

## As 'superbug' rises, new antibiotics fall

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BY ROBERT COHEN

WASHINGTON -- As concerns have grown about the increase in drug-resistant and potentially deadly bacterial infections, the pharmaceutical pipeline for new antibiotics has been drying up.

Faced with high research costs and greater profits to be made from other types of medications, many big pharmaceutical companies began abandoning the field of antibiotic development years ago. This has resulted in a significant slowdown in the introduction of new antibiotics now needed to protect the public health.

"Right now, the outlook is grim. We have hit rock bottom. There are not enough drugs for our current needs," said Brad Spellberg, an assistant professor at the UCLA School of Medicine and an infectious-disease specialist. "The consequence is that we will increasingly see drug-resistant infections we can't treat."

The "superbug" issue has been in the headlines lately with reports about the virulent and often drug-resistant bacterium known as methicillin-resistant *Staphylococcus aureus*, or MRSA. The Centers for Disease Control and Prevention reported about 19,000 people died in 2005 from MRSA, and about 95,000 were infected -- with the most serious problems occurring at hospitals, nursing homes and showing up in schools.

The Infectious Diseases Society of America, an organization of physicians, scientists and health-care professionals, said the concern has been building for some time, and involves not only worry about MRSA but about other strains of bacteria for which there are no treatments.

According to the society, there were 16 new antibiotics approved by the Food and Drug Administration between 1983 and 1987, and 14 between 1988 and 1992 -- an average of three a year. Those numbers have been steadily dwindling in the past 15 years, with only five new antibiotics -- an average of one a year -- winning approval between 2003 and today.

The group said companies with track records in antibiotic research and development have been withdrawing from the market, including Aventis, Abbott Laboratories, Bristol-Myers Squibb, Eli Lilly, Proctor & Gamble, Roche and Wyeth.

Laura Hortas, a spokeswoman for Bristol-Myers Squibb in Princeton, said the company "decided not to continue research and development efforts in antibiotics based on an assessment of their commercial profile, as well as the ongoing transition of the Bristol-Myers Squibb pharmaceutical strategy to a specialty-driven focus."

"Certain existing antibiotics in the Bristol-Myers Squibb portfolio continue to be commercialized in various regions of the world," she said. "The company continues to focus on infectious disease through our intensive commitment to fighting HIV/AIDS."

### LONG WAITS

A spokesman for Madison-based Wyeth said the company received approval in 2005 for the antibiotic Tygacil to treat a range of bacterial infections, and despite assertion by the Infectious Diseases Society, is "continuing to do research in anti-infectives." The spokesman said Wyeth has one new compound, as well as a vaccine, in the early stages of development, meaning it could be a very long time before they are available if proven safe and effective.

Johnson & Johnson received approval last month for Doribax, an antibiotic for complicated urinary tract and other infections, and is awaiting FDA approval for Cefto biprole, an antibiotic to treat diabetic foot infections, including some caused by MRSA.

"We remain dedicated to the area of anti-infective research," said Amy Firsching, a spokeswoman for New Brunswick-based Johnson & Johnson.

Ken Johnson, the senior vice president for the Pharmaceutical Research and Manufacturers of America, a major industry trade group, said there are 61 vaccines in the pipeline to help treat patients suffering from infectious diseases, and 34 antibiotic treatments in development. Many of these antibiotics are years away from being considered for approval by the FDA.

## **HIGH COSTS**

For drug companies such as Johnson & Johnson, Bristol-Myers and Wyeth, it takes hundreds of millions of dollars, years of difficult research and costly clinical trials to develop new medications and bring them to market.

Since antibiotics tend to work well and are not generally used repeatedly by individuals or for long periods of time, they do not have as large a market as drugs used to treat chronic, long-term conditions, and therefore cannot achieve the profit margins desired by the companies.

The inevitable development of resistant strains of bacteria also tends to limit the long-term use of most antibiotics. At the same time, doctors often recommend against frequent use of the most highly effective antibiotics in hopes of saving them for the most serious situations when other alternatives are not available, further eroding the profit potential.

In addition, the FDA has set a high burden of proof for antibiotics, making the approval process difficult.

## **REAL THREATS**

A number of small biotech companies have been seeking to fill some of the gaps, but experts such as David Perlin of the Public Health Research Institute of New Jersey said involvement of the big companies is critically important because the development costs are "so expensive that they almost always have to have Big Pharma as a partner to pay for it."

"This is not yet a public-health emergency, but the threat is real, and we have to take it seriously and really have to address this in a way that allows us to be proactive in avoiding a catastrophe down the road," Perlin said.

Perlin said "the science is complex" and "the easy targets are not there." He said a comprehensive strategy is needed, including new scientific approaches, more FDA flexibility, changes in way the antibiotics are used by doctors, better infection controls and new federal economic incentives for drug makers.

Rep. Mike Ferguson (R-7th Dist.) said during the negotiations over the recently approved FDA user fee and drug safety bill, a House proposal to increase the patent life for breakthrough antibiotics was removed at the insistence of the Senate.

The New Jersey congressman said there "doesn't seem to be political will in the Senate to offer that kind of incentive."

Ferguson and Rep. Jim Matheson (D-Utah) have offered a different approach, including legislation that would create a federal office to coordinate the activities of agencies involved in drug resistance, collect data on antibiotic use and improve current surveillance efforts. In addition, the bill calls for a federal strategic research plan for drug resistance.

Ferguson said the measure, also introduced in the Senate, takes "common sense steps," with a focus aimed at prolonging the life of existing drugs and spurring development of new drugs through coordinated research efforts.