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**Natural Products Research Center Director Appeals
for Unified Effort to Stem Antimicrobial Resistance**

Congressional leaders are warned of public health crisis

UNIVERSITY, Miss. — The growing resistance of disease-causing pathogens to the drugs used to combat them represents a potentially massive public health crisis that only immediate, concerted research efforts can avert, a panel of health and pharmaceutical experts told congressional leaders Wednesday morning in Washington.

Such efforts should include a range of basic and applied research by scientists from academia, government and the private sector, said Dr. Alice Clark, director of the National Center for Natural Products Research and F.A.P. Barnard Professor of Pharmacognosy at The University of Mississippi. Clark was among the witnesses presenting information and recommendations to the Labor, Health and Human Services Subcommittee of the Senate Appropriations Committee.

“Different strategies must be employed, and all will be important,” Clark said. “We would no more rely on a single strategy to achieve a military victory than we should to achieve important victories against public health enemies. There will be no single answer, no single strategy, no single hero, no magic bullet; true success only will be achieved through combined efforts.

“The time is now to invest in people, facilities and equipment, in collaborative multidisciplinary strategies that maximize our information and resources, and in creating and sustaining both physical and intellectual environments that foster partnerships between academia, government and the private sector to develop innovative solutions.”

The hearing, chaired by Sen. Thad Cochran, also included testimony by Jane E. Henney, commissioner of the U.S. Food and Drug Administration; Dr. Jeffrey Koplan, director of the Centers for Disease Control; Dr. F.E. Thompson, state health officer for the Mississippi Department of Health; Dr. Martin Rosenberg, senior vice president and director, anti-infectives, SmithKline Beecham Pharmaceuticals; Dr. Merle A. Sande, professor and chairman of the Department of Medicine and the Clarence

M. and Ruth N. Birrer Presidential Endowed Chair in Internal Medicine, University of Utah School of Medicine; and Dr. Mark L. Nelson, senior director of chemistry at Paratek Pharmaceuticals Inc.

“All humankind is at risk,” said Sen. Cochran. “The most susceptible to the threat are the most vulnerable, those who are sick in hospitals and the young in day-care centers. But drug-resistant infections are now occurring in all urban and rural settings and among all populations. ... The threat is growing at a time when our society cannot afford the social or financial costs of a drug-resistant outbreak or infectious diseases. ... I hope we can get suggestions from the experts about how the federal and state governments, the private sector and academia can work together to deal with the threat.”

Cochran said the Senate already had recognized the problem, passing a recent amendment to fund pilot projects in antimicrobial resistance surveillance and research, and referred to another pending bill to provide authorization for federal programs to address the issue.

Antimicrobial resistance has been observed for decades, but the problem has been compounded by the overuse and misuse of popular antibiotics and a diminished emphasis on research aimed at understanding, preventing and controlling resistance, Clark said.

“The rapid development of resistance to vancomycin by *Enterococcus* is a deadly combination of the most commonly acquired hospital infection with the last resort drug — raising the fearful question no one wants to ask or hear: Now what?” Clark said. “Many of the pathogens that concern us are, presently, familiar only to the healthcare professional. We must do whatever is necessary to prevent terms like VRE, VISA and MRSA from becoming so common in the community that they become household names. But resistant *Pneumococcus* jumped from virtually nonexistent in the early '80s to as high as 30 percent or more in some parts of the country today.”

Pharmaceutical firms introduce new antimicrobial drugs each year, partly to counter resistance problems, but few of those drugs represent totally new classes of antimicrobial agents. To adequately restock mankind's chemotherapeutic arsenal, researchers must develop new drugs that act by novel mechanisms to kill pathogens.

University research teams play a vital role in this effort, Clark said.

“The frontiers of knowledge are pushed forward every day by academic researchers throughout this country,” she said. “The information that is generated in academic laboratories will be a major contribution to our overall success in turning the tide of antimicrobial resistance — everything from understanding the magnitude of the problem to understanding the specific mechanisms by which pathogens evade the action of antimicrobial drugs to identifying new leads for drug development.”

Drug discovery and development is a lengthy and expensive process that can take a decade or more, so it is important to get new antimicrobial agents into the drug pipeline quickly, she said. Investments made now will pay off 10 to 20 years in the future.

One approach used to develop new antimicrobials is to study the pathogens and design something that interferes with a critical process within the bacteria. Recent advances in genomics bring hope of new breakthroughs in this area.

Another approach is to find substances in natural products that have antimicrobial properties. This method has been successful in other areas, including the anticancer drugs taxol and camptothecin, and natural products could yield important new weapons against pathogenic bacteria, Clark said.

“We must broaden our search to include other organisms, especially plants, marine life and microorganisms from unusual environments,” she said. “We’ve not begun to tap the full potential of nature, which is a vast and virtually unlimited source of novel chemical structures with a variety of biological effects.”

The National Center for Natural Products Research is the nation’s only university-affiliated research center devoted to improving human health and agricultural productivity through the discovery, development, and commercialization of pharmaceuticals and agrochemicals derived from natural products. Center research focuses on discovering new drugs for unmet therapeutic needs such as cancer and infectious diseases, improving the quality and safety of dietary supplements, and discovering new, effective agrochemicals that will not harm the environment.

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