Letters

Antimicrobial Drug R&D

David M. Shlaes' excellent article ("New Antibiotics—Government Intervention Versus Market Forces, *Microbe*, February 2007, p. 56) underscores the urgent need to develop new anti-infective therapeutics. He emphasizes the importance of government incentives for pharmaceutical discovery and advanced development, and notes that until the creation of the Biomedical Advanced Research and Development Authority within the Department of Health and Human Services in December 2006, "none of the (federal) agencies (had) the specific competence or desire to become or to establish all those coordinated activities that are embodied within pharmaceutical companies (from basic science through manufacturing and marketing)." The need to coordinate pharmaceutical development through FDA licensure is addressed in the Department of Defense Chemical and Biological Defense Program (CBDP).

Within the CBDP, the Department of Defense (DOD) has launched the Transformational Medical Technologies Initiative (TMTI) as an innovative $1.5 billion biodefense program to develop broad-spectrum medical countermeasures, including antimicrobial agents, against biological weapons threats including intracellular bacterial pathogens, hemorrhagic fever viruses, and novel or genetically engineered pathogens. The program office incorporates pharmaceutical industry concepts, organization, and methods. Program management integrates all phases of product development, from early drug discovery through phase I clinical trials and new drug application. The TMTI goal is to submit at least two IND applications within five years with an ultimate goal of FDA licensure. This is the first DOD biodefense program to integrate early and advanced development into one office.

The TMTI staff is matrixed from both the Defense Threat Reduction Agency's Joint Science and Technology Office for Chemical and Biological Defense, providing expertise in early discovery and preclinical development, and the Joint Program Executive Office for Chemical and Biological Defense, providing expertise in advanced development and acquisitions. Team members bring experience from industry, academia, the National Institutes of Health, the Food and Drug Administration, and military biodefense and acquisitions programs.

Projects are executed through partnerships with private industry, academia, and federal laboratories. Products in development include small molecules and protein-based and antisense therapeutics. Strategies include the identification and targeting of highly conserved microbial genes and gene products, and host genes and pathways essential to microbial intracellular survival, replication, and pathogenesis; short-term enhancement of innate immunity; and the development of rapidly adaptable platform technologies that could be readily modified for use against novel pathogens. Although the primary market for TMTI-sponsored products will be federal biodefense stockpiles, there could be additional market incentives if products are broadly active against bacterial and viral infections encountered in hospital or community-based medical practice.

Although the TMTI effort has only recently been initiated (first contracts in 2006), we believe it provides an example of the vision, expertise, and capability needed within the federal government to coordinate the development of new anti-infective pharmaceutical products.

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David Shlaes wrote an interesting and important article about the reduced research activities in the pharmaceutical industry over the last couple of decades in regard to new antibiotic drug development for the treatment of infectious agents, including resistant pathogens (*Microbe*, February 2007, p. 56–67). He pointed out that a plan is needed to stimulate research in this area and discussed several scenarios, including the establishment of a governmentally owned pharmaceutical company, the offering of incentives to the private sector, or the development via market forces.

I read recently a related article that discussed the same problem but focused more on the ethics of antimicrobial drug development (A. E. Aiello, N. B. King, and B. Foxman, Am. J. Public Health **96:**1910–1914, 2006). The authors used the example of methicillin-resistant *Staphylococcus aureus* (MRSA) and discussed the different viewpoints of drug companies, the general public, as well as physicians and patients. Aiello et al. believed that an approach of treating antimicrobial drugs as a public good might serve us best in the long term in combination with public health prevention regarding infection control and management.

There is no doubt that we are in a crisis situation: On the one hand, antibiotics can help us maintain/restore public health and are thus "socially desirable products;" on

Correction

The recent Current Topics article on *Toxoplasma gondii* (*Microbe*, March 2007, p. 119) stated that *T. gondii* is the causative agent of cat scratch fever. This is incorrect; though *T. gondii* can cause disease in humans, *Bartonella henselae* is the causative agent of cat scratch fever. *Microbe* regrets the error.

the other hand, they are often considered by companies simply as "profit-generating products" that help corporations to survive. So, the big question is, what do we value most as a society? Should we put the emphasis more on what is socially desirable or on what has impact on profit generation? If we can answer this question, I believe we will find the most appropriate solution. We should not forget that the pathogens we try to control are not waiting for our solution; they will most certainly use every opportunity we give them to get the upper hand in the fight for survival.

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GenBank, RefSeq, TPA, and UniProt

At a recent workshop on microbial genomes held at the National Center for Biotechnology Information (NCBI) and attended by bacterial annotation groups, sequencing centers, and members of ASM, some attendees expressed confusion about the differences between several nucleotide and protein databases and requested that NCBI summarize these resources and their differences. NCBI has prepared a document in response. While there was some input from the European Bioinformatics Institute on UniProt and Swiss-Prot, the document represents an NCBI perspective. The document, "GenBank, RefSeq, TPA and UniProt: What's in a Name?," is available through the online edition of this issue.

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Vaccine Development and Production: Who Should Do It?

I am writing regarding the article entitled "Amid anthrax vaccine debacle, BARDA amends biodefense efforts" written Jeffrey Fox that appeared in the March 2007 issue of *Microbe*. I am a retired professor of microbiology of University of Louisville School of Medicine in Louisville, Ky., living in Florida.

It seems to me that there are many bacterial or viral infections for which vaccines or antitoxic sera can be produced, but production of such products does not make commercial sense because the number of patients are so small that producers will not make enough money to recoup the cost of research. In addition, there is always the possibility of litigation associated with clinical use of these products when some untoward reactions occur. This is the reason that commercial companies are not interested in producing these biological medicines or vaccines. I think the only way we can produce them is to have government laboratories produce them. Most of the socialist countries, such as Russia, China, and even Cuba, have government laboratories that produce these biological products. I am wondering why American government has to insist on having private, civilian laboratories producing these things.

I am the one who discovered the exotoxin of *Pseudomonas aeruginosa* that functions like diphtheria toxin. By around 1970 I realized that it was relatively easy to make antitoxin against this infection to save lives of patients. However, I could not find any company that would be interested in making this antitoxin. The reason was that there would not be much money to be made with such antitoxin and there was the possibility of litigation. Eventually I made contact with a Chinese bacteriologist at the Biological Products Institute (BPI) in Chengdu, China, to do this type of work. I visited the BPI in 1985 by an invitation of Dr. Shi-peng Wang. This institute is one of the six such institutes that produced all of the antisera and vaccine needed by people in China, and they were planning to build a few more to serve the underserved area in southern China. They also had another group of institutes that specialized in vaccines needed for animals. BPI was actually a city of about 5,000 population with its own police system, transportation system, housing and hospital for employees and schools for children of employees in addition to the production facilities that included a farm with thousands of animals. They were able to exports these vaccines and antisera to foreign countries, mostly to those countries in eastern Europe.

I also contacted a doctor in Cuba who works at the Finlay Institute, which specializes in the production of vaccines and antisera. I have been corresponding with her for almost 20 years and I am impressed by the fact that even a small country like Cuba has an institute specializing in production of vaccine and antitoxin while a big country like America, which is wasting hundreds of billions of dollars in a war in Iraq, does not have a laboratory specializing in the production of the type of vaccines and antisera that are commercially not profitable enough to be done by private companies. It seems to me that people in ASM ought to push for establishment of one such government laboratory to produce biological products that are not likely to be done by private companies.

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Lyme Disease

The article by Bernard Dixon in the March 2007 issue, p. 114, evoked a disastrous episode in the history of public health. As he recounted, a moderately efficacious vaccine against Lyme disease (as shown by two separate double-blind trials) was withdrawn by the manufacturer because of tepid recommendations by the Centers for Disease Control and Prevention (CDC) and the false beliefs of uninformed lay and medical people. Yet *Borrelia burgdorferi* continues to cause thousands of infections in the Northeast and Midwest regions of the United States, to say nothing of borrelial infections in Europe.

It is not surprising that vaccine manufacturers will not again touch the subject of Lyme disease unless the medical and public health community demands it. Since the withdrawal of the vaccine, a number of discoveries offer the possibility to improve the original product both with respect to efficacy and to the putative safety issues.

ASM should urge other organizations to act on this otherwise ignored problem.

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Author's note: Sanofi Pasteur does not have a Lyme disease vaccine, nor does it intend to develop one.