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New agency would bolster biodefense

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After two years of delays, Congress is poised to pass biodefense legislation next month that would create a new federal agency to speed development of drugs for an array of infectious diseases that are bioterror threats.

That prospect has scientists and biotechnology entrepreneurs anticipating a resurgence of government-sponsored research that could significantly benefit the pub lic by producing drugs that counter not just a single biological threat, but whole classes of viruses as well, from anthrax and Ebola to influenza and hepatitis.

The bill that would establish the Biomedical Advanced Research and Development Authority, or BARDA, was passed unanimously by the Republican-controlled House of Representatives in September. The Senate's new Democratic majority leader, Harry M. Reid of Nevada, has called the legislation a priority for the December lame-duck session of Congress.

The broader social implication of BARDA, and its proposed $1 billion fund, is the promise of breakthroughs in the treatment of infec tious diseases, research that pharmaceutical companies have largely abandoned in the past two decades.

"It's sort of taken bioterrorism to wake us up to the fact that in fectious diseases are a real problem," said Iain Hay, a microbiolog ist at the University of Buffalo's New York State Center of Excel lence in Bioinformatics and Life Sciences.

"They're not funding us for research into the common cold, but the technology we're developing for exotic diseases could be used for the more common diseases," he said. "While the investment is coming from anti-bioterrorism funding, there is a benefit for the man or woman on the street."

It is particularly significant in light of the fact that hundreds of diseases, many of them zoonotic (passed from animals to humans), are emerging for the first time, or are re-emerging in new places, sometimes in more virulent forms.

A SLUGGISH PIPELINE

But progress in designing drugs to counter potential biological weapons has been slow. Vaccines in particular are enormously complex to design, take years and hundreds of millions of dollars to bring to the market and have limited use. Cur rently, there are only four major vaccine manufacturers left in the world. In 1967 there were 26.

"Development of countermea sures (drugs to treat bioterror pathogens) is unattractive to private investors because there are no markets outside of governments for most of these products," Tara O'Toole, a medical doctor and biosecurity expert, told a congressional committee earlier this year. These drugs, she said, "cannot generate profits comparable to successful medicines for chronic diseases."

The Project Bioshield Act, passed in 2004, was Congress' first attempt at encouraging the pharmaceutical

industry to develop medicines to treat bioterror pathogens, but its $5.6 billion fund was used primarily to procure drugs that already had made their way through the development stage.

BARDA is meant to help bridge that "death valley" gap between drug discovery and market by pumping much-needed cash into small research compa nies. The legislation had stalled, however, over clauses exempting BARDA from disclosure require ments under the Freedom of Information Act. Those stipulations were dropped when the bill was reintroduced, and passed, two months ago.

COMMON GROUND

"At this point, the policy issues are narrowed down to a core that everyone agrees is good," said Brad Smith, a microbiologist and senior associate at the Center for Biosecu rity, University of Pittsburgh Medical Center. "I think it could be approved in December."

If passed by the Senate and signed by President Bush, BARDA will become an office under the Department of Health and Human Services, which already spends $4.2 billion a year to address bioterror threats.

Another main contributor to government bioterrorism research is the Defense Threat Reduction Agency. Part of the Department of Defense, the agency has a $2.6 billion annual budget, most of which goes to intelligence regarding weapons of mass destruction and to combat support. A portion, however, goes to technology development, including medical defenses against biological weapons.

In the past month alone, the agency awarded at least a half- dozen contracts to small biotech companies to develop either antibiotics or antivirals that are broad-spectrum, meaning they are capable of working against a wide variety of germs. Among them: PTC Therapeutics in South Plainfield ($17.2 million), Achaogen in San Francisco ($24.7 million) and Microbiotix Inc. in Worcester, Mass. ($5.06 million).

"In addition to funding research in the traditional academic areas, the agency also supports 'high-risk, high payoff' ideas, novel collaborations and numerous projects that may seem like science fiction today, but which we'll take for granted tomorrow," said Irene Smith, spokesperson for the Defense Threat Reduction Agency.

Among those novel collabora tions is the nonprofit Calspan- University of Buffalo Research Center and a small San Francisco-based medical therapeutics company called Prosetta. Earlier this month, the Defense Threat Reduction Agency awarded the team a grant of $8.5 million to develop radically new broad-spec trum antiviral therapies to treat hemorrhagic diseases such as Ebola, Marburg and Rift Valley fever, which represent major bioterrorism threats.

CURES REMAIN ELUSIVE

It has been particularly difficult to find treatments for these diseases because they are viruses, far simpler than bacteria and therefore presenting fewer avenues for disruption. Viruses are known as zom bies -- not quite alive, but not exactly lifeless, either. In essence, vi ruses act like parasites, invading cells and taking over their energy- producing machinery in order to survive and replicate. Until re cently, scientists did not understand how a virus, once inside a cell, built the protective cover, called a capsid, that allows it to continue to flourish.

"The capsid is the house; it's made up of building blocks of proteins," said Davis. "If the virus doesn't have a house, it isn't effective -- it's just a piece of nucleic acid. The whole idea is to produce new antivirals that are active not just against a single virus, but maybe against a whole class of vi ruses, by interrupting capsid formation."

Such an antiviral could prove effective not only against, say, Ebola, but also influenza, herpes, hepatitis -- even the common cold.

"A key feature of strategy for HHS is to move from fixed defenses, what's called 'one bug, one drug,' to flexible defenses," said Smith. "This is a reflection of what a lot of people have been saying about how to develop new drugs and vaccines. The only way out of (the bioterror threat) is to make a broad defense against a wide array of infectious diseases both here and outside the U.S. -- that's our vision of victory."

Davis believes that since the anthrax attack in the U.S. in 2001, in fectious diseases are finally getting the attention they deserve.

"We went to sleep," he said, "but now, strangely, by looking at the biological threat, we've finally woken up."

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