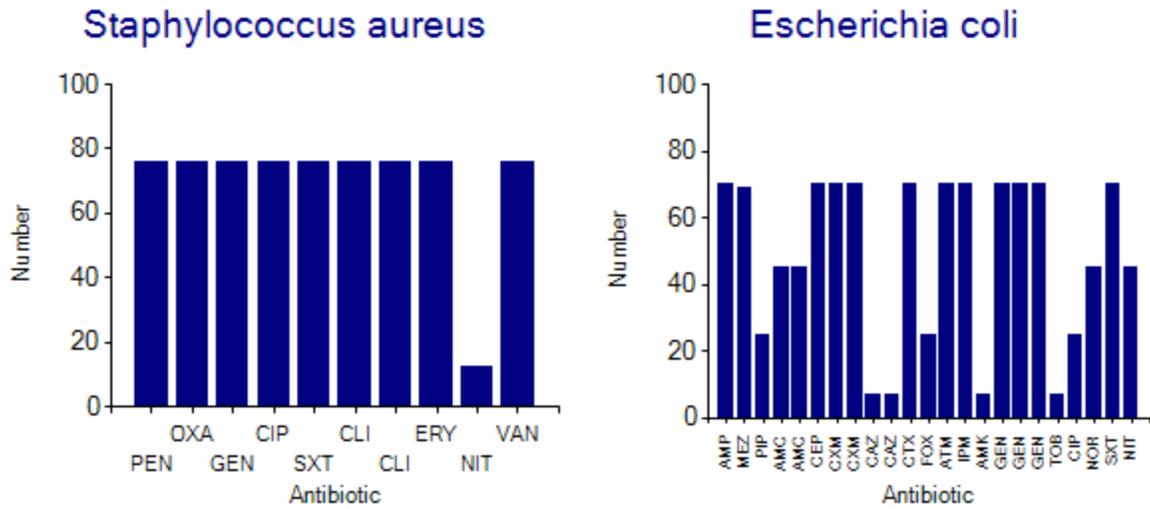
Figure 2: Frequency of antibiotic testing for Staphylococcus aureus and Escherichia coli

Organism	Number of antibiotics	Core antibiotics	Number of isolates tested against all antimicrobials (%)
Staphylococcus aureus	7	Penicillin G, Erythromycin, Clindamycin, Oxacillin, Gentamicin, Trimethoprim/Sulfamethoxazole, Ciprofloxacin	86/86 (100%)
Escherichia coli	9	Cephalothin, Ampicillin, Gentamicin, Trimethoprim/Sulfamethoxazole, Cefotaxime, Imipenem, Cefuroxime, Mezlocillin, Aztreonam	84/86 (98%)

4.4 Antimicrobial susceptibility test measurements

There is great value in measuring, recording, and analyzing antimicrobial susceptibility test measurements, such as the disk diffusion zone diameter and the MIC value.

- Necessary to provide the correct test interpretation to the clinician
- Necessary to compare old results with new results if the breakpoints change
- More detailed characterization of resistance mechanisms associated with high, moderate, and low levels of resistance.
- Improved strain tracking
- Assessment of the quality of laboratory test reagents and the quality of laboratory test performance

	Disk diffusion
Quantitative results	4,918
Number of test results	4,918
% Quantitative	100%

Table 9: Number of tested results and the percentage of results with quantitative test results such as disk diffusion zone diameters or MIC results

5. Quality control alerts

WHONET offers a number of quality control alerts to facilitate the recognition of possible deficiencies in test performance. It is important to note that a quality control alert does not necessarily indicate that a result is incorrect, but repeat testing and confirmation are often warranted.

WHONET addresses four types of quality control alert.

- Intrinsic resistance: The organism is lacking a resistance characteristic typical of the species, for example Klebsiella pneumoniae susceptible to ampicillin
- Discordant test results: In some cases, the results are biologically implausible, such as an Escherichia coli susceptible to ampicillin but resistant to ampicillin/sulbactam. In other cases, the results may be correct, but are relatively rare. For example, most isolates of Escherichia coli resistant to amikacin will also be resistant to gentamicin. However, in South America, there are many isolates have been confirmed to be amikacin resistant but gentamicin susceptible.
- Rare resistance: Resistance to some antimicrobials is extremely rare for some species, and may suggest an error in the organism identification or in the antimicrobial susceptibility test result, such as Staphylococcus aureus resistant to vancomycin.
- Incorrect test method: There are some organisms and some organism-antibiotic combinations that should not be tested by certain test methods. For example, Neisseria meningitidis should always be tested by the MIC method. Staphylococcus aureus should not be tested with the oxacillin or vancomycin disk, and Streptococcus pneumoniae should not be tested by the oxacillin disk.

Organisms	Alert	Number of isolates	Priority	TST
Acinetobacter baumannii	Penicillins or Cephalosporin I or Cephamycins = Susceptible	4	Low priority	4
All organisms	Penicillins and Beta-lactam+Inhibitor = Discordant results	12	Medium priority	12
All organisms	Penicillins = Discordant results	1	Medium priority	1
Citrobacter sp.	Cephalosporin III = Susceptible	4	Low priority	4
Citrobacter sp.	Penicillins or Cephalosporin I or Cephalosporin II or Cephamycins = Susceptible	4	Low priority	4
Enterobacter sp.	Cephalosporin III = Susceptible	5	Low priority	5
Enterobacter sp.	Penicillins or Cephalosporin I or Cephalosporin II or Cephamycins = Susceptible	9	Low priority	9
Enterobacteriaceae	Cephems = Discordant results	6	Medium priority	6
Klebsiella sp.	Penicillins = Susceptible	25	Low priority	25
Moraxella (B.) catarrhalis	Ciprofloxacin = Susceptible	14	Low priority	14
Morganella sp.	Penicillins or Cephalosporin I or Cephalosporin II = Susceptible	14	Low priority	14
Neisseria meningitidis	Antibiotic = Tested by disk diffusion	2	Low priority	2
Providencia sp.	Penicillins or Cephalosporin I or Cephalosporin II = Susceptible	1	Low priority	1
Pseudomonas aeruginosa	Aminoglycosides = Discordant results	1	Medium priority	1
Pseudomonas aeruginosa	Penicillins or Cephems = Susceptible	31	Low priority	31
Pseudomonas aeruginosa	Trimethoprim/Sulfamethoxazole = Susceptible	2	Low priority	2
Serratia sp.	Cephalosporin III = Susceptible	6	Low priority	6
Serratia sp.	Penicillins or Cephalosporin I or Cephalosporin II or Cephamycins = Susceptible	11	Low priority	11
Stenotrophomonas maltophilia	Aminoglycosides = Susceptible	7	Low priority	7
Stenotrophomonas maltophilia	Penicillins or Cephems = Susceptible	3	Low priority	3
Streptococcus pneumoniae	Beta-lactams = Tested by disk diffusion	2	Medium priority	2
Streptococcus viridans	Penicillin or Ampicillin = Tested by disk diffusion	18	Low priority	18

Table 10: Quality control alerts for unlikely and infrequent findings. The results are stratified by laboratory to facilitate feedback to laboratories on possible issues in the reliability of test results.