Testimony of

Dr. John Bartlett

October 6, 2004

Statement of the Infectious Diseases Society of America (IDSA) Concerning "BioShield II: Responding to An Ever-Changing Threat"
Presented by John G. Bartlett, MD
Before the U.S. Senate Committee on Health, Education, Labor, and Pensions and the U.S. Senate Committee on the Judiciary
October 6, 2004

Chairman Gregg, Chairman Hatch, Ranking Member Kennedy, Ranking Member Leahy, and Members of the Senate Committee on Health, Education, Labor and Pensions (HELP) and Senate Judiciary Committee, thank you for inviting the Infectious Diseases Society of America (IDSA) to present our views on the critical need for new drugs, vaccines and diagnostics to treat, prevent and detect infectious diseases agents. I am Dr. John Bartlett, chair of the IDSA Task Force on Antimicrobial Availability, Past President of IDSA, and Chief, Division of Infectious Diseases, Johns Hopkins University School of Medicine.

I am testifying today on behalf of IDSA to communicate our strong support for the creation of new legislation that will remove financial disincentives to antiinfective research and development (R&D) so that U.S. physicians will have the tools necessary to take care of very sick patients suffering from infectious diseases. New medicines and diagnostics are critically needed across all areas of infectious diseases medicine.

IDSA represents nearly 7,800 physicians and scientists devoted to patient care, education, research, and community health planning in infectious diseases. The Society's members focus on the epidemiology, diagnosis, treatment, prevention, and investigation of infectious diseases in the U.S. and abroad. Our members include researchers who study infectious microbes, including agents of bioterrorism as well as naturally occurring microbes. Our members also include scientists involved in the development of new pharmaceuticals and vaccines to control, prevent, and treat such infections. Also among our members are the ID clinicians who will be integrally involved should a bioterrorism event or spontaneous natural outbreak occur--an ID specialist discovered the anthrax case that occurred in Florida in 2001. ID clinicians care for patients of all ages with serious infections, including meningitis, pneumonia, tuberculosis, those with cancer or transplants who have life-threatening infections caused by unusual microorganisms, food poisoning, and HIV/AIDS as well as new and emerging infections, such as severe acute respiratory syndrome ("SARS") and West Nile virus. Housed within IDSA is the HIV Medicine Association ("HIVMA"), which represents physicians working on the frontline of the HIV/AIDS pandemic. HIVMA members conduct research, administer prevention programs and provide

clinical services to individuals with HIV disease. Together, IDSA and HIVMA are the principal organizations representing infectious diseases and HIV physicians in the United States.

As Senate leaders move forward to develop new legislation, commonly referred to as "BioShield II," IDSA and its members urge you to extend the new legislation's scope beyond pathogens designated as relevant to "bioterror" and apply any new incentives broadly to cover drugs, vaccines and diagnostics needed to treat all areas of infectious diseases, particularly antibiotics to treat antibiotic-resistant organisms. There is an inextricably linked, synergistic relationship between R&D efforts needed to protect against both natural occurring infections and bioterrorism agents. As such, we believe this approach makes perfect sense.

Let me be very clear from the start: IDSA is here today on behalf of patients. We are not here at the request of the pharmaceutical or biotechnology industries nor is our "bad bugs, no drugs" advocacy campaign financed in any way by industry.

Background

On July 21, 2004, the same day that President Bush signed "The Project Bioshield Act" ("Bioshield I"), IDSA issued its landmark report entitled, "Bad Bugs, No Drugs, As Antibiotic Discovery Stagnates, A Public Health Crisis Brews." Copies of that report are available here today. Our report calls attention to a serious public health problem--at the same time that emerging infections and antibiotic resistance are increasing, drug companies are withdrawing from antiinfective R&D. IDSA is particularly concerned about antibiotic R&D, an area in which many pharmaceutical and biotechnology companies have shown the least commitment in recent years, either withdrawing totally or seriously downsizing their dedicated resources and staff. Infectious diseases (ID) and HIV physicians on the frontline of patient care see patients every day who face lengthy hospitalizations, painful courses of treatment and even death because of drug-resistant and other infections. We desperately need new weapons to protect our patients.

Members of Congress are beginning to see the connection between naturally occurring infections and bioterrorism and understand our vulnerability. In their reports on "Bioshield I" in 2003, both the House Government Reform Committee and the Energy and Commerce Committee linked natural conditions, including antimicrobial resistance and dangerous viruses, to national security concerns. The Energy and Commerce Report stated "advancing the discovery of new antimicrobial drugs to treat resistant organisms ... may well pay dividends for both national security and public health."

Why Policymakers Should be Concerned

Policymakers have recognized the urgent need to spur R&D related to biodefense, which led to the enactment of "Bioshield I" earlier this year. While the concern about bioterrorism is highly appropriate, it is important to keep things in perspective. Not one American has died from bioterrorism since President Bush first announced "Bioshield I" in February of 2003, but drug-resistant bacterial and other infections have killed tens of thousands of Americans in hospitals and communities across the United States and millions of people across the world during that same short period of time.

Here are some important facts about infectious diseases reported by the World Health Organization and others:

? Infectious diseases are the second leading cause of death in the world and, by far, the leading cause of premature death and disability.
? Worldwide, 15 million deaths annually are caused by infectious diseases.
? Three of the biggest killers--HIV, tuberculosis (TB) and malaria--account for nearly 40 percent of deaths caused by infectious diseases (5.6 million deaths in 2001).
? Diarrheal diseases and respiratory infections are equally as deadly, accounting for 5.8 million deaths in 2001.
? Influenza accounts for 36,000 deaths and more than 200,000 hospitalizations in the United States and 250,000 to 500,000 deaths globally each year. A pandemic influenza outbreak could kill millions in the U.S. alone.
? "Neglected" infectious diseases that primarily affect the poorest populations living in remote areas of the world leave nearly 1 billion people with a lifetime of debilitating illnesses and deformities. These diseases include lymphatic filariasis (5.6 million disability life adjusted years [DALYs--the number of healthy years of life lost due to premature death and disability]), intestinal nematode infections (4.7 million DALYs), leishmaniasis (2.4 million DALYs), schistosomiasis (1.8 million DALYs), sleeping sickness (1.6 million DALYs), onchocerciasis (1.0 million DALYs), dengue (0.7 million DALYs), chagas disease (0.6 million DALYs), and leprosy (0.2 million DALYs). Despite this enormous disease burden, very few public or private resources have been devoted to research on these diseases.
? According to the Global Forum for Health Research, only about 10 percent of health research funding is targeted to diseases that account for 90 percent of the global health burden.

Here are some surprising facts about drug-resistant bacterial infections in the United States:

? Infections caused by resistant bacteria can strike anyone--the young and the old, the healthy and the chronically ill. Antibiotic resistance is a particularly serious problem for patients whose immune systems are compromised, such as people with HIV/AIDS and patients in critical care units.
? About 2 million people acquire bacterial infections in U.S. hospitals each year, and 90,000 die as a result. About 70 percent of those infections are resistant to at least one drug. The trends toward increasing numbers of infection and increasing drug resistance show no sign of abating.
? Resistant pathogens lead to higher health care costs because they often require more expensive drugs and extended hospital stays. The total cost to U.S. society is nearly $5 billion annually.
? The pipeline of new antibiotics is drying up. Major pharmaceutical companies are losing interest in the antibiotics market because these drugs simply are not as profitable as drugs that treat chronic (long-term) conditions and lifestyle issues.
? Resistant bacterial infections are not only a public health problem; they have national and global security implications as well.
? The Institute of Medicine and federal officials have identified antibiotic resistance and the dearth of antibiotic R&D as increasing threats to U.S. public health.

Emerging and Re-emerging Infectious Diseases

Market forces alone will not solve the current crisis in infectious diseases drug, vaccine and diagnostic R&D--that's why we need innovative public policy changes such as those that the Senate HELP and Judiciary Committees are now contemplating.

Robust R&D programs are needed to respond successfully to existing infectious diseases as well as new threats on the horizon. More than three-dozen new infectious diseases have been identified since the 1970s that have impacted the United States and more vulnerable countries. The list includes HIV/AIDS, severe acute respiratory syndrome (SARS), West Nile virus, Lyme disease, hepatitis C, a new form of cholera, waterborne disease due to Cryptosporidium, foodborne disease caused by E. coli 0157:H7, and a plethora of neglected diseases that primarily affect patients in the developing world.

Some of these diseases have no treatment except for supportive care. For diseases that do have effective treatments, complacency can stifle new research and allow us to be caught off guard when current treatments become less effective due to resistance. This has been the case with tuberculosis (TB). It has been 30 years since a new class of antibiotic was approved to treat TB despite the fact that it is the second most common microbial cause of death in the world. Doctors also are concerned about the rapid rate at which other bacterial infections, such as gonorrhea and syphilis, are becoming resistant to drugs. Finally, for diseases such as TB, AIDS, and malaria, which have notoriously complex and sometimes toxic treatment regimens, there is a substantial need for new drugs that are not only more effective but easier to deliver to the patient so that greater drug adherence and, ultimately, successful care and treatment will be achieved.

Antibiotic-Resistant Bacterial Pathogens: Why IDSA is Concerned

New treatments, preventions, and diagnostics are clearly needed in all areas of infectious diseases medicine. However, IDSA is particularly concerned that the pharmaceutical pipeline for new antibiotics is drying up. Infectious diseases physicians are alarmed by the prospect that effective antibiotics may not be available to treat seriously ill patients in the near future. There simply aren't enough new drugs in the pharmaceutical pipeline to keep pace with drug-resistant bacterial infections, so-called "superbugs." Antibiotics, like other antimicrobial drugs, have saved millions of lives and eased patients' suffering. The withdrawal of companies from antibiotic R&D is a frightening twist to the antibiotic resistance problem and, we believe, one that has not received adequate attention from federal policymakers.

Until recently, company R&D efforts have provided new drugs in time to treat bacteria that became resistant to older antibiotics. That is no longer the case.

A recent analysis published in the journal Clinical Infectious Diseases found only five new antibiotics in the R&D pipeline out of more than 506 drugs in development. The authors evaluated the websites or 2002 annual reports of 15 major pharmaceutical companies with a track record in antibiotic development and seven major biotechnology companies. Their analysis revealed four new antibiotics being developed by pharmaceutical companies, and only one antibiotic being developed by a biotech company. By comparison, the analysis found that the pharmaceutical companies were developing 67 new drugs for cancer, 33 for inflammation/pain, 34 for metabolic/endocrine disorders, and 32 for pulmonary disease. The biotech companies

were developing 24 drugs for inflammation/immunomodulators, 14 drugs for metabolic/ endocrine disorders, and 13 for cancer.

The end result of the decline in antibiotic discovery research is that the Food and Drug Administration (FDA) is approving few new antibiotics. Since 1998, only 10 new antibiotics have been approved, two of which are truly novel--i.e., defined as having a new target of action, with no cross-resistance with other antibiotics. In 2002, among 89 new medicines emerging on the market, none was an antibiotic.

The Institute of Medicine's (IOM) 2003 report on microbial threats reinforces the point, noting that although at first glance the situation with respect to antibiotics currently in clinical development looks encouraging, not one new class of antibiotics is in late-stage development. "Rather these 'new' antibiotics belong to existing classes, including macrolides and quinolones, that have been used to treat humans for years," IOM said.

Unfortunately, both the public and private sectors appear to have been lulled into a false sense of security based on past successes. The potential crisis at hand is the result of a marked decrease in industry R&D, government inaction, and the increasing prevalence of resistant bacteria.

IDSA has investigated the decline in new antibiotic R&D for more than a year, interviewing stakeholders from all sectors. We have met with officials from FDA, the National Institute of Allergy and Infectious Diseases (NIAID), the Centers for Disease Control and Prevention (CDC), congressional members and staff, executives from leading pharmaceutical and biotechnology companies, representatives from public-private partnerships that are focused on infectious diseases-related product development, patients, and other stakeholders. Based on our investigation, IDSA is convinced that the pharmaceutical and biotechnology industries are clearly best situated to take the lead in developing new antibiotics needed to treat bacterial diseases. They are the only player with a track record of success. Consequently, industry action must become the central focus of an innovative federal public health effort designed to stimulate antibiotic R&D.

Why Naturally Occurring Infections Should Be Included Within
"Bioshield II" & "Bioshield I"

IDSA strongly supports including all infectious diseases, and particularly antibiotics used to treat antibiotic-resistant organisms, within the scope of "Bioshield II." Research related to both naturally occurring infections and bioterrorism agents seeks to understand how these organisms cause disease, the immune system response to these pathogens, the development of drug resistance, and how antibiodies and medicines protect against them. As such, infectious diseases and bioterrorism countermeasure R&D are inextricably linked. In the end, we need antibiotics, anti-virals, and other drugs that can be utilized against a variety of diseases, and vaccines that can be adapted to a variety of organisms. Extending the scope of "Bioshield II" to include infectious diseases that are naturally occurring will enhance the research needed to develop bioterrorism countermeasures and vice versa.

We also urge that the "guaranteed market" provisions of "Bioshield I" be expanded to be applied to the development of all antibiotics, not just those intended to fight bioterror agents of present

concern. Antibiotic resistant organisms that currently threaten Americans in hospitals and communities can have future national and global security implications as well. Virtually all of the antibiotic-resistant pathogens that exist naturally today can be bio-engineered through forced mutation or cloning. In addition, genetic manipulation of existing pathogens could render them resistant to currently available antibiotics. A better understanding of the mechanisms related to drug resistance and tools that could be derived from such research may help U.S. public health officials as they monitor and respond to any future bioterrorism episodes that involve genetically engineered resistant pathogens. Thus, expanding the procurement provisions found in "Bioshield I" to antibiotics used to treat natural occurring bacterial infections will spur the development of new antibiotics that would provide benefits against naturally occuring infections and bioterrorism.

While "BioShield I" loosely could be applied to the development of antibiotics used to treat naturally occurring resistant organisms, it is not likely that such antibiotics will be listed as a priority of the Administration under "BioShield I." "BioShield I"-related funding mostly or entirely will be utilized for procurement of bioterrorism countermeasures where the government is the sole market. There is a substantial civilian market for antibiotics, with the government only a marginal player. In those cases, it won't be the government that is the principal purchaser. However, the government could contribute to and administer a pool of funds from federal and charitable sources that will make up the guarantee pool. Then it can add the tax, intellectual property, and other incentives from "Bioshield II" to make it all work. This approach would be consistent with our needs for bioterrorism preparedness and provide a much-needed benefit to our public health infrastructure.

Pharmaceutical Charity Helps, But Is Not the Solution

Some policymakers and members of the public place the onus on the pharmaceutical industry, saying that companies should act responsibly and ensure that new drugs and vaccines are available as needed. The pharmaceutical industry supports many good works pro bono. Some examples include Merck & Co.'s efforts related to River Blindness; efforts by Bristol-Myers Squibb, Pfizer, and other drug companies related to global AIDS; and GlaxoSmithKline's malaria and AstraZeneca's TB drug discovery initiatives. Nevertheless, companies are responsible to their shareholders and cannot alter their fundamental business strategies in ways that would place their bottom lines at risk.
Drug and vaccine R&D is expensive, risky, and time-consuming. As such, companies are most likely to invest in products for which a strong return on investment is likely, such as drugs that treat long-term, chronic illnesses, lifestyle issues, and products that benefit people in developed countries who can afford to pay for them. Most antiinfectives, particularly antibiotics, which are used for short durations (7-14 days), face restricted use to avoid the development of resistance, resistance limits effectiveness and profitability, etc.; vaccines; and medicines desperately needed in the developing world are being left out.

Policymakers and the public should have no illusions that future pharmaceutical charity will be sufficient to address the existing and emerging infectious pathogens that threaten U.S. and global health. Instead, IDSA believes the onus is on the federal government to lure industry to antiinfective R&D as a means to protect U.S. public health and strengthen national security.

Potential Solutions

IDSA's report, "Bad Bugs, No Drugs, As Antibiotic Discovery Stagnates, A Public Health Crisis Brews," offers a number of solutions for policymakers to consider, and builds upon several solutions included in the "Biological, Chemical, and Radiological Weapons Countermeasures Research Act" (S. 666), introduced by Senators Lieberman and Hatch in 2003. IDSA's investigation of the "bad, bugs, no drugs" problem has revealed that the solutions most likely to spur R&D within major pharmaceutical companies include those that provide financial benefits prior to a drug's approval (e.g., tax credits for R&D), commence at the time of approval (e.g., wild-card patent extension), reduce the costs of clinical trials (e.g., FDA flexibility concerning the evidence necessary to demonstrate safety and efficacy; NIAID-sponsored research to develop rapid diagnostics tests, screen candidates, etc.), and reduce companies' risks (e.g., liability protections). R&D at smaller biotechnology companies also could be stimulated through statutory and administrative changes. Specific recommendations for FDA and NIAID action may be found in IDSA's report.

Following is a list of potential legislative solutions that may help to spur R&D of drugs, vaccines, and diagnostics to treat, prevent, and detect bacteria, viruses, parasites, fungi and other infectious organisms. IDSA does not claim to possess all of the answers, but we believe a combination of the legislative solutions listed below will help. Critical priority incentives that we believe will have the greatest impact are indicated. Policymakers should use these recommendations to shape a framework for governmental action.

Commission to Prioritize Antimicrobial Discovery [CRITICAL PRIORITY]
Establish and empower an independent Commission to Prioritize Antimicrobial Discovery to decide which infectious pathogens to target using the legislative R&D incentives listed below.

Supplemental intellectual property protections:
? "Wild-card patent extension." [CRITICAL PRIORITY]
A company that develops and receives approval for a priority antiinfective could extend the market exclusivity period of another FDA-approved drug as long as the company commits to invest a portion of the profits derived during the extension period back into antiinfective R&D.
? Restoration of all patent time lost during FDA's review of and clinical trials undertaken related to priority antibiotics and antiinfectives
? Extended market and data exclusivity similar to what has been successfully implemented for pediatric and orphan drugs

Other potential statutory incentives:
? Tax incentives for R&D of priority antiinfectives [CRITICAL PRIORITY]
? Measured liability protections [CRITICAL PRIORITY]
? Additional statutory flexibility at FDA regarding approval of antibiotics and other antiinfectives, as needed
? Antitrust exemptions for certain company communications
? A guaranteed market similar to that provided in Bioshield I for priority antibiotics that target resistant bacterial and other antiinfectives, as appropriate

Establish similar statutory incentives to spur R&D for rapid diagnostic tests for targeted pathogens, which will help to reduce the cost of clinical trials

Potential statutory incentives of interest to small biopharmaceutical companies:
? Waive FDA supplemental application user fees for priority antibiotics and other antiinfectives
? Tax credits specifically targeting this segment of the industry
? Small business grants

Support synergistic partnerships that focus on infectious diseases medicines:
A growing number of international public-private partnerships are focusing on the discovery of medicines to treat infectious diseases in the United States and globally. Initiatives like the International AIDS Vaccine Initiative, the Medicines for Malaria Venture, and the Global Alliance for TB Drug Development offer promising opportunities to advance product R&D in areas that have languished in the past. Public-private partnerships have adopted business models that exploit the venture capital approach to investment in new product R&D. Such initiatives receive the bulk of funding from the public and philanthropic sectors. They involve for-profit partners by seeking in-kind contributions from industry. The commitment of U.S. public dollars for these and similar initiatives would take advantage of the entrepreneurial spirit possessed by many researchers and humanitarians.

In addition to funding public-private partnerships, policymakers should seriously consider ways to prompt companies to inventory their shelves for promising drug candidates that could be donated to the partnerships for development. Such candidates exist, and companies recently have shown some interest in donating them. This is not a current priority for companies, however, because the resources required would have to be diverted from other efforts.

Conclusion

The time for talk has passed--it's now time to act. The "bad bugs, no drugs" problem is growing more severe, and patients are suffering. Even if all of the incentives outlined in our testimony were implemented today, it likely would take 10 or more years for companies to move safe and effective new drugs, vaccines and diagnostics to market. The federal government must take decisive action now to address the burgeoning problem of infectious diseases, particularly the lack of antibiotics to treat resistant organisms.

Government-sponsored research and refinement of existing regulations, policies, and guidance can help to address the overall problem, fill in some of the gaps in drug, vaccine, and diagnostics development, and help to reduce the cost of discovery and development. Industry action, however, must remain policymakers' central focus. Policymakers must remove financial disincentives to antiinfective R&D as a means to stimulate pharmaceutical and biotechnology companies to invest in the discovery of tools to treat, prevent, and detect infectious diseases.

Specific to antibiotics, the past two decades of antibiotic development clearly have demonstrated that we no longer can rely on existing market forces to keep companies engaged in this area of drug discovery and development. Should additional companies' antibiotic R&D infrastructures be dismantled, it will take years to establish new programs--or this expertise could simply be lost forever. New antibiotics are desperately needed to treat serious as well as common infections.

The bacteria that cause these infections are becoming increasingly resistant to the antibiotics that for years have been considered standard of care, and the list of resistant pathogens keeps growing. It is not possible to predict when an epidemic of drug-resistant bacteria will occur--but we do know it will happen.

Drugs, vaccines and diagnostics also are needed across the spectrum of infectious diseases medicine. Conquering AIDS, TB, malaria, the neglected diseases found primarily in developing countries, and the next emerging infection will require renewed vision, creative policymaking and righteous action.

"Bioshield II" provides a critical opportunity to spur the development of new tools to protect Americans and the global community against the scourge of infectious diseases, particularly antibiotic resistant organisms, and bioterrorism. We urge congressional leaders to show bold leadership in creating this legislation and urge its quick passage.

We appreciate the opportunity to testify before the Senate Health, Education, Labor and Pensions Committee and Senate Judiciary Committee. We look forward to working with you in the coming months to develop federal legislation to spur the tools infectious diseases and HIV/AIDS physicians need to treat our seriously ill patients.

Thank you.