Table 1 Anthrax countermeasures in development

Company	Product	Stage of development	BARDA contract
Human Genome Sciences	ABthrax (raxibacumab), a human mAb against anthrax protective antigen (PA)	Biologic license application	$151 million
Emergent BioSolutions	AV-7909, a combination of BioThrax (aluminum-adsorbed cell-free filtrates of unencapsulated *Bacillus anthracis*) and Coley Pharmaceutical's VaxImmune (an unmethylated CpG-motif oligonucleotide that acts as an agonist of Toll-like receptor 9)	Phase 2	$447.6 million
	Anthrax immune globulin (AIGIV), polyclonal antibodies raised against BioThrax	Phase 1/2	$13 million
Elusys Therapeutics	Anthim (ETI-204), a humanized mAb against PA	Phase 1	Up to $143 million
PharmAthene	SparVax, an injectable rPA absorbed on to hydrogel	Phase 2	$3.9 million NIAID
DynPort Vaccine	Anthrax vaccine, an injectable rPA vaccine	Phase 1	NA
Medarex, a subsidiary of Bristol-Myers Squibb	Valortim (MDX-1303), a fully human mAb against PA	Phase 1	$1 million from the US Department of Defense (DoD) payable to partner PHarmAthene
Advanced Life Sciences	Restanza, a once-daily oral ketolide cethromycin that inhibits *B. anthracis* protein synthesis	Preclinical	$3.8 million from DoD

Sources: Sagient Research, BiomedTracker and BARDA. NA, Not available.

Even with government support, PharmAthene and other companies working under biodefense contracts face the stark reality of drug development: 30% of all candidates that reach phase 3 clinical trials within the eight-year BARDA procurement time are likely to fail. According to some policy experts, this ought to be a good reason for the government to contract with large pharmaceutical companies. "There's a systemic problem, which is that most of the contracts for developing new biodefense measures are with small biotech companies," says Gregory Koblentz, an assistant professor at George Mason University and deputy director of the Biodefense Graduate Program, "and these companies tend to be undercapitalized, understaffed and don't have the depth and breadth of experience to take a drug from the research and development phase through clinical trials, scale-up to large-scale production and licensure."

But pharma has so far has been notably absent from biodefense contract competitions. One possible explanation is the perception that government is a bad customer. At least this was the experience for Bayer (Leverkusen, Germany) during the anthrax attacks of 2001. As the demand for Bayer's antibiotic Cipro (ciprofloxacin) soared, a faction led by Senator Charles Schumer (D-NY) suggested that the government should use existing law to issue a compulsory purchase order suspending Bayer's patent. This would have allowed other manufacturers to make generic Cipro and charge a lower price. In the end, this threat was never enacted, and experts doubt it could have been under the circumstances. However, the incident is well remembered (and resented) and raises the question of whether any company with a patent covering an important bioterrorism countermeasure could risk its patent being threatened at a later date.

For the US government, anthrax treatment remains a critical element in its biodefense strategies. Emergent Solutions currently manufactures the only approved vaccine for anthrax based on protective antigen (PA). This is an older 'legacy' vaccine and, although considered safe and effective, requires six injections over 18 months to be fully effective. The hope for the next-generation, or rPA, anthrax vaccines is that they will provoke a stronger immune response and not require such a cumbersome vaccination schedule. Antibiotics and therapeutics are also important pieces of the anthrax countermeasure puzzle because an anthrax infection has different phases and because it can be so rapidly lethal. Antibiotics are effective against active bacterial infection, for example, but not spores and not a late-stage infection.

Emergent BioSolutions is responding to the withdrawn RFP by refocusing on development of its original anthrax vaccine (BioThrax; aluminum-adsorbed cell-free filtrates of unencapsulated *Bacillus anthracis*), seeking FDA approval for a modified, four-dose regimen. Meanwhile, the company's $400 million procurement contract with the Centers for Disease Control and Prevention of Atlanta, Georgia, to manufacture and deliver 14.5 million doses of BioThrax for the strategic national stockpile remains unchanged. "This is just one of many starts and stops along the way that we've seen in the past four years. We understand that process well, as we have been a player in this space for more than a decade," says Daniel Abdun-Nabi, president and COO of Emergent BioSolutions.

The BioShield budget announced last month is more flexible than those of previous years, as it can allocate resources for R&D and for companies running projects at early stages of development. But there is no ready market for biodefense countermeasures other than the government. As Elizabeth Posillico, president and CEO of Elusys, points out, "There's one customer and the company has little control over the decision to purchase the drug. It's not driven by the market so much as the customer's needs." So chasing government contracts alone, however lucrative, will continue to be a risky strategy for biotech.

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Ride 'n Drive on government waste

Danish enzyme manufacturer Novozymes invited journalists to burn up official waste by taking a spin on the flex-fuel Chevy HHR truck at the Washington Auto Show in January. The engine was powered by paper discarded by White House offices.

Novozymes