Antibacterial Resistance Leadership Group 2.0: Back to Business

Henry F. Chambers,1 Scott R. Evans2, Robin Patel3, Heather R. Cross,4 Anthony D. Harris,5 Yohei Doi,5,7 Helen W. Boucher,3 David van Duin,5,6 Ephraim L. Tsai,5,10 Thomas L. Holland,9,10 Melinda M. Pettigrew,5,6 Pranittra B. Tamma,5,6,8 Kathryn R. Hodges,4 Maria Souli,11 and Vance G. Fowler, Jr.4,11

1Division of HIV, Infectious Diseases, and Global Medicine, Department of Medicine, Zuckerberg San Francisco General Hospital, University of California, San Francisco, California, USA; 2Biostatistics Center, Department of Biostatistics and Bioinformatics, Milken Institute School of Public Health, George Washington University, Washington, D.C., USA; 3Department of Clinical Microbiology, Department of Laboratory Medicine and Pathology, Division of Infectious Diseases, Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA; 4Department of Epidemiology and Public Health University of Maryland School of Medicine; Baltimore, Maryland, USA; 5Division of Infectious Diseases, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA; 6Division of Geographic Medicine and Infectious Diseases, Tufts Medical Center, Boston, Massachusetts, USA; 7Division of Infectious Diseases, Department of Medicine, University of North Carolina, Chapel Hill, North Carolina, USA; 8Department of Medicine, Duke University Medical Center, Durham, North Carolina, USA; 9Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, Connecticut, USA; and 10Division of Infectious Diseases, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

In December 2019, the Antibacterial Resistance Leadership Group (ARLG) was awarded funding for another 7-year cycle to support a clinical research network on antibacterial resistance. ARLG 2.0 has 3 overarching research priorities: infections caused by antibiotic-resistant (AR) gram-negative bacteria, infections caused by AR gram-positive bacteria, and diagnostic tests to optimize use of antibiotics. To support the next generation of AR researchers, the ARLG offers 3 mentoring opportunities: the ARLG Fellowship, Early Stage Investigator seed grants, and the Trialists in Training Program. The purpose of this article is to update the scientific community on the progress made in the original funding period and to encourage submission of clinical research that addresses 1 or more of the research priority areas of ARLG 2.0.

Keywords. Antibacterial Resistance Leadership Group; clinical research; mentoring.
study led to the practice-changing observation that all-cause mortality and global outcomes were significantly better with ceftazidime-avibactam compared with colistin-based regimens [8]. Experience gained with CRACKLE led to the creation of the Multi-Drug Resistant Organism (MDRO) Network, an international research network to conduct observational studies in hospitalized patients with MDR bacteria. More than 6400 patients with CRE, carbapenem-resistant *Pseudomonas aeruginosa*, or carbapenem-resistant *Acinetobacter baumannii* complex from more than 80 hospitals in 11 countries on 4 continents have been enrolled to date. The ARLG’s global initiatives have been further advanced through a formal collaboration with its European counterpart, COMBACTE. Europe’s largest clinical and laboratory research network, COMBACTE will soon transit into the European Clinical Research Alliance on Infectious Diseases.

The ARLG also conducted several diagnostic studies. MASTERMIND (MASTER protocol for Evaluating Multiple INfection Diagnostics) studies use an innovative trial design that allows evaluation and comparison of multiple diagnostic tests on biological samples from a single patient. This strategy simultaneously supports US Food and Drug Administration (FDA) approval/clearance of multiple new diagnostic tests, including from different companies, in a single clinical trial [9]. The first MASTERMIND study, MASTER-GC, evaluated the performance of multiple diagnostic assays to detect extragenital infection with *Neisseria gonorrhoeae* or *Chlamydia trachomatis* in more than 2500 study participants [10,11]. The data generated from this trial supported FDA approval of 2 diagnostic assays [12].

The challenge in differentiating bacterial from viral etiologies of respiratory tract infection drives a significant amount of inappropriate antibacterial use. Based on observations that bacterial and viral infections induce distinct immunological responses [13], RADICAL (Rapid Diagnostics in Categorizing Acute Lung Infection) study investigators discovered host gene expression signatures that can discriminate between bacterial and viral infections [14]. This approach was validated in 623 emergency department patients with acute respiratory illness (viral infection AUC, 0.92; bacterial infection AUC, 0.90). The work is moving into clinical and analytical validation to support regulatory clearance.

The ARLG performed 2 studies to evaluate the clinical impact of rapid diagnostics on the management and outcome of patients with positive blood cultures. BCID (Blood Culture IDENTification) assessed a rapid multiplex polymerase chain reaction panel in patients with positive blood cultures. Use of the rapid diagnostic platform was associated with reduced treatment of blood culture contaminants, reduced use of broad-spectrum antibiotics, and enhanced antimicrobial deescalation when combined with active stewardship initiatives [15]. A subsequent study, RAPIDS-GN (RAPid IDENTification and Susceptibility testing for Gram Negative bacteremia), assessed rapid phenotypic susceptibility testing for patients with gram-negative...
bacilli (GNB) in blood cultures. RAPIDS-GN showed that rapid organism identification alongside rapid phenotypic susceptibility testing directly from positive blood cultures led to more appropriate antibiotic therapy for gram-negative bacteraemia [16].

Standard Course Outpatient Therapy of Community Acquired Pneumonia in Children (SCOUT-CAP) was a randomized, double-blind, placebo-controlled, superiority trial that compared 5 days to 10 days of β-lactam antibiotic therapy for outpatient community-acquired pneumonia in children. This trial, conducted in partnership with the National Institute of Allergy and Infectious Diseases Vaccine and Treatment Evaluation Units, used an innovative design [17] pioneered by the ARLG in which desirability of outcome ranking (DOOR) was the primary outcome. The global experience of each child was ranked into an ordinal clinical response (OCR) that combined response to treatment and antibiotic adverse effects 11–15 days after the start of therapy. For those patients with equivalent OCR, documented days of antibiotics was used to further rank outcome with the assumption that shorter antibiotic exposure was more desirable. In an intention-to-treat analysis, children who received a 5-day therapy course had a higher probability of a more desirable clinical outcome than those who received 10-day therapy (probability, 69%; 95% confidence interval, 63–72; P < .001) [18].

ARLG 2.0 Organizational Structure
ARLG 2.0 consists of 4 closely interactive centers to advance its scientific mission (Figure 2): the Scientific Leadership Center (SLC), the Clinical Operations Center (COC), the Statistical and Data Management Center (SDMC), and the Laboratory Center (LC). The SLC is responsible for the overall administrative and scientific leadership of the ARLG by ensuring effective governance, prioritization of the research agenda, collaboration with external stakeholders, and effectiveness of the ARLG’s robust mentoring and training portfolio. The COC provides operational support, management, and oversight for the network’s clinical studies and trials, including protocol development, site selection, and study execution. The LC leads the development, implementation, and evaluation of the laboratory and diagnostic aspects of the ARLG research agenda. The SDMC collaborates in all stages of the ARLG research [19], including study design, execution, analysis, and interpretation. It also contributes innovative statistical methods and ensures integrity of study design.

Figure 2. Organization of ARLG. Abbreviations: ARLG, Antibacterial Resistance Leadership Group; PI, primary investigator; U, university; UCLA, University of California–Los Angeles; UCSF, University of California–San Francisco; UNC, University of North Carolina.
ARLG 2.0 Scientific Priorities

ARLG 2.0 has 3 overarching research priorities: infections caused by MDR gram-negative bacteria, infections caused by MDR gram-positive bacteria, and diagnostic tests to optimize use of antibiotics. To ensure this prioritization was aligned with the expectations of the scientific community, the ARLG conducted a survey of infectious diseases (ID) practitioners and investigators. Potential study questions were developed within the ARLG for each research priority area and then submitted as a web-based survey to the broader ID community for ranking (Table 1). Administered online from 17 April 2020 until 6 May 2020, the questionnaire (see the Supplementary Material) was distributed to members of the Infectious Diseases Society of America (IDSA) via the IDSA website and amplified via the ARLG's Twitter handle.

A total of 161 professionals from 8 geographic regions (North America, South America, European Union, Asia, Africa, Central America, Middle East, and Oceania) participated. Most respondents (88%) practiced medicine in the United States. Respondents ranked infectious syndromes where they perceived evidence-based data to be lacking (1, highest need to 5, lowest need): pneumonia (mean rank, 1.9), bloodstream infection (BSI; mean, 2.1), urinary tract infection (UTI; mean, 2.6), and other (mean, 3.3). Study questions within these areas were prioritized as follows: which drug to use (mean, 1.9), how long to treat (mean, 2.2), how much drug to use (mean, 2.9), and etiology (mean, 2.9). Full survey results are provided in the Supplementary Material.

Table 1 provides the questions identified for each research priority area, their ranking in the survey, and the ARLG research response to each question. Importantly, these data confirm alignment between the ARLG’s scientific agenda and priorities of the ID community. Based on this information, the ARLG formulated specific needs within each of the 3 priority areas and will conduct studies to address them.

Infections Caused by MDR Gram-Negative Bacteria

The Gram-Negative Subcommittee established the following scientific objectives: to identify and evaluate novel treatments and strategies for infections caused by MDR GNB, to identify strategies that optimize administration of antibiotics for the treatment of GNB, and to evaluate novel strategies to prevent the emergence of resistance in GNB. The ARLG is currently pursuing 2 trials involving GNB.

The ARLG is conducting a phase 1/2, multicenter, randomized, double-blind, placebo-controlled trial, the Study of the safety and microbiological activity of bacterioPHAGEs in persons with cystic fibrosis colonized with P. aeruginosa (PHAGE), to investigate the safety and microbiological activity of a single intravenous dose of phage therapy in cystic fibrosis volunteers colonized with P. aeruginosa. A preformed phage cocktail will be administered at a range of dosages to clinically stable volunteers colonized with P. aeruginosa without concomitant antibiotic therapy. This study will enable a thorough safety analysis of bacteriophage therapy and define the activity of bacteriophage on bacterial burden. Phage pharmacokinetics and emergence of resistance will also be investigated. This work will lay the foundation for future studies investigating the impact of a bacteriophage therapy in patients with active infections.

Extended spectrum beta lactamase–producing Enterobacteriales were recently identified as the second most common cause of MDR bacterial infections in the United States [20]. The ARLG is currently designing a randomized, open-label, randomized controlled trial (RCT), Oral step down for BSIs, to compare tebipenem, an oral carbapenem, to standard intravenous therapy to complete treatment of BSI caused by extended-spectrum cephalosporin-resistant Enterobacteriales in patients who have achieved clinical stability on initial therapy. Study outcomes are expected to advance management of gram-negative BSI.

Table 1. Antibacterial Resistance Leadership Group Research Agenda and Community Prioritization of Scientific Agenda Questions

<table>
<thead>
<tr>
<th>Question</th>
<th>ARLG Project</th>
<th>Status</th>
<th>Rank in Community Survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are there safe and effective alternatives to prolonged IV therapy for complicated Staphylococcus aureus bacteremia?</td>
<td>DOTS</td>
<td>Start-up</td>
<td>1</td>
</tr>
<tr>
<td>Are there safe and effective alternatives to prolonged IV therapy for complicated S. aureus infective endocarditis (including oral options)?</td>
<td>DOTS</td>
<td>Start-up</td>
<td>2</td>
</tr>
<tr>
<td>Are novel long-acting anti-MRSA agents (dalbavancin or oritavancin) noninferior to standard of care for therapy of MRSA osteomyelitis?</td>
<td>DOTS</td>
<td>Start-up</td>
<td>3</td>
</tr>
<tr>
<td>What is the role of combination antibiotic therapy for the treatment of complicated MRSA bacteremia and endocarditis?</td>
<td>VENOUS</td>
<td>Complete</td>
<td>4</td>
</tr>
<tr>
<td>What is the best therapy for vancomycin-resistant enterococci bacteremia?</td>
<td>VENOUS</td>
<td>Complete</td>
<td>5</td>
</tr>
<tr>
<td>Are there safe and effective alternatives to prolonged IV therapy for complicated strep infections (e.g., Streptococcus pyogenes, Streptococcus agalactiae, viridans group streptococci)?</td>
<td>DOTS</td>
<td>Start-up</td>
<td>6</td>
</tr>
</tbody>
</table>
Infections Caused by MDR Gram-Positive Bacteria

A centerpiece effort of ARLG 2.0, directly responsive to the top priorities identified by survey respondents, is the Dalbavancin as an Option for Treatment of S. aureus Bacteremia (DOTS) trial. DOTS is a phase 2b, superiority-design, RCT comparing a 2-dose regimen of dalbavancin to standard intravenous therapy for treatment of complicated S. aureus BSI. DOTS will enroll key populations for whom high-quality treatment data are lacking, including patients with osteomyelitis and those who inject drugs. A blinded adjudication committee will establish...
A Framework (BED-FRAME) [25] introduces the diagnostic benefit-risk evaluation of diagnostics: a flexible quantitative framework that evaluates the desirability of diagnostic errors, providing a tool for communicating the expected impact of diagnostic application and trade-offs of diagnostic alternatives to guide decision-making. Average weighted accuracy extends BED-FRAME to allow pragmatic assessment of diagnostic utility [29]. DOOR for the Management of Antimicrobial Therapy (DOOR MAT) [30] is a flexible quantitative framework that evaluates the desirability of antibiotic selection and is used to evaluate the utility of stewardship strategies. Finally, the ARLG has a web-based catalogue that offers the research community access to clinically, phenotypically, and genotypically well-characterized MDR bacteria [19].

Other Priority Areas for ARLG 2.0
Mentoring
The goal of the ARLG Training and Mentoring Program (ARLG-TMP) is to develop the next generation of clinical researchers in antibacterial resistance. It was successful in the initial funding...
Table 2. Antibacterial Resistance Leadership Group Innovation in Clinical Trials Design

<table>
<thead>
<tr>
<th>Clinical trial design</th>
<th>Program</th>
<th>Purpose</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOOR</td>
<td>Uses partial credit strategies involving an ordinal ranking of global outcome to analyze patients</td>
<td>Published. Used in interventional trials [18] and cohort studies [2, 8].</td>
<td></td>
</tr>
<tr>
<td>National Institutes of Health–FDA collaboration</td>
<td>Creates standardized, validated, publicly available DOOR and QOL end points for common entry indications in infectious diseases to be available for use by industry as exploratory end points within registrational clinical trials of novel antibiotics for FDA approval</td>
<td>Bloodstream infection; published, validated, and integrated QOL [17, 21] and DOOR [23] measures into clinical trial (DOTS). Acute bacterial skin and skin structure infection, complicated urinary tract infection, hospital-acquired/ventilator-associated bacterial pneumonia, intra-abdominal infection; in progress.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnostics trial design</th>
<th>Program</th>
<th>Purpose</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMART COMPASS (Sequential, Multiple-Assignment, Randomized Trials for COMparing Personalized Antibiotic Strategies)</td>
<td>Allows for pragmatic assessment of patient-management strategies that span empiric and definitive therapy choices</td>
<td>Published [24].</td>
<td></td>
</tr>
<tr>
<td>BED-FRAME (Benefit-Risk Evaluation of Diagnostics: A Framework)</td>
<td>Introduces the diagnostic yield concept and incorporates prevalence and the relative importance of diagnostic errors</td>
<td>Published [26]. Used to evaluate rapid molecular diagnostics in carbapenem-resistant Enterobacteriales [26], Pseudomonas aeruginosa [27], and Acinetobacter baumannii [28].</td>
<td></td>
</tr>
<tr>
<td>ANA (Average Weighted Accuracy)</td>
<td>Extends BED-FRAME to allow pragmatic assessment of diagnostic utility</td>
<td>Published [29].</td>
<td></td>
</tr>
<tr>
<td>DOOR MAT (DOOR for the Management of Antimicrobial Therapy)</td>
<td>Quantitatively evaluates the desirability of antibiotic selection to evaluate utility of stewardship strategies</td>
<td>Published [30].</td>
<td></td>
</tr>
<tr>
<td>Isolate Biorepository</td>
<td>Web-based catalogue that offers the research community access to clinically, genotypically, and phenotypically well-characterized multidrug-resistant bacteria for research and development</td>
<td>Active: &gt;2300 isolates provided to research community to date [19].</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: DOOR, desirability of outcome ranking; FDA, US Food and Drug Administration; MASTERMIND BSI, MASTER protocol for evaluating Multiple Infection Diagnostics for rapid detection of bloodstream infection; QOL, quality of life.

period (Figure 1). Because the needs of trainees differ at different career stages, the ARLG-TMP developed 3 opportunities for mentoring support: the ARLG Fellowship, Early Stage Investigator Seed Grants, and the Trialists in Training Program. These 3 mechanisms are summarized in Table 3.

Diversity
Diversity, access, equity, and inclusion are core values of the ARLG. Although these principles are vital for excellence and innovation in scientific research [33], the diversity of medical professionals and clinical trial participants does not always reflect US population demographics [34, 35]. We are working to ensure full integration of these core values throughout ARLG operations. Our goals include increasing diverse representation and participation in ARLG-associated clinical trials and research studies; expanding outreach to underrepresented groups to encourage pursuit of careers in antibacterial resistance; promoting pipeline, mentorship, and career development activities within the ARLG; and recommending methods to assess, monitor, evaluate, and hold ourselves accountable for progress toward these goals.

Community Engagement in the ARLG
A number of improvements were initiated in ARLG 2.0 to enhance awareness of the ARLG and ARLG resources and opportunities. We created a Twitter handle (@ARLNetwork), expanded the ARLG quarterly newsletter recipient list, and enhanced website content to include posting of key ARLG activities, summaries and top-line results of recently completed ARLG studies, links to the ARLG twitter feed, and posts of the ARLG quarterly newsletter. These social media resources are being used to disseminate ARLG study results to the scientific community. In addition, the ARLG is actively collaborating with the IDSA and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) to contribute to ESCMID weekly newsletters.

CONCLUSIONS
ARLG 2.0 recently commenced its 7-year competitive renewal. Building on the experience gained in the initial funding period, ARLG 2.0 has developed a robust research agenda that aligns with the expressed priorities of the scientific community. A portfolio of clinical trials that leverages the ARLG’s unique combination of international
networks, innovative study design, and a strong operational infrastructure are well positioned to address our nation's most important threats posed by antibacterial resistance. Mentoring and diversity are core values of ARLG 2.0 as we train the next generation of researchers focused on antibacterial resistance. Collectively, ARLG 2.0 is well positioned to engage with investigators, clinicians, and trainees to identify, prioritize, design, and implement clinical research that improves diagnosis and treatment of antibacterial-resistant bacteria.

**Supplementary Data**

Supplementary materials are available at Clinical Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

**Notes**

**Financial support.** This work was supported by the National Institutes of Health (NIH; grant UM1-A1104681).

### Table 3. Antibacterial Resistance Leadership Group Engagement Opportunities

<table>
<thead>
<tr>
<th>Mentoring</th>
<th>Applications available at <a href="https://arlg.org/">https://arlg.org/</a></th>
</tr>
</thead>
</table>
| **ARLG Fellowship** | • Competitive award for post-doctoral fellows interested in pursuing research, training, and a subsequent career in patient-oriented research in antibacterial resistance  
• Salary for 2 years  
• Mentoring in antibacterial resistance research, tuition support for formal master's degree training in clinical trials, and integration into the ARLG committee infrastructure  
• Trainee serves on the Steering Committee and Scientific Subcommittees of the ARLG  
• Fellows pursue a research project and receive formal instruction in quantitative and methodological principles of clinical research; applications for the ARLG fellowship are submitted online via the ARLG website using established ARLG forms |
| **Early Stage Investigator seed grant** | • Provides up to $50,000 in direct costs to support research in antibacterial resistance by MD, PhD, or PharmD students, graduate or post-graduate trainees, or individuals with a faculty appointment for ≤5 years |
| **Trialist in Training** | • For trainees able to commit to projects for longer than the usual 2 years of the ARLG fellowship  
• Candidates “embedded” in day-to-day operations of an ARLG clinical trial  
• Salary support to develop protocols and participate in clinical trials implementation and data management  
• Authorship on publications that result from the project |
| **Outreach** | • Two Blood Stream Infection Task Force Surveys  
• Raised awareness and drove traffic with newsletter items, website news, IDSA emails and message board posts, communications kits to ARLG members, Twitter  
• Fellowship campaign  
• Updated fellowship website page (including new video and infographic); drove traffic with newsletter items, website news, IDSA emails and message board posts, communications kits to ARLG members, Twitter, promotional toolkits for stakeholders (included banner ads, Twitter and LinkedIn posts, infographic, ID Colleague email, news story, and video)  
• Gram-negative communication plan to solicit proposals  
• Raised awareness and drove traffic with social media, email blasts, newsletter mentions, and news item on website  
• IDSA Outreach Campaign  
• Solicited survey information on top research priorities to develop the ARLG scientific agenda |

**Twitter** | • Access Twitter handle, @ARLGnetwork |
| **Other** | Information available at https://arlg.org/ |
| **Contact ARLG link** | • Submit questions and comments directly to the ARLG |
| **ARLG newsletter** | • Subscribe to quarterly newsletter that highlights the progress of the ARLG scientific agenda and studies and members of the ARLG community |
| **Clinical trial site** | • Join the ARLG site network to be considered for current and future ARLG study participation |
| **Data sharing** | • Request datasets from ARLG studies |
| **Virtual biorepository** | • Access a web-based system that provides unique access to clinically well-characterized gram-positive and gram-negative bacteria for the development of diagnostic tests, novel antimicrobial compounds and for studies evaluating mechanisms of resistance |
| **Physical biorepository** | • Access clinically characterized isolates and clinical specimens from ARLG studies that are stored in a centralized facility and are available to the scientific community |
| **Protocol concept** | • Submit a protocol concept consistent with the ARLG's 3 prioritized areas of research for funding |
| **Industry collaboration** | • Engage with subject matter experts and key opinion leaders in antibacterial resistance to inform research agendas and product/device development |

**Abbreviations:** ARLG, Antibacterial Resistance Leadership Group; ID, infectious disease; IDSA, Infectious Disease Society of America.

Potential conflicts of interest. V. G. F. reports personal consultancy fees from Novartis, Novadigm, Durata, Debiopharm, Genentech, Achaogen, Affinium, Medicines Co., Cerexa, Tetrathaphe, Trius, MedImmune, Bayer, Theravance, Basilea, Affinergy, Janssen, xBiotech, Contrafect, Regeneron, Basilea, Destiny, Amplifihi Biosciences, Integrated Biotherapeutics, C3J, Armata, Valanbio, Akagera, and Aridis; MedImmune, Allergan, Pfizer, Advanced Liquid Logics, Theravance, Novartis, Merck, Medical Biosurfaces, Locus, Affinergy, Contrafect, Karius, Genentech, Regeneron, Basilea, and Janssen; royalties from UpToDate; stock options from Valanbio; a patent pending in sepsis diagnostics; educational fees from Green Cross, Cubist, Cerexa, Durata, Theravance, and Debiopharm; and an editor's stipend from the Infectious Diseases Society of America (IDSA). R. P. reports grants from Merck, ContraFect, TenNor Therapeutics Limited, Hylomorph, and Shionogi; is a consultant to Curetis, Specific Technologies, Next Gen Diagnostics, PathoQuest, Sefus Diagnostics, 1928 Diagnostics, PhAST, and Qvella (monies are paid to Mayo Clinic); is also a consultant to Netflix; has a patent on Bordetella pertussis/paparussis polymerase chain reaction issued, a patent on a device/method for sonication with royalties paid by Samsung to Mayo Clinic, and a patent on an anti-biofilm substance issued; receives an editor's stipend from IDSA; and receives honoraria from the National Board of Medical Examiners, Up-to-Date, and the Infectious Diseases Board.
Review Course. D. v. D. is a consultant for Actavis, Tetraphase, Sanofi-Pasteur, MedImmune, Astellas, Merck, Allergan, T2Biosystems, Roche, Achaogen, Neumedicus, Shionogi, Pfizer, Entasis, Qixpex, Wellspring, Karius, and Utility; receives an editor’s stipend from BSAC; and reports grants from NIH outside the submitted work. Y. D. reports personal scientific advisory board fees from Gilead, Shionogi, Janssen, Entasis, VanetoxRx, bioMerieux, and MSD; reports speaking fees from AstraZeneca and FujiFilm; and reports grants from NIH, Japan Agency for Medical Research and Development (AMED), Shionogi, Janssen, MSD, Astellas, Pfizer, and Kanto Chemical. H. W. B. reports personal fees from Antimicrobial Agents & Chemotherapy, Sanford Guide, and Infectious Diseases Clinics of North America outside the submitted work. H. F. C. reports being co-primary investigator of an NIH/ National Institute of Allergy and Infectious Diseases (NIAID) Antibacterial Resistance Leadership Group (ARLG) grant outside the submitted work. A. D. H. reports honorarium from UpToDate outside the submitted work. T. L. H. reports consulting fees from Basilea Pharmaceutica (ceftobiprole) and Genentech (immunotherapeutic) and scientific advisory board and consulting fees from Motif Bio (ilaprazolam) outside the submitted work. S. R. E. reports grants from NIAID/NIH during the conduct of the study; personal fees from Takeda/Millennium, Pfizer, Roche, Novartis, ACTTION, Genentech, Amgen, American Statistical Association, the US Food and Drug Administration, Osaka University, National Cerebral and Cardiovascular Center of Japan, Society for Clinical Trials, Statistical Communications in Infectious Diseases (DeGruyter), AstraZeneca, Teva, Austrian Breast and Colorectal Cancer Study Group / Breast International Group and the Alliance Foundation Trials, Taylor and Francis, Vir, Shire, Alexion, Gilead, Clinical Trials Transformation Initiative, Tracon, Deming Conference, Antimicrobial Resistance and Stewardship Conference, Advantagene, Cardinal Health, Microbition, Stryker, Atricure, BENEFIT, Roivant, Neovasc, Nobel Pharma, Horizon, Roche, Rakuten, Duke University, University of Pennsylvania, Takeda, Nuvelution, AbbVie, Clover, FHI Clinical, Lung Biotech, SAB Biopharm, CIOMS, and SVB LEERINK outside the submitted work. E. L. T. reports being co-founder with equity of Predigen Inc and has US patent 8599 859 539 B2 issued and patents PCT/US2016/040437 and PCT/US18/13832 pending. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

29. Wilson B, Viala R, Perez F, et al. Corrigendum to: 1757, using the desirability of outcome ranking for management of antimicrobial therapy (DOOR-MAT) to assess antibiotic therapy guided by rapid molecular diagnostics (RMD) in
bloodstream infection (BSI) caused by *Escherichia coli* and *Klebsiella pneumoniae*. Open Forum Infect Dis 2019; 6: ofz267.


