One Health – One Method of Antimicrobial Susceptibility Testing

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Antimicrobial resistance is a globally recognized issue; therefore, efforts to combat this problem have been initiated by international organizations such as the World Health Organization (WHO), the Office International des Epizooties (OIE) as well as national antibiotic action plans in the United States, the European Union, and other countries. Many associations, stakeholders and professional societies have made commitments to fulfilling various components of these plans to combat antimicrobial resistance.

One of the fundamental technical aspects in these initiatives begins in the clinical microbiology laboratory with antimicrobial susceptibility testing (AST). Laboratories that identify and test bacterial isolates for susceptibility to antimicrobial agents report the results that are used by epidemiologists, veterinarians, physicians, and research scientists, and other stakeholders, for many purposes. Clinicians use the data for treatment decisions, epidemiologists evaluate the data for trends in resistance prevalence, and researchers use the data for advancing new innovations to mitigate resistance.

Standardized antimicrobial susceptibility (AST) testing methods are used to generate minimal inhibitory concentration (MIC) data or zone of (growth) inhibition data. The MIC or "zone size" data is "translated" at specific "breakpoints" into the categories of Susceptible, Intermediate or Resistant. These categories provide guidance to clinicians (physicians or veterinarians) to assist in antibiotic treatment decisions as a component of Responsible Use guidelines.

From a research viewpoint, an MIC frequency histogram is compiled from the cumulative results of tests over time, geography or other parameters so that epidemiologists and monitoring program researchers can ascertain the presence of wild-type populations (isolates with low MICs) vs. non-wild type (higher MIC isolates) populations.

Moreover, regulatory agencies may recommend standardized AST methods within guidance documents to ensure validity and comparability for test data. Researchers may use AST methods to evaluation of new agents compared to existing agents.

The U.S. National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB) calls for validated methods to document antimicrobial resistance in order to "… facilitate identification and implementation of interventions to reduce the spread of antibiotic-resistance." The OIE Terrestrial Manual (2013) [2], the WHO Action Plan [3], the National Antimicrobial Resistance Monitoring System (NARMS) [4], the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) [5], and Judicious Therapeutic Use Guidelines generated by veterinary and human medical professional societies and organizations have all identified the need for standardized methodology for antimicrobial susceptibility testing.

The Clinical and Laboratory Standards Institute (CLSI), an international standards organization, has produced through its internationally constituted volunteer subcommittees specific technical standards documents for human and animal pathogen AST that provide reproducible and validated methods that allow for global implementation which can address the need for harmonized AST methodology[6,7]. Simply put, while is possible to make local therapeutic decisions that rely on determining "resistant" or "susceptible", it is very difficult to perform national-scale resistance monitoring and surveillance that allows trans-national comparisons unless an approved AST standard method is used that is globally implemented.

The CLSI is the only organization in the world that provides testing methods and interpretive categories for both animal and human pathogens. The value of CLSI standards is that they have been in use for many decades, are continually updated, aligned with the International Standards Organization and have been integrated into many AMR surveillance programs, clinical diagnostic laboratories, and regulatory guidelines; therefore, they offer a "one method" approach that will enable global harmonization. The benefits of globally uniform and standardized antimicrobial susceptibility testing methods include:

- Harmonization and alignment across diagnostic, research and reference laboratories, countries and time to ensure comparability of MIC data.
- Quality-controlled data for pathogens, zoonotic and commensal bacteria, regardless of the species of origin, for the major classes of antibiotics.
- The use of breakpoints and interpretive categories is intimately connected to the AST method used, so it is not appropriate to use an AST method that is different than the one used to set the interpretive category or to apply a breakpoint using a different method. Interpretation of MIC frequency histograms is a fundamental data presentation that cannot be achieved unless the data comes from laboratories that all use the same standardized method. The CLSI Interpretive Categories are now available online at:
    - Animal Pathogen Tables: http://vet01s.edaptivedocs.com/Login.aspx
    - Human Pathogen Tables: http://clsi.org/m100/
- Accurate antimicrobial susceptibility test results and interpretive categories provide veterinarians and physicians with information upon which to make appropriate antibiotic treatment decisions further ensuring responsible and judicious use of antimicrobial agents.

In conclusion, within the spirit of One Health, a One Method approach provides a means to ensure that antimicrobial susceptibility testing methods are aligned and uniformly applied on an international basis to facilitate information exchange, provide comparability across boundaries and time, and minimize confounding of data that may be generated by other means.

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References

1. Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria. National action plan for combating antibiotic-resistant bacteria. 2014.

https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf

2. OIE Terrestrial Manual. http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/

3. WHO Global Action Plan on Antimicrobial Resistance. 2015. http://www.who.int/drugresistance/global_action_plan/en/

4. National Antimicrobial Resistance Monitoring System. http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/default.htm

5. Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS). Public Health Agency of Canada. http://www.phac-aspc.gc.ca/cipars-picra/index-eng.php

6. CLSI documents: http://shop.clsi.org/veterinary-medicine-documents/

7. CLSI documents: http://shop.clsi.org/microbiology-documents/