Incentives for Addressing Unmet Needs in Antibiotic Development:

Focusing the GAIN Bill for Patients in Greatest Need

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Good morning. Thank you for inviting me to testify. I am a practicing infectious disease and internal medicine physician and a medical researcher who actively cares for patients. I was a scientist at FDA for almost a decade and while there I was one of the co-chairs of the Inter-agency Task Force on Antimicrobial Resistance. I would like to share with you today my perspectives as a clinician, researcher and patient myself on appropriately developing incentives for antibiotics where there is the greatest need. My remarks are my own views and I am not representing any agency or organization, but I am here speaking on behalf of the patients for whom I care. Several consumer and public health groups and advocates have expressed the same views I will present here today.

Government intervention is needed to spur antibiotic development because antimicrobials are less profitable for drug companies than other therapeutic areas, resulting in decreased investment in new antibiotic development. The Get Antibiotic Incentives Now or GAIN bill provides incentives to develop new antibiotics.

In any policy making as in science, one must first outline the problem, come up with potential solutions while minimizing unintended consequences, implement the policy and then measure whether it has had its intended effects. The problem of serious diseases for which there are no effective therapies has been well-outlined. The question is how best can GAIN address these problems? If the public is to make an investment on new antibiotics the public should get something of measurable value in return while not worsening the problem.

Several changes to GAIN might help it focus to best address public health needs while limiting potential adverse consequences.

First, GAIN should focus on patients and diseases, not organisms. I have never had a patient tell me their *E. coli* hurts or their *Klebsiella* is killing them. Patients present with disease syndromes like pneumonia. The human body contains more bacterial than human DNA. Organisms do not cause problems for patients until they cause disease. Any list of organisms in the bill would be quickly outdated. In addition, FDA regulations appropriately point out that drugs are approved for "recognized diseases or conditions" and organisms are neither. Use of antibiotics to eliminate organisms in the absence of disease would paradoxically increase antibiotic resistance.

Second, GAIN should focus on the treatment of serious and life-threatening diseases where lack of safe and effective therapies result in death or serious disability. Antibiotic resistance in the test tube has little effect on patient outcomes in self-resolving disease, but it is inappropriate use in these settings that has worsened antibiotic resistance. Despite efforts by CDC, FDA and others a substantial proportion of antibiotic prescriptions are not warranted, provide no benefit to patients and cause the problem we are trying to control.

Third, there should be valid scientific evidence based on FDA's standard of substantial evidence from adequate and well-controlled trials that drugs meet unmet medical needs. In 1979 in a landmark Supreme Court case Thurgood Marshall pointed out that people

with terminal disease should not receive less protection under the law from unsafe and ineffective drugs than persons with curable diseases. Test tube and animal studies are helpful in choosing drugs to study in people, people are not rodents. Three fourths of antibiotics submitted to FDA for review with promising test tube data and animal studies ultimately fail to show safety and efficacy in human disease. Approving antibiotics today hoping for some future promise makes no sense as resistance is inevitable with all antibiotics, sometimes occurring before a drug is even marketed. There is no guarantee that a drug approved today will address resistance tomorrow. Almost half of antibiotics approve since 1980 have disappeared from the market, either because of safety and efficacy issues or because of poor sales because they did not address public health needs, therefore number of drugs approved is not a measure of the public health benefits.

Fourth, we need new tools to evaluate antibiotics that will make trials more efficient. Determining who needs antibiotics and developing better outcome measures to evaluate how patients feel and function are urgently needed so we can get the valid evidence we need to know if drugs meet the claims made for them.

Fifth and finally, any incentives should go hand in hand with programs for appropriate stewardship of antibiotics. For any scarce resource, conservation should accompany increased production. Unfortunately, we as physicians have been only moderately successful at policing ourselves to appropriately use antibiotics. FDA should be given the authority to develop strategies to evaluate and ensure appropriate use of antibiotic where they are most needed and minimize antibiotic resistance. An HHS level internal group to

address issues related to antibiotic resistance would help strengthen ongoing efforts of the Inter-Agency Task Force.

Focusing the GAIN bill in the five ways I have just outlined will result in addressing the goal it sets out to achieve – developing new safe and effective drugs with an appropriate evidence base to positively affect patients' lives while limiting antibiotic resistance.