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April 9, 2012

Senator Tom Harkin
Chairman
U.S. Senate Committee on Health, Education, Labor, and Pensions
731 Hart Senate Office Building
Washington, DC 20510

Senator Michael B. Enzi
Ranking Member
U.S. Senate Committee on Health, Education, Labor, and Pensions
379A Russell Senate Office Building
Washington, DC 20510

Re: Senate HELP Committee discussion draft for proposal to incentivize new antibiotic development

Dear Senators Harkin and Enzi:

Public Citizen, representing more than 250,000 members and supporters nationwide, appreciates the opportunity to comment on the March 29 discussion draft of legislation amending the Federal Food, Drug, and Cosmetic Act to incentivize new antibiotic development that was prepared by the Senate Committee on Health, Education, Labor, and Pensions.

The draft legislation would provide drug companies with large financial incentives to develop new antibiotics and mandate that the Food and Drug Administration (FDA) review these drugs more rapidly. We have serious concerns about these proposals because these incentives would come at a significant price: an increase in health care costs to patients from the delayed entry of generic drugs into the market and a shifting of resources within the FDA away from the review of other drugs. More importantly, the legislation has the potential to promote the development of antibiotics that are ineffective and unsafe.

First, the language of the draft bill implies that test-tube and animal studies are adequate for a drug to fulfill an unmet medical need and be granted status as a "qualified infectious disease product." This implication is misleading and inaccurate because most drugs with promising test tube and animal data are not effective when studied in humans with infectious disease. This was demonstrated recently with the increased mortality from use of tigecycline for treatment of a number of serious, life-threatening infections despite promising test-tube and animal studies with this drug. It does not make sense to designate a drug as a "qualifying infectious disease product" — a status that cannot be revoked for any reason once granted — based on these preclinical studies when it is possible to show that these drugs are effective against infections due to resistant bacteria only through the conduct of adequately powered, well-designed human clinical

studies. Also, FDA approval of a drug based on positive results from clinical trials does not mean that the drug is effective against resistant bacteria, unless these trials were designed to show this in a specific population of patients with these resistant infections. The bill should clearly state that to be granted "qualifying infectious disease product" status, an antibiotic must be shown, through human clinical trials designed to evaluate this question, to fulfill an unmet medical need.

Second, the draft legislation would extend exclusivity and priority review to antifungal drugs in the absence of any evidence that these drugs need such incentives. The number of antifungal drug approvals for serious diseases has increased over the last decade, and antifungal drugs for serious diseases are prescribed for longer periods of time, often at costs of tens to hundreds of thousands of dollars per patient. The incentives in the legislation should be confined to those areas in which they are needed, namely antibacterial drugs.

Third, the list of organisms in the draft bill is not needed, and it facilitates unsubstantiated claims of efficacy without evidence from clinical studies. Incentives should be provided for drugs that offer additional benefits over existing therapies, regardless of whether or not the disease is due to resistant organisms. Many, if not most, patients die of infectious diseases due to "susceptible" pathogens. "Resistance" is defined based on test-tube data and is not based on worse clinical outcomes in patients. Again, the basis for approval should be demonstrating added benefits for patients rather than focusing on organisms.

Fourth, the proposed legislation should be revised to include provisions to promote the good stewardship and judicious use of antibiotics. This would address one of the most important causes of infections due to resistant bacteria: the rampant use of antibiotics by clinicians when they are not needed, which promotes resistance against existing, overused therapies. The draft legislation does nothing to counter the incentive for companies to sell more antibiotics and continue to promote antibiotic resistance. Rather, the bill creates incentives only for companies to develop and promote the use of more antibiotics.

Lastly, any discussions of the FDA with "medical experts" outside the FDA, as suggested in the draft bill, should be done through the Federal Advisory Committee Act, with appropriate controls for conflicts of interest. Meetings with these experts should be conducted in an open, public forum through the FDA advisory committee process.

Although the draft legislation would provide incentives for companies to develop new antibiotics, it does not address the unmet medical need of combating infections due to resistant bacteria for which existing therapies are inadequate. Patients have little to gain from this legislation and much to lose: They will be exposed to new, heavily marketed antibiotics that may seem effective in a laboratory setting but are ineffective in actual clinical care. We implore you to rework this bill to balance the financial incentives to companies with measures that benefit patients.

Thank you for your consideration of our comments regarding these important issues. We would welcome the opportunity to meet with your committee to further discuss our recommendations.

Sincerely,

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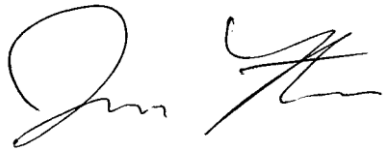

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