New Antimicrobial Agents . . . but No Susceptibility Tests!

TO THE EDITOR—It was with great interest that we read the invited article by Humphries and Hindler [1] highlighting the importance of timely antimicrobial susceptibility testing (AST) to confirm susceptibility, detect resistance, and guide patient therapy. With the increasing emergence of multiderug-resistant organisms, it is necessary to evaluate pathogen susceptibility to new antimicrobials to generate local antibiograms for hospital formulary decision making and optimize antimicrobial stewardship [2–4]. Ideally, US Food and Drug Administration (FDA)-cleared commercial AST (cAST) systems should be available when an antimicrobial is launched, but there is invariably a significant delay.

The lengthy lag between antimicrobial launch and access to FDA-cleared automated cAST systems is an ongoing concern to pharmaceutical companies that invest in the development of key cAST systems. The underlying reasons for the lag are multifactorial, and include long development timelines for automated systems with complex software, potential drug-specific technical issues, access to contemporary isolates having specific resistance mechanisms, and multiple competing drug candidates uncertain of gaining New Drug Application (NDA) approval. Currently AST manufacturers submit a 510(k) premarket notification to the Center for Devices and Radiological Health (CDRH) after NDA approval and establishment of breakpoints by the Center for Drug Evaluation and Research (CDER). We believe that focusing on the following areas will expedite access to cAST systems: (1) early collaboration between drug and device manufacturers; (2) coordinated clinical development (eg, Pharma to provide AST manufacturers access to clinical trial isolates; trials to encompass multiple device types); and (3) mechanisms for concurrent review of drug and cAST systems [4].

An estimated 37 investigational antimicrobials [5] with the potential to treat life-threatening infections are reported in clinical development for the US market. A total of 63 unique molecules have received Qualified Infectious Disease Product (QIDP) designation under the Generating Antibiotic Incentives Now Act, allowing for “fast-track” status and expedited review of marketing applications by FDA [6]. Because no “fast-track” designation exists for cAST systems, we propose the creation of an analogous pathway for these test systems so that they may be available at launch to provide clinical value for patient management.

We are encouraged that CDER and CDRH are drafting guidance on the coordinated development of antimicrobials and cAST systems, to facilitate timely access to FDA-cleared cAST systems soon after antimicrobial approval [7–9]. We urge the FDA to prioritize this guidance, and look forward to working collaboratively with all relevant stakeholders on implementation upon its release.

We therefore call for multistakeholder discussions encompassing the FDA, policy makers, drug developers, cAST manufacturers, standard-setting organizations, coordinators of sentinel surveillance of antimicrobial resistance, clinical laboratory staff, physicians, and patient representatives to review the data needed to support contemporaneous marketing authorization of antimicrobial agents and cAST systems and to devise concrete, actionable solutions that ensure timely access to cAST systems.

We know that significant progress can be made through focused partnerships and collaboration. Given the threat to public health posed by antimicrobial resistance, and the numerous QIDP-designated drugs in clinical development, this multifaceted challenge must be addressed as a matter of urgency.
Note

Potential conflicts of interests. J. E. A. is an employee of Wockhardt, a previous employee of Merck Research Laboratories (formerly Cubist Pharmaceuticals), and a former employee and shareholder of AstraZeneca Pharmaceuticals; she has been a consultant to Achaogen Inc and ContraFect Corp. K. M. K. is an employee of and shareholder in Achaogen, and was a previous employee of Cereza Inc. J. N. S. is an employee of Paratek Pharmaceuticals; has been a consultant to Tetraphase Pharmaceuticals, Inc; and formerly was an employee of Merck Research Laboratories. N. E. S.-O. and L. A. M. are employees of and shareholders in GlaxoSmithKline. S. S. B. is an employee and shareholder of Wockhardt Ltd, Wockhardt Research Centre. A. W. S. is an employee and shareholder of Achaogen, L. C. and N. M. M. are employees of and shareholders of Cubist Pharmaceuticals. M. R. M. is an employee and shareholder of Merck Sharp & Dohme Corp. I. A. C. is an employee and shareholder of Allergan, plc; has been a consultant to Actavis plc; and was previously employed by Cereza Inc. J. P. I. and G. G. S. are employees of and shareholders in AstraZeneca Pharmaceuticals. J. A. is an employee of and shareholder in Bayer HealthCare Pharmaceuticals Inc. L. X. is an employee of and shareholder in VenatoRx. S. P. M. is an employee of Melinta Therapeutics and former employee of Durata Therapeutics and Cubist Pharmaceuticals, and is a shareholder of Pfizer. D. F. V. is an employee of and shareholder in Shionogi Inc, and a former employee of and shareholder in Bayer HealthCare Pharmaceuticals Inc. T. G. S. is an employee of and shareholder in Tetraphase Pharmaceuticals, Inc. R. M. E. is a consultant to Shionogi Inc. G. W. is a consultant to Actavis plc, Achaogen Inc, Cempra Inc, Wockhardt Bio AG, and Roberta’s. P. A. B. is a consultant to ContraFect Corp and Tetraphase Pharmaceuticals Inc; is a shareholder of AstraZeneca and Pfizer; and was formerly employed by AstraZeneca Pharmaceuticals. 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.

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Clinical Infectious Diseases® 2016;63(11):1528–1 © The Author 2016. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved.

For permissions, e-mail journals.permissions@oup.com. DOI: 10.1093/cid/ciw603

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