nature biotechnology

US biodefense—shocking and awful

Almost six years after the anthrax attacks, the US BioShield Program has singularly failed to add new products to the nation's stockpile.

Last month, the US Food and Drug Administration's (FDA) Vaccines and Related Biological Products Advisory Committee declared Acambis's modified vaccinia Ankara smallpox vaccine safe and efficacious. This makes somewhat baffling the US Department of Health and Human Services' (DHSS) decision to cancel Acambis's BioShield contract six months earlier. But then baffling decisions have become the signature of BioShield, a biodefense procurement program synonymous with bureaucratic backtracking, political opportunism, poor accountability, cronyism and fiscal mismanagement. If the US government truly still harbors aspirations to attract interest from industry, the recently created Biodefense Advanced Research and Development Authority (BARDA) must act swiftly and decisively to communicate its vision and ensure consistent decision-making across BioShield.

The Pandemic and All-Hazard Preparedness Act passed by the US Congress last December mandates the reorganization of the $5.6 billion BioShield program and its oversight by the new agency, BARDA. As a further incentive to industry, the Act also contains an indemnity clause that would protect any companies participating in Bioshield from personal injury litigation. BARDA's mission is to coordinate biodefense efforts and provide bridge funding to span the so-called 'valley of death' between basic research spending (the province of the US National Institute of Allergy and Infectious Disease; NIAID) and product procurement (supported by BioShield). Ostensibly to safeguard the nation's vulnerabilities, BARDA will operate outside the Freedom of Information Act, which does not bode well for increased transparency or accountability.

One of the first tasks BARDA will face is to make sure the past mistakes of BioShield are not repeated. And there have been many.

For vaccine procurement in particular, poor communication between DHSS officials and companies under contract, internal politics, government personnel turnover and external pressures have prompted abrupt changes in contract terms, often for projects in midstream and full swing. In some cases, shifting goalposts have led to cancelled contracts, leaving companies bewildered, or worse, bankrupt.

A case in point is the first ever BioShield contract, which was awarded to VaxGen in November 2004. The company was contracted to manufacture 75 million doses of a recombinant anthrax vaccine that would supplement the existing stockpile—a vaccine that is a crude filtrate of attenuated *Bacillus anthracis,* manufactured by Emergent BioSystems (formerly BioPort).

Things started going south for VaxGen when FDA identified problems with the stability of its vaccine, causing the firm to miss several contract deadlines. These problems were seized upon by Emergent, which subsequently pumped millions of dollars into a campaign to smear VaxGen's credentials and boost the prospects of its own 1950s'-era anthrax vaccine. The upshot of all this was the purchase by DHSS of an additional five million doses of Emergent's vaccine in May 2006 and ultimately the termination of VaxGen's contract last December.

In March, DHSS cancelled the contract of another biotech company, Hollis Eden Pharmaceuticals. The official line was that the firm's lead candidate (Neumune; 5-androstenediol)—intended to treat acute radiation syndrome—was "technically unacceptable" and "no longer competitive." This was a surprise to Hollis Eden executives, however, as DHSS had designated the proposal "within competitive range" as recently as October 2006 and had not requested any additional safety or efficacy data in the interim. According to DHSS insiders, the panel of scientific experts in charge of the request for proposals on radiation remedies kept going back and forth revising the criteria, until earlier this year, it decided to scrap the entire proposal and start again.

Such shifting decisions affect lives and livelihoods. Within weeks of the VaxGen cancellation, the company had replaced its chief executive, dispensed with its stake in a Korean manufacturing facility and fired half of its staff. Similarly, termination of Acambis's vaccine contract last November was followed by a management overhaul and the layoff of 15% of its staff.

Little wonder then that biotech firms are wary of getting involved.

If BARDA is to have any hope of reinvigorating BioShield, a first priority should be to draw up a clear and standardized pathway for how biologic countermeasures should be developed, indicating the exact role in the process of such agencies as the FDA and NIAID.

It must also clarify the rationale for the few contracts granted so far—only a fraction of the $5.6 billion allocated to BioShield has actually been awarded—and failing that for grants going forward. The fact that contracts were awarded to several companies with no experience in manufacturing raises questions about the competency of BioShield administrators.

Most of all, BARDA needs to articulate a clear vision for BioShield. Nearly three years after the latter's inception, it is still not clear whether the aim is to stockpile existing vaccines and therapies, optimized versions of old vaccines or entirely novel agents against unmet needs, such as Marburg or Ebola virus. Is the emphasis on stockpiling a few doses of agents against every possible biological threat, on gathering agents that could protect the entire populace against the most common bioterrorism agents or on providing broad-spectrum agents that could also benefit public health as a whole, which would likely save many more lives?

In other words, what's the plan? Industry insiders tell us that they can't get answers to these questions—of course it's difficult to get answers when no one appears to be in charge.

As of this writing, BARDA has not appointed a director. And without an influential director in place—someone with the necessary clout and resources to coordinate the unwieldy US biodefense complex—it is difficult to see much progress being made.

To paraphrase President Bush, it's hard work to protect the US against all that might harm it. But almost six years after 9/11, it's long past time to have a coherent plan.