2012 VALUE PROPOSITION

THE ALLIANCE FOR THE PRUDENT USE OF ANTIBIOTICS (APUA):
ANTIBIOTIC RESISTANCE EXPERTISE

Since 1981, the Alliance for the Prudent Use of Antibiotics (APUA) has been the leading global non-governmental organization fighting to preserve the effectiveness of antimicrobials. See the Appendix for more detailed information.

APUA OBJECTIVES

- Increase public awareness and knowledge
- Strengthen infectious disease prevention capability and treatment
- Improve institutional and governmental antimicrobial policy
- Build local microbiology surveillance and diagnostics capacity

APUA OFFERS

- Boston-based headquarters and staff with expertise in medicine, microbiology, public health, and policy
- Affiliations with Tufts University School of Medicine and international expert advisory board
- Global network of local APUA chapter affiliates in 66 countries in Africa, Asia, and South America
- Extensive experience in developing countries

RESEARCH

- Coordination of large research consortia and sub-grants in industrial and developing countries
- Multi-country research of bacterial spread in humans, animals, soil, and water
- Food and water safety and other bio-defense applications
- Ability to detect and monitor resistance emergence, spread, and evolution
- Management of large databases on antimicrobial resistance (AMR)
- Building capability for bacterial surveillance at global and local levels
- Wet laboratory capacity for direct testing and analysis
- Expert advisory groups to interpret and analyze the data
- Laboratory assessments and capacity building in resource-poor countries
- Health systems research and tools to assess antibiotic supply distribution and use
- Economics and cost effectiveness studies

EDUCATION AND ADVOCACY

- Public policy advocacy based on original research and peer-reviewed publications
- International community organization and public health education
- Consumer and provider education via listservs, APUA blog, Web site and major media outlets
- Fact sheets and white papers for health providers, patients, and policy makers
- Quarterly clinical newsletter on infectious disease issues
- Regulatory and policy research (national and international)
- Engagement of diverse stakeholders to forge consensus on controversial policy
**CHIEF EXECUTIVE OFFICERS**

**Stuart B. Levy, M.D.;** Chairman and President  
Dr. Levy is past president of the American Society for Microbiology and a world renowned microbiologist and physician. He discovered the mechanism for tetracycline resistance (efflux) and was among the first to document the transfer of drug resistance among animals and humans. Dr. Levy has authored over 250 scientific and medical papers as well as authoring *The Antibiotic Paradox: How Miracle Drugs Are Destroying the Miracle.* He has served as advisor on health policy committees including: the NIH Fogarty Center; the U.S. Office of Technology; the EPA Subcommittees on Health and Antibiotic Resistance; and WHO Scientific Advisory Groups. Dr. Levy has also served as a consultant for the U.S. FDA, the National Institutes of Health and U.S. national security projects. He is currently a Professor of Medicine and Molecular Biology/Microbiology and the Director of the Center for Adaptation Genetics and Drug Resistance at Tufts University School of Medicine, as well as a Staff Physician at the New England Medical Center.

**Thomas F. O’Brien, M.D.;** Vice President  
Dr. O’Brien is a leading authority on antibiotic resistance control and surveillance. An infectious disease specialist and microbiologist, Dr. O’Brien helped develop the WHONET surveillance program. He also initiated the WHO Collaborating Center for Surveillance of Resistance to Antimicrobial Agents at Brigham and Women’s Hospital in Boston in 1985, which has established an international network of over 60 microbiology laboratories tracking AMR patterns and developing guidelines based on these data. Dr. O’Brien has performed field consultations to improve clinical services in African hospitals and served as an advisor on numerous national and international committees, including the NIH Task Force on Antibiotic Resistance (which he chaired from 1984 to 1986); the WHO Scientific Working Group on AMR (1981); the FDA’s Veterinary Medicine Advisory Committee (since 1994); the Office of Technology Assessment Advisory Panel on Impacts of Antibiotic-Resistant Bacteria; the Inter-Agency (FDA, CDC, USDA) Working Group on Antimicrobial Resistance; and the CDC Working Group on Drug-Resistant Streptococcus pneumoniae. He has also served as a consultant on antimicrobial resistance to WHO (in Geneva and Manila), PAHO, the British House of Lords, and the National Health Research Institute of Taiwan, among others. Medical Director of the Microbiology Laboratory at Brigham and Women’s Hospital for the past 20 years, Dr. O’Brien has been a pioneering researcher in the area of AMR since the mid-1960s.

**Kathleen T. Young;** Executive Director  
Ms. Young has over 25 years of experience in executive administration of health care payer, provider, consumer and governmental organizations. Ms. Young is responsible for oversight of all APUA operations, programs development, and strategic initiatives and currently serves on the U.S. FDA Anti-Infective Drugs Advisory Group. Ms. Young has served as president and board member of health advocacy groups and director of strategic planning at a major international health provider organization.
ABOUT APUA

Antibiotic resistance is one of the major public health threats of the 21st century. Since 1981, the Alliance for the Prudent Use of Antibiotics has been the premier organization dedicated to promoting appropriate antibiotic use and curbing antibiotic resistance. APUA conducts large-scale national and international research and educational projects to control and monitor antibiotic resistance. We facilitate the exchange of up-to-date information by forging national and international partnerships among scientists, healthcare providers, consumers, and policy makers.

APUA’s resources include: a professional staff with expertise in medicine, microbiology, economics, health education, ecology, international program development, and health systems research; affiliations with Tufts University School of Medicine and Tufts Health Plan; APUA chapters in more than 60 countries; and an advisory board of leading clinical and scientific experts including Nobel laureates and members of national academies of medicine and science. For more information, read the APUA Progress Report (FY 2010-2012) or visit the APUA website.

APUA’s multidisciplinary research program applies basic science, epidemiology, and surveillance to identify trends in susceptible and drug resistant infections and promising interventions. By conducting research on many aspects of this far-reaching public health problem, APUA’s work advances the ecological approach towards “One World, One Health.” APUA studies have provided groundbreaking data which have influenced national and international public health policy on antimicrobial resistance, including: the first hospital study to rigorously document the economic burden of drug resistance; studies used by the FDA to support their pursuit of curbing the non-therapeutic use of antibiotics in food animals; and reports to promote targeted sanitation and hygiene measures to control the spread of infectious disease. APUA staff and board members regularly publish the results of their research and consult in national and international planning initiatives with IDSA, USFDA Anti-Infective Advisory Committee, WHO Patient Safety Committee, Global Development Council, Institute of Medicine, Center for Global Development, and others.

APUA is the sister organization of the Center for Adaptation Genetics and Drug Resistance at the Tufts University School of Medicine, allowing us to enjoy a close relationship with Tufts Medical Center and its affiliates: Cambridge Hospital, Metro West Medical Center, St. Elizabeth’s Medical Center, Lahey Clinic Medical Center, and Tufts Managed Care Institute. We have also conducted projects with the Tufts University Friedman School of Nutrition and the Tufts University Cummings School of Veterinary Medicine.

Antibiotic resistance is fueled by misuse and overuse of antibiotics. Bacteria become resistant to the very medicines developed to treat and cure the infection they cause. Major ARIs (antibiotic resistant infections) include methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococcus (VRE), C. difficile and a growing number of deadly Gram-negative infections. APUA specializes in study of drug-resistant infections – one of the most expensive types of healthcare-acquired infection and the most difficult to contain. APUA’s research interests are focused on documenting and controlling bacterial infections through improved surveillance, antibiotic stewardship and infection control. For more information on APUA work on antimicrobial resistance containment for infection control, see the archives of the APUA Clinical Newsletter.
RESEARCH APPROACH AND EXPERIENCE

APUA has a long history of working in collaboration with local, national, and international organizations. We have developed protocols for projects with PAHO, USAID, U.S. CDC, USDA-ARS, NIH, and NIAID; state organizations such as the Massachusetts Department of Public Health and the Massachusetts Infectious Disease Society; corporations such as Pfizer, Clorox, Procter & Gamble, and bioMérieux; and other nonprofit organizations such as the Gates Foundation and the Pew Charitable Trusts. We have also worked closely with both domestic and international government healthcare infrastructure.

APUA’s research initiatives go through a rigorous pipeline with high standards of scientific methodology before they reach completion. The model for all APUA research projects consists of: 1) gathering data and/or reviewing published studies; 2) analyzing data (statistic/mathematical/economic analysis or qualitative analysis) with the collaboration of a panel of internationally recognized experts, individually selected for each project; and 3) publishing a summary of findings as a press release, report, or peer-reviewed publication. Both the expert panels for individual projects and the Scientific Advisory Board that provides leadership to APUA as an organization are made up of health professionals with extensive field experience in the industrial and the developing world, including the world’s top infectious disease experts in treating HIV, TB, malaria, and many other diseases.

The findings of our research projects have been published in the form of numerous white papers, reports, and articles in prestigious peer-reviewed journals such as Clinical Infectious Diseases, Emerging Infectious Diseases, Clinical Microbiology Reviews, Microbe, and Nature Medicine. Our publications have been used as resources for WHO, the Transatlantic Task Force (TATFAR), the Institute of Medicine, and for staff briefings of the U.S. Congress.

Study design and planning: quantitative and qualitative data management and analysis

APUA has extensive experience in designing and implementing survey-based studies. Some studies focused on the collection, management, and statistical analysis of qualitative data. We conducted the nationwide opinion survey “Antibiotics and the Consumer: Perceptions and Use” to identify incorrect practices in procuring or using antibiotics and the beliefs and circumstances that motivate such behaviors. The “Pilot Survey of Massachusetts Physicians” documented the factors that were most influential in physicians’ decision-making and prescribing practices, indicating that diagnostic uncertainty and patient requests for antibiotics were usually responsible for inappropriate prescriptions of antibiotics. A similar survey of physicians was conducted in “Physician Antibiotic Prescribing Practices and Knowledge in Seven Countries in Latin America and the Caribbean.”

Other studies focused on quantitative data management and statistical analysis. The FAAIR project (“Facts and Antibiotics in Animals and their Impact on Resistance”) implemented a systematic survey to obtain quantitative estimates of antibiotic usage in U.S. food animal production, for the purpose of guiding regulatory decision-making. Its findings were published as the comprehensive report “Animal Antimicrobial Use Data Collection in the United States: Methodological Options” in Preventive Veterinary Medicine. In Uganda and Zambia, APUA performed comprehensive needs assessments in the pharmaceutical sectors of close to 100 health centers and hospitals with over 10,000 outpatients to analyze drug quality and rates of emerging resistance.

Literature review and analysis

APUA has experience in many aspects of primary and secondary research related to infectious disease and antibiotic use, such as literature reviews, database development, statistical and mathematical analysis, and economic analysis. Several of APUA’s research initiatives have reviewed and analyzed existing literature and studies in the field of antimicrobial resistance. The FAAIR report evaluated published studies first on antibiotic usage in agriculture, then on antibiotic usage in food animal production, resulting in two publications in Clinical Infectious
Diseases and Preventive Veterinary Medicine. APUA also hosted a roundtable meeting of experts in Paris in 2010 to discuss the EU ban on the use of antibiotics for growth promotion in agriculture, which led to 16 background papers and the publication of a review article in Microbe.

**Laboratory research**

Extensive research in genetics, biochemistry, molecular biology, and pharmacology is carried out in collaboration with APUA by Dr. Stuart Levy’s Center for Adaptation Genetics and Drug Resistance at Tufts University School of Medicine. Hygiene studies have surveyed large community populations to examine the relationships between antibacterial use and the emergence and propagation of antibiotic resistance in household kitchens and bathrooms (Frequency of antibiotic-resistant bacteria in homes differing in their use of surface antibacterial agents; Current Microbiology [submitted]) and on the hands (Antimicrobial Chemotherapy 2008; Antimicrobial Agents and Chemotherapy 2004), as well as the potential health impacts of microbial contamination of wind instruments (International Journal of Environmental Health Research 2011).

**Database development**

Effective database design, creation, and maintenance have also been essential to many APUA projects that focused on tracking resistance rates and trends in infectious disease organisms. APUA first compiled annotated, peer-reviewed publications as well as field data from commensal isolates into the ROAR (Reservoirs of Antibiotic Resistance) database to create a Web-based bioinformatics tool that could analyze the trends and patterns of antibiotic resistance in harmless, commensal bacteria and use it to statistically model the emergence of antibiotic resistance genes in pathogens. The database compiled during the ROAR project became the foundation for the subsequent ISRAR (International Surveillance of Reservoirs of Antibiotic Resistance) project, which assisted in national biodefense efforts by examining genotypes and phenotypes of resistant bacteria to determine which could potentially be used as enhancers of agents of biological terrorism. These projects assimilated data on approximately 2000 environmental and clinical isolates of eight major genera from animal, soil, water, and plant sources in the U.S. and seven global countries.

**Informatics: risk analysis and economic analysis**

As well as statistical and mathematical modeling, APUA has also used risk analysis and economic analysis to contribute quantitative evidence for the significance of antimicrobial resistance as a threat to global health. In 2008, APUA initiated a study involving a national expert advisory panel and the John H. Stroger, Jr. Hospital of Cook County to document the economic impact of antibiotic misuse and antibiotic-resistant infections (ARIs). “Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: implications for antibiotic stewardship” was published in the October 2009 issue of Clinical Infectious Diseases. The study found that the medical costs attributed to these ARIs ranged from $18,588 to $29,069 per patient, while the duration of hospital stay was extended 6.4 – 12.7 days for affected patients. Additionally, the excess mortality attributed to ARIs alone was 6.5% — a death rate two-fold higher than in patients without ARIs. The authors also estimated the societal costs incurred at this hospital as a result of the ARIs to be between $10.7 and $15 million. These findings have since become the “gold standard” for quantitative evaluations of clinical healthcare settings.

**Education and outreach**

APUA has more than 30 years of experience in producing evidence-based education and outreach materials for both consumers and healthcare practitioners. We have published multiple consumer-targeted fact sheets about antimicrobial resistance on our website, and have been part of the CDC’s Get Smart campaign to spread public awareness about the appropriate use of antibiotics since 2010. APUA’s own publication, the APUA Clinical Newsletter, is published three times a year and distributed on a complimentary basis to our extensive network over 10,000 infectious disease practitioners who support and collaborate with us in more than 100 countries. The Clinical
Newsletter is supplemented by monthly APUA Highlights, which keeps subscribers updated on new developments from APUA’s research projects, policy work, publications, and international chapter reports.

“Hygiene for a Healthy Household” was a research and education campaign in which APUA used risk-reduction analysis to identify a small number of priority hygiene practices that were low-cost, easy to implement, and most likely to reduce levels of disease transmission, and developed promotional material to disseminate this information to consumers. APUA also provided a CME (Continuing Medical Education) curriculum program at the Massachusetts College of Pharmacy and Health Sciences and at the American Academy of Nurse Practitioners to educate pharmacists, nurse practitioners, physicians, and other healthcare providers on trends in antibiotic resistance, clinical treatment guidelines, and pharmacological and clinical approaches to combating antibiotic resistance in the community.

POLICY EXPERIENCE

APUA has initiated and been a member of national coalitions and campaigns to promote antimicrobial resistance surveillance and control, maintain incentives for the creation of better drugs and diagnostic devices, and preserve antibiotics for medical treatment. APUA also endorsed the Infectious Disease Society of America’s “10x’20” initiative to develop ten new antibiotics by 2020.

APUA maintains a watch and weighs in on antimicrobial resistance policy developments by giving testimonies and statements to Congress, and sponsoring a congressional staff briefing on Capitol Hill. Dr. Stuart Levy and APUA staff have testified before Congress over the years. A Congressional staff briefing in 2005 brought attention to the lack of effective treatment for Gram-negative bacilli and the rise of Clostridium difficile infections in hospitals, and called for health plans that would better address the challenge of antimicrobial resistance in clinical settings. Through our work with The Pew Charitable Trusts, APUA has also campaigned to strengthen FDA regulations against the irresponsible use of antibiotics in the national food supply.