Hazardous microbe rules raise biosecurity debate to a new level

Even before the fatal anthrax mailings in 2001 were traced to a government lab worker, US regulators had been grappling with how to change to the rules governing research with dangerous pathogens so as to keep hazardous agents out of the hands of would-be bioterrorists. One solution, suggested last month by an intergovernmental working group, is for biological agents considered to have high potential as weapons to be stratified on the basis of risk.

The group's report, released on 7 January, recommended dividing the current list of 'select agents'—which contains 82 pathogens and toxins—into several tiers of security. The working group found that such a tier system would further research on agents judged to be less of a threat by requiring less bureaucracy and fewer costly security measures. Simultaneously, it would encourage research institutions to focus more resources on agents with the greatest potential for harm.

"What everyone seems to recognize is that not all of these agents are created equal," says working group co-chair Carol Linden, the principal deputy director of the US Biomedical Advanced Research and Development Authority. "Right now, there is a somewhat blanket approach to security for everything. That isn't necessarily providing the best security for the most dangerous agents; meanwhile, it's needlessly preventing important work on others."

The panel does not recommend a specific grading system; instead, it calls for one to be created through a collaborative effort between the government agencies that currently regulate select agents and public agencies such as the National Academy of Sciences (NAS) and the American Society for Microbiology.

However, legislation that is currently awaiting a vote in the Senate has proposed a three-tiered security system, with the most hazardous agents regulated as potential weapons of mass destruction by the Department of Homeland Security. Although the legislative move to refine the list is widely applauded, this highest level of security has caused concern among many scientific organizations.

"It's a mistake to treat these agents like nuclear weapons," says Gerald Epstein, a security policy expert at the American Association for the Advancement of Science (AAAS) in Washington, DC. Rather than adding additional safety gauges, he says, the Senate's proposed oversight system would mainly impede research by adding unnecessary costs and red tape.

In November, the AAAS sent an open letter to the senators who sponsored the bill, calling on the government to work within its existing framework while attempting to foster a network and culture of self-regulation similar to the US National Institutes of Health's biological surety program, which covers all personnel who work in biosafety level 4 laboratories.

"What is important is to move the burden of responsibility away from a static list and toward real-time evaluation and judgment," says David Relman, an infectious disease researcher at Stanford University School of Medicine in California who chairs the NAS forum on microbial threats. Last month, Relman coauthored a perspective article arguing that the select agents list, in its current incarnation, hinders research into vaccines and therapeutics, thereby making society more vulnerable to biological attacks and natural epidemics (*Nat. Rev. Microbiol.* **8**, 149–154, 2010).

A list of dangerous agents is inherently flawed, Relman says, in part because pathogenic strains vary greatly, even within a single species. What's more, they can be genetically altered to either be dangerous or benign. Instead of a rigid classification scheme, systematic ways of evaluating the potential danger of organisms on a case-by-case basis need to be developed, he adds.

"The truth is that we're doing our best—a more intelligent, stratified list is a step in the right direction," he says. "We don't have the technology or the knowledge right now to evaluate everything we work with, but that's a goal worth working toward."

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Slump in UK trials blamed on strict rules

Britain's historically strong role in clinical trials seems to be diminishing. Slow returns on drug investment and poor relations between industry and the UK National Health Service (NHS) have been cited as two reasons for this decline.

The slump has occurred despite more funding. Pharmaceutical investment in the UK between 1999 and 2007 grew from £2.5 billion ($4.4 billion) to £4.5 billion—jumping from 22% to 28% of Britain's total industry research and development investment, according to the Association of the British Pharmaceutical Industry. Kent Woods, chief executive of the UK's Medicines and Healthcare products Regulatory Agency, said in a statement that the annual number of applications to run UK clinical trials has remained between 1,000 and 1,200 in recent years and that rejection rates have remained stable at 1–2% a year.

But the UK's share of global clinical trials shrank from 6% to 2% from 2000 to 2006, according to figures provided to the country's Department of Health by the Centre for Medicines Research, a British consultancy. And the Medicines and Healthcare Products Regulatory Agency has now said that the total numbers of commercial clinical trial applications in 2007, 2008 and 2009 were 853, 979, and 759, respectively.

Industry criticism is nothing new. A decade ago, an industry figure accused the NHS of becoming a "less attractive place" for trials (*BMJ* **321**, 1041, 2000). The ability to conduct trials in cheaper markets lacking the UK's strict patient protection rules accounts for much of the market loss, says Andrew Smith, editor of *Clinical Research focus,* published by the Institute of Clinical Research. UK agencies are testing improvements meant to speed up their trials.

British rules governing medical research began tightening after pathologist Dick van Velzen of the Alder Hey Children's Hospital was caught ordering the removal of dead infants' organs without relatives' consent.

International rules such as the 1997 International Conference on Harmonization Good Clinical Practice guidelines and the 2004 EU Clinical Trials Directive also tightened trial protocols. These rules, although delaying and raising the cost of clinical trials, "have made it much harder to conduct poor-quality research, a publicly desirable outcome," Smith says.

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