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Antimicrobial Testing Leadership and Surveillance

ATLAS: Fully-searchable Global Antibiotic Resistance Database to Fight AMR

Michael J. Dowzicky, MSc, MT ASCP
Senior Scientific Director, Hospital Business Unit

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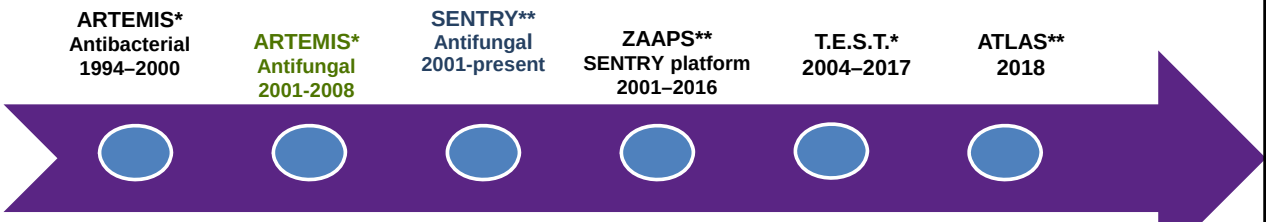
History of Pfizer-sponsored surveillance programs



- Unasyn
- Zithromax
- Trovan
- Diflucan
- Vfend
- Diflucan
- Vfend
- Eraxis
- Zyvox
- Tygacil added in 2011
- Tygacil
- Zosyn
- Caz/Avi
- Zinforo
- AZT/Avi

- *Susceptibility testing performed by participating sites
- ** Susceptibility testing performed by a central laboratory

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Pfizer's ATLAS Surveillance Database
A Key Tool in the Fight Against AMR

Antimicrobial Testing Leadership and Surveillance

What is it: The Antimicrobial Testing Leadership and Surveillance (ATLAS) database, which now represents the integration of three surveillance programs (TEST, AWARE, INFORM), is offered as a fully searchable, interactive, user-friendly website and as a mobile application enabling rapid access – by anyone – to critical resistance information[1,2]

Objective: Enable physicians to determine the appropriate antibiotic therapy and to inform AMS practices while partnering with them to advance publication of regionally and locally relevant ATLAS data. This will help to strengthen our positioning as the holistic solutions provider

ATLAS Features: Global Website and App

- Antimicrobial susceptibility geographic heat maps
- Data filterable by year, country, pathogens & antimicrobials
- Configurable MIC frequency distribution analyses
- Interactive tables, line plots and bar charts (2D and 3D)
- Export data to Excel

What Has ATLAS Done So Far?

ATLAS by the Numbers

- **15** Year of cumulative data
- From more than **73** countries
- Updated every **6–8** Months
- Over **750** Congress presentations
- Includes source information from more than **780** sites
- Over **600,000** Isolates tested (pure strain of microbe separated from a mixed population of microbe)
- Over **55** Peer-reviewed publications **based on data**

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References: 1 Pfizer. Pfizer unveils ATLAS, an interactive, user-friendly website that provides global antibiotic resistance surveillance data across 60 countries. April 21 2017. Available at: http://www.pfizer.com/news/press-release/press-release-detail/pfizer_unveils_atlas_an_interactive_user_friendly_website_that_provides_global_antibiotic_resistance_surveillance_data_across_60_countries. Last accessed August 2018. 2 Pfizer. Antimicrobial Testing Leadership and Surveillance. Available at: https://atlas-surveillance.com/ Last accessed August 2018.

ATLAS in the Mainstream

Antimicrobial Testing Leadership and Surveillance

- "Surveillance of resistance patterns is crucial for clinicians and public health officials in assessing both the nature and scope of emerging resistance locally and nationally. ATLAS is the only database of its kind capable of providing such a broad scope of reliable, readily available information in an easy-to-use platform."

  KOL- Infectious Disease

- "We have wonderful surveillance data i.e. [ATLAS], this is an opportunity to turn this data into knowledge."

  KOL- Microbiology

- "You are 100% on the right track. This could become a powerful tool to help local understanding of the time to make changes in prescribing and improve stewardship."

  KOL- Infectious Disease

- "[ATLAS] stands out among all AMR surveillance programmes identified by the Benchmark, as it is completely accessible to the public."

  ATM report

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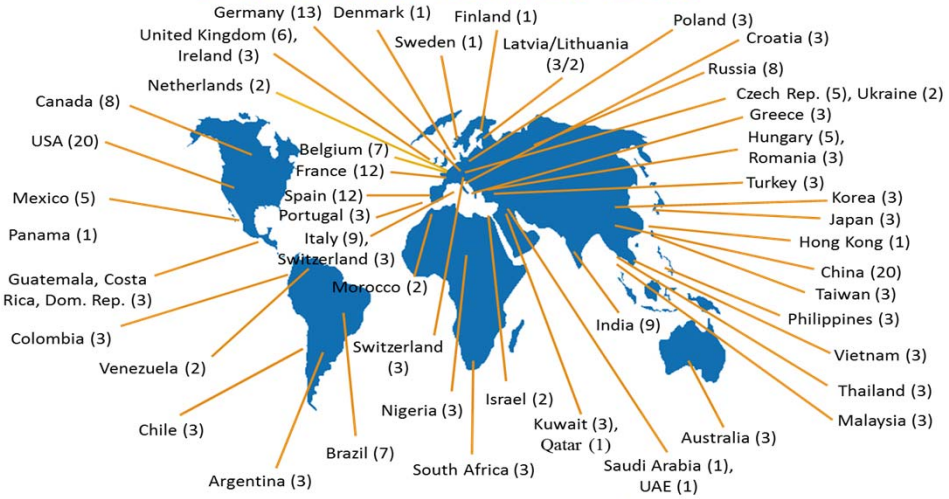
ATLAS Study: 241 Global Centers 2019[a]



[a] PROJECTED for 2019- subject to change

Source: www.atlas-surveillance.com

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ATLAS 2019 Scope

- Global cumulative data for 2019 from 241 sites yielding 50,172 unique bacterial strains

– Gram Positives
- 2260 *Streptococcus pneumoniae*
- 2260 Other Beta-Hemolytic *Streptococci*
- 6780 *Staphylococcus aureus*
- 1130 *Staphylococcus epidermidis*
- 1130 *Staphylococcus haemolyticus*
- *2260 Enterococcus faecalis*
- 1130 *Enterococcus faecium*

– Gram Negatives
- 3390 *Acinetobacter* spp.
- 5650 *Pseudomonas aeruginosa*
- 1130 *Citrobacter* spp.
- 5650 *Escherichia coli*
- 7910 *Klebsiella* spp.
- 2260 *Enterobacter* spp.
- 678 *Proteus vulgaris*
- 678 *Proteus mirabilis*
- 1130 *Serratia marcescens*
- 678 *Morganella morganii*
- 678 *Providencia* spp.

– Fastidious
- 1130 *Moraxella catarrhalis*
- 2260 *Haemophilus influenzae*

– Anaerobes
- 150 *Clostridium* spp.
- 150 *Peptostreptococcus* spp.
- 150 *Bacteroides fragilis* group
- 150 *Prevotella* spp.

Source: 2019 ATLAS protocol; Data on file

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ATLAS 2019 Scope

- Target Pathogens by testing site

- Gram-positive Pathogens - 75 isolates
  - 10 *Streptococcus pneumoniae*
  - 10 Other Beta-Hemolytic *Streptococci*
  - 30 *Staphylococcus aureus*
  - 5 *Staphylococcus epidermidis*
  - 5 *Staphylococcus haemolyticus*
  - 10 *Enterococcus faecalis*
  - 5 *Enterococcus faecium*
  - 5 *Moraxella catarrhalis*
- Gram-negative Pathogens - 132 isolates total
  - 10 *Haemophilus influenzae*
  - 15 *Acinetobacter* spp.
  - 25 *Pseudomonas aeruginosa*
  - 5 *Citrobacter* spp.
  - 25 *Escherichia coli*
  - 35 *Klebsiella* spp.
  - 10 *Enterobacter* spp.
  - 3 *Proteus vulgaris*
  - 3 *Proteus mirabilis*
  - 5 *Serratia marcescens*
  - 3 *Morganella Morganii*
  - 3 *Providencia* spp.
- Fastidious Pathogens – 15 isolates total
  - 10 *Haemophilus influenzae*
  - 5 *Moraxella catarrhalis*
- Anaerobe Pathogens – 40 isolates total
  - Applicable to 15 sites located in Belgium, Czech Republic, France, Germany, Hungary, and Spain ONLY
  - 10 *Clostridium* spp.
  - 10 *Peptostreptococcus* spp.
  - 10 *Bacteroides fragilis* group
  - 10 *Prevotella* spp.

Source: 2019 ATLAS protocol; Data on file

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ATLAS 2019 Scope

- Acceptable Sources
  - Urinary Tract Infection (UTI)
  - Intra-abdominal Infection (IAI)
  - Blood
  - Skin and Skin Structure Infection (SSSI)
  - Lower Respiratory Tract Infection (LRTI)

Source: 2019 ATLAS protocol; Data on file

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ATLAS 2019 Scope

- Collection Criteria

Inclusion Criteria

- Clinically relevant causative isolate - The isolate must meet the laboratory criteria of "significant pathogen" and be considered the "probable causative agent" of a hospital or community acquired infection.
- Isolates collected on or after December 1, 2018.
- Sources - All body sites are acceptable clinical sources for isolates to be included in this study. However, no more than 25% of all isolates can come from urine cultures.
- Within study group - Only isolates defined by protocol are to be included.

Source: 2019 ATLAS protocol; Data on file

ATLAS 2019 Scope

- Collection Criteria (Cont.)

Exclusion Criteria

- Limited isolates from sources - No more than 25% of all isolates from this study will be derived from urine cultures.
- No banked or stored isolates - Isolates collected prior to December 1, 2018 will not be accepted.
- **No duplicate isolates** - Only one isolate per patient is permitted.
- Outside study group - Any isolate other than those defined by protocol.

Source: 2019 ATLAS protocol; Data on file

ATLAS 2019 Scope

- Success Criteria for Site Participation
  - Local microbiology laboratories
    - Quickly respond to study invite and return enrollment forms as soon as possible.
      - Number of sites allocated in each country decided by Global Medical and Global Commercial Leads interactions.
      - Sites selected by interaction with Regional and local medical/commercial colleagues
    - Adhere to study timelines – all study isolates collected and shipped to the central laboratory by January 31 of the subsequent year.
    - Collect all 222 aerobic bacterial isolates as defined by the study protocol or all 40 anaerobic bacterial isolates as defined by study protocol
    - Record required demographic data on IHMA supplied Organism Report Forms (ORFs)

Source: 2019 ATLAS protocol; Data on file

ATLAS 2019 Scope

- Success Criteria for Site Participation (Cont.)
  - Local microbiology laboratories
    - Ship bacterial isolates and ORFs to central laboratory within the defined shipping dates.
    - Store a copy of study isolates until testing for each year is complete and annual participation is closed
    - Actively participate in publication opportunities
    - Access and utilize the ATLAS website and data analytics tool

Source: 2019 ATLAS protocol; Data on file

ATLAS 2019 Testing

- Centralized Laboratory Testing
  - Study isolates are tested at IHMA's central laboratory in Chicago IL, USA
    - India and China are the exceptions – government regulations prohibit the export of bacterial isolates
      - Local Central Laboratories test all isolates respective of each country

Source: 2019 ATLAS protocol; Data on file

ATLAS 2019 Testing (Cont.)

- Benefits of Centralized Laboratory Testing
  - Enhances integrity of data through more standardized susceptibility testing
    - Limits the number of individuals reading MICs
    - Allows for consistency of data generation in a global study
    - Generally viewed as the preferred method for surveillance studies
      - Minimizes concerns of publication reviewers around data integrity
  - Central location of all isolates
    - All isolates are stored and collected at Central lab and we "own" the rights to all of them.
    - Allows for further testing and analysis as needed – particularly molecular characterization

Source: 2019 ATLAS protocol; Data on file

ATLAS 2019 Testing

Antimicrobials Tested by Broth Microdilution
Gram-negative Bacteria – 2 panels per isolate

- Amikacin
- Amoxicillin/clavulanic acid
- Ampicillin
- Aztreonam
- Aztreonam/avibactam
- Cefepime
- Cefoperazone/sulbactam
- Ceftaroline
- Ceftazidime
- Ceftazidime/avibactam
- Ciprofloxacin
- Colistin
- Gentamicin
- Imipenem
- Levofloxacin
- Meropenem
- Piperacillin/tazobactam
- Tigecycline
- Trimethyl/Sulfa

Source: 2019 ATLAS protocol; Data on file

ATLAS 2019 Testing

Antimicrobials Tested by Broth Microdilution
Haemophilus Bacteria – 1 panel per isolate

- Amoxicillin/clavulanic acid
- Ampicillin/sulbactam
- Ampicillin
- Azithromycin
- Ceftaroline
- Ceftazidime
- Ceftazidime/avibactam
- Ceftriaxone
- Levofloxacin
- Meropenem
- Piperacillin/tazobactam
- Tigecycline

Source: 2019 ATLAS protocol; Data on file

ATLAS 2019 Testing

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Antimicrobials Tested by Broth Microdilution
Staphylococcus, Enterococci and Moraxella Bacteria – 1 panel per isolate

- Ampicillin/sulbactam
- Ampicillin
- Ceftaroline
- Clindamycin
- Daptomycin
- Erythromycin
- Gentamicin
- Levofloxacin
- Linezolid
- Oxacillin
- Teicoplanin
- Tigecycline
- Trimethyl/Sulfa
- Vancomycin

Source: 2019 ATLAS protocol; Data on file

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ATLAS 2019 Testing

Antimicrobial Testing Leadership and Surveillance

Antimicrobials Tested by Broth Microdilution
Streptococcus Bacteria – 1 panel per isolate

- Ampicillin/sulbactam
- Cefoperazone/sulbactam
- Ceftaroline
- Ceftriaxone
- Clindamycin
- Erythromycin
- Levofloxacin
- Linezolid
- Meropenem
- Penicillin
- Piperacillin/tazobactam
- Teicoplanin
- Tigecycline
- Vancomycin

Source: 2019 ATLAS protocol; Data on file

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ATLAS 2019 Molecular Testing

- Selected *Enterobacteriaceae* and *Pseudomonas aeruginosa* tested by multiplex PCR at Central Lab
- Meropenem non-susceptible *P. aeruginosa* isolates and *Enterobacteriaceae* (specifically *Escherichia coli, Klebsiella pneumoniae, K. oxytoca,* and *Proteus mirabilis*) that are ESBL-screen
- Approximately 30% of the *P. aeruginosa* and 80% of the ESBL+ *Enterobacteriaceae* isolates falling into the two categories above will be characterized, "randomly" selected but also ensure that each site participating in Atlas will have similar percentages of their strains meeting the criteria characterized.
- Estimated at ~1,500 *P. aeruginosa* and ~3,025 *Enterobacteriaceae*

Source: 2019 ATLAS molecular protocol; Data on file

ATLAS 2019 Molecular Testing (Cont.)

- Testing will cover the genes specified below for the species shown:
  - *P. aeruginosa*: TEM, SHV, VEB, PER, GES OXA-24 group, KPC, NDM, IMP, VIM, GIM, SPM
  - *Enterobacteriaceae*: TEM, SHV, CTX-M-1/2/8/9/25 groups, VEB, PER, GES, OXA-48 group, plasmid-encoded AmpC (ACC, ACT, CMY, DHA, FOX, MIR, MOX), KPC, NDM, IMP, VIM, GIM, and SPM.
  - All detected genes, excluding bla_{SHV} and bla_{TEM} that do not encode ESBLs, are amplified and sequenced in their entirety.

Source: 2019 ATLAS molecular protocol; Data on file

ATLAS Antimicrobial Testing Leadership Surveillance External Web Site

- Pfizer's ATLAS website is a core & comprehensive resource for Pfizer anti-infectives
- Aim: To provide up-to-date antimicrobial resistance data to enable medical professionals to better understand regional or local resistance patters to help the fight against antimicrobial resistance
- The ATLAS website includes:
  - The long-standing searchable database, providing MIC and susceptibility data on various organisms against a panel of commonly used antimicrobials
    - Data from additional surveillance studies which were added during 2018
    - www.atlas-surveillance.com

ATLAS App: The Future of Bedside Patient Management

- A mobile ATLAS App showing geographical heat maps of antimicrobial resistance is currently under enhancement and was released December 2017
- The App provides physicians with the option of bedside evaluation of resistance trends Globally, Regionally or locally.
- The App was introduced to physicians at ECCMID 2017 (April, Vienna, Austria)