

## Globalization and Biosecurity

A common argument since the terrorist attacks in New York and Washington, D.C., on September 11, 2001, is that while economic globalization brings enhanced efficiency, this comes at the cost of greater vulnerability to terrorism. Audrey Kurth Cronin maintains, "The current wave of international terrorism, characterized by unpredictable and unprecedented threats from nonstate actors, not only is a reaction to globalization but is facilitated by it."<sup>1</sup> "It would be naïve to assume," says Cronin, "that what is good for international commerce and communication is not also good for international terrorists."<sup>2</sup> Similarly, Kurt Campbell contends, "Much has been written about the forces of globalization—the relentless expansion of market forces and the constant search for greater economic efficiencies. . . . Many of the things that have left Western societies vulnerable to terrorist attacks are the very efficiencies that have come as a consequence of the relentless search for efficiency and the maximization of productivity, by person, companies, and countries."<sup>3</sup> Stanley Hoffman argues that Islamic terrorism is partly fueled by "a resistance to 'unjust' economic globalization. . . . Insofar as globalization enriches some and uproots many, those who are both poor and uprooted may seek revenge and self-esteem in terrorism."<sup>4</sup>

This perspective is not just wrong; it is also dangerous. Economic globalization is a double-edged sword: It has the potential both to enhance and to reduce the terrorist threat simultaneously. It is crucial to reduce the number of vulnerabilities associated with economic globalization, such as by developing

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1. Audrey Kurth Cronin, "Behind the Curve: Globalization and International Terrorism," *International Security*, Vol. 27, No. 3 (Winter 2002/03), p. 30.
  2. *Ibid.*, p. 51.
  3. Kurt Campbell, "Globalization at War," *Washington Post*, October 22, 2001, p. A19; see also Kurt Campbell, "Globalization's First War?" *Washington Quarterly*, Vol. 25, No. 1 (Winter 2002), p. 10.
  4. Stanley Hoffman, "The Clash of Globalizations," *Foreign Affairs*, Vol. 81, No. 4 (July/August 2002), p. 112.
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more rigorous border inspection procedures.<sup>5</sup> Yet it also must be recognized that many of the most effective tools for dealing with the terrorist threat are themselves partly the products of globalization. Many scholars now focus on the potential need to restrict economic globalization to reduce the terrorist threat.<sup>6</sup> In contrast, we argue that globalization presents opportunities, not just challenges, in the effort to deal with international terrorism.

In this article, we show that the full range of effects of economic globalization need to be considered when examining the bioterrorist threat and how best to respond to it. Improving defenses against a biological weapons (BW) attack is a principal security issue facing the United States and the world in the twenty-first century.<sup>7</sup> Even before the anthrax attacks in the fall of 2001, there was a growing understanding within the security and global health communities that pathogens pose a threat equal to, if not greater than, military might.<sup>8</sup> Biological weapons offer a relatively inexpensive and surreptitious method of inflicting mass casualties.<sup>9</sup> As one recent analysis concludes, "Biotechnology is one of only two technologies that truly deserve the label 'agent of mass destruction' and it is by far the more accessible of the two."<sup>10</sup> Given the difficulties of policing their proliferation or tracing their source once deployed,

5. See Stephen E. Flynn, "America the Vulnerable," *Foreign Affairs*, Vol. 81, No. 1 (January/February 2002), pp. 60-75; and Stephen E. Flynn, "Beyond Border Control," *Foreign Affairs*, Vol. 79, No. 6 (November/December 2000), pp. 57-68.

6. See, for example, Richard Betts, "The Soft Underbelly of American Primacy: Tactical Advantages of Terror," *Political Science Quarterly*, Vol. 117, No. 1 (Spring 2002), p. 30.

7. See, for example, David F. Gordon, Lt. Col. Don Noah, and George Fidas, "The Global Infectious Disease Threat and Its Implications for the United States," National Intelligence Estimate 99-17D (January 2000); William S. Cohen, *Annual Report to the President and the Congress* (Washington, D.C.: U.S. Department of Defense, April 1997); Richard A. Falkenrath, Robert D. Newman, and Bradley A. Thayer, *America's Achilles' Heel: Nuclear, Biological, and Chemical Terrorism and Covert Attack* (Cambridge, Mass.: MIT Press, 1998); Andrew T. Price-Smith, *The Health of Nations: Infectious Disease, Environmental Change, and Their Effects on National Security and Development* (Cambridge, Mass.: MIT Press, 2001); Jessica Stern, "Dreaded Risks and the Control of Biological Weapons," *International Security*, Vol. 27, No. 3 (Winter 2002/03), pp. 94-99; and Gregory Koblentz, "Pathogens as Weapons: The International Security Implications of Biological Warfare," Ph.D. dissertation, Massachusetts Institute of Technology, forthcoming.

8. See, for example, Gordon, Noah, and Fidas, "The Global Infectious Disease Threat and Its Implications for the United States"; Cohen, *Annual Report to the President and the Congress*; Falkenrath, Newman, and Thayer, *America's Achilles' Heel*; and Price-Smith, *The Health of Nations*.

9. According to one study, 100 kilograms of aerosolized anthrax is sufficient to cause 3 million deaths in a densely populated area. Office of Technology Assessment, *Proliferation of Weapons of Mass Destruction: Assessing the Risks*, OTA-ISC-559 (Washington, D.C.: U.S. Government Printing Office, 1993), p. 53.

10. John Steinbruner, Elisa Harris, Nancy Gallagher, and Stacy Gunther, *Controlling Dangerous Pathogens: A Prototype Protective Oversight System*, CISSM Working Paper (College Park, Md.: Center for International Security Studies at Maryland, February 5, 2003), <http://www.puaf.umd.edu/CISSM/Publications/AMCS/finalmonograph.pdf>.

biological weapons will remain attractive to any individual, group, or nation with a desire to inflict harm and to avoid detection. The biological threat is grave, and it is here to stay.

Although it is misleading to assume that it will be possible to devise a technological “fix” to this threat, advances in science and technology lie at the core of U.S. efforts to develop a comprehensive biodefense strategy. Yet, as with economic globalization, science and technology possess a double-edged quality. Although open systems of research, communication, and commerce facilitate the development of biomedical countermeasures such as new vaccines, therapeutics, and diagnostics, these systems also support advances in the development of biological weapons. How is it possible to maximize innovation and efficiency in the development of technologies to thwart bioterrorists while minimizing the potential abuses of biotechnology? To assess the influence of globalization on U.S. biodefense strategies, we examine the dynamics of innovation for a core biodefense technology: vaccines.

The first section of this article argues that investment in better defensive measures is crucial for the United States and other countries that are vulnerable to the threat of bioterrorism, and that no credible defensive effort can move forward without accelerating the rate of biodefense vaccine development. As we show, however, the rate of vaccine development has fallen far behind the growing number of biological threats over the past several decades.

In the second section, we demonstrate that international collaboration among firms has more potential benefits for furthering vaccine development than scholars currently recognize. A number of recent analyses have stressed the need to preserve international openness in the academic sector to promote advances in the biological sciences.<sup>11</sup> An issue that has so far been neglected, yet holds greater near-term significance for U.S. biodefense capabilities, is the importance of globalization in commercial sectors that contribute to the advancement of biodefense technologies.

In the third section, we examine the implications of the new regulatory framework for governing biological research and commerce that federal agen-

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11. See, for example, Stern, “Dreaded Risks and the Control of Biological Weapons”; Eugene Skolnikoff, “Research Universities and National Security: Can Traditional Values Survive?” in Albert H. Teich, Stephen D. Nelson, and Stephen J. Lita, eds., *Science and Technology in a Vulnerable World: Supplement to AAAS Science and Technology Policy Yearbook 2003* (Washington, D.C.: American Association for the Advancement of Science, 2002); and Vincent Chan, Jerome Friedman, Stephen Graves, Harvey Sapolsky, and Sheila Widnall, *In the Public Interest: Report of the Ad Hoc Faculty Committee on Access to and Disclosure of Scientific Information* (Cambridge, Mass.: Massachusetts Institute of Technology, June 12, 2002).

cies and lawmakers in the United States put in place in the aftermath of the September 2001 terrorist attacks. This new regulatory framework is designed to enhance U.S. security by reducing the ability of terrorists to access the information and materials needed to produce biological weapons. As we show, however, the framework is likely to have an unintended negative influence on the current U.S. effort to develop enhanced biodefense capabilities, because it creates incentives to shift away from international collaboration in biodefense research and production.

In the fourth section, we argue that U.S. biodefense policy needs to be adjusted in light of the significance of economic globalization. To ensure that the globalization of biodefense continues, we maintain that the best way forward is to harmonize regulations concerning biological research and commerce through the creation of an international biosecurity regime.

### *The Growing Vaccine Gap*

To reduce the threat of biological terrorism, rapid progress in vaccine development is paramount. This section outlines two issues concerning the role of vaccines in biosecurity: the strategic value of vaccines relative to other threat reduction measures and the problems surrounding vaccine development and supply.

#### THE STRATEGIC VALUE OF VACCINES

The U.S. national strategy to reduce the biological weapons threat comprises three tactics: nonproliferation, counterproliferation, and defense—or “consequence management.”<sup>12</sup> The strategy recognizes that no one tactic is sufficient to address the threat and that all three must be pursued simultaneously. Although all three are useful for countering the threat from bioterrorism, a comparison of their potential efficacy reveals that improving defenses must become central to this strategy and that vaccines lie at the heart of this effort.

U.S. biological weapon nonproliferation policy rests on a collection of arms control measures that, thus far, have failed to prevent the spread of biological weapons technology, in large part due to the twin challenges of monitoring and enforcement. In 2001, President George W. Bush’s administration withdrew support from efforts to strengthen the cornerstone of the U.S. non-

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12. White House, *The National Strategy to Combat Weapons of Mass Destruction*, December 2002, <http://www.whitehouse.gov/news/releases/2002/12/WMDStrategy.pdf>.

proliferation strategy—the Biological and Toxin Weapons Convention (BTWC)—arguing that the draft verification protocol put forth at the Fifth Review Conference would not effectively limit proliferation. Given the current challenge of achieving international consensus on an enforceable verification protocol, the strength of legally binding multilateral treaty solutions in this area remains uncertain.<sup>13</sup> Apart from the BTWC, the U.S. government has supported export controls through the Australia Group, composed of a committee of thirty-three countries and the European Commission. Through a non-legally binding agreement, members limit the export of materials and technologies relevant to the production of chemical and biological weapons to proliferant countries.<sup>14</sup> However, given the dual-use nature of the materials controlled under this agreement and the global expansion of the biotechnology and pharmaceutical sectors, scholars strongly doubt the effectiveness of export controls over the long term.<sup>15</sup> Finally, the Harvard Sussex Program on Chemical and Biological Weapons Armament and Arms Limitation has called for an international convention to criminalize chemical and biological weapons development and related activities.<sup>16</sup> Such a law would promulgate a valuable normative prohibition against biological weapons among states. As the experience of weapons inspectors in Iraq in the early and mid-1990s demonstrated, however, determining whether a state possesses biological weapons can be extremely difficult: Without sufficient evidence, international courts will be unable to successfully prosecute suspected violators.

U.S. BW counterproliferation policy relies on a range of deterrents, including surveillance and interdiction, political persuasion, and the threat of overwhelming military force to preempt or respond to a biological attack.<sup>17</sup> All of these strategies have limited utility, however, because biological weapons easily escape early detection, favor the attacker, and are difficult to trace.<sup>18</sup> Al-

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13. Mark Wheelis and Malcom Dando, "On the Brink: Biodefence, Biotechnology, and the Future of Weapons Control," *CBW Conventions Bulletin*, No. 58 (December 2002), p. 3; statement by Jonathan B. Tucker before the Subcommittee on International Security, Proliferation, and Federal Services of the U.S. Senate Committee on Governmental Affairs, "The Proliferation of Chemical and Biological Weapons Materials and Technologies to State and Sub-State Actors," 107th Cong., 1st sess., November 7, 2001.

14. For a description of the agreement, see <http://www.australiagroup.net>.

15. Tucker, "The Proliferation of Chemical and Biological Weapons Materials and Technologies to State and Sub-State Actors"; and Steinbruner et al., "Controlling Dangerous Pathogens."

16. Matthew Meselson, "Averting the Hostile Exploitation of Biotechnology," *CBW Conventions Bulletin*, No. 48 (June 2000), pp. 16–19.

17. White House, *The National Strategy to Combat Weapons of Mass Destruction*.

18. See the discussion in Koblenz, "Pathogens as Weapons."

though not traditionally considered a deterrent, vaccines are one of the few remaining tools available to deter a biological attack.<sup>19</sup> By limiting the efficacy of biological weapons, vaccines reduce their attractiveness and thereby offer some means of deterring their use.

Given the current limitations of U.S. BW nonproliferation and counterproliferation strategies, security planners have a clear need to emphasize defense.<sup>20</sup> Limiting the severity of a biological attack will hinge on a variety of factors. One is the ability to detect and diagnose the release of a select agent through heightened surveillance and medical training. Another is the ability to prevent, respond to, and recover from a biological attack.<sup>21</sup> To this end, vaccines not only are a crucial defensive resource, but they also enable other defensive measures to work more effectively. As Philip Russell (former commander of the U.S. Army R&D Command) argues, the success of any U.S. response to the deliberate release of a highly infectious organism will depend on “the rapidity of the public health response, the effectiveness of a vaccination campaign, and, most importantly, the availability of vaccine.”<sup>22</sup> Building capacity in the health care system to respond to a large-scale biological attack, devising and practicing quarantine protocols, and developing protective equipment such as building filters and respiratory gear—all will have much greater efficacy in conjunction with vaccines. For example, vaccinated emergency and health care workers can enter biologically contaminated areas to triage victims and administer vaccines that will, in turn, shorten the length of the quarantine. Vaccines can also be used to protect surrounding populations from secondary waves of infection.

As with all other threat-reduction strategies, however, vaccines cannot offer perfect security. Given the potentially wide range of pathogens that could be used in a biological attack, attempting to vaccinate the U.S. population as a

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19. Other medical countermeasures, such as antivirals and broad-spectrum antibiotics, would also be useful in efforts to deter or mitigate biological attacks. We focus our discussion on vaccines, however, because, relative to antivirals, their development is more feasible within a ten-year time frame. National Research Council, *Making the Nation Safer: The Role of Science and Technology in Countering Terrorism* (Washington, D.C.: National Academies Press, 2002), p. 87. Although it may be more feasible to develop broad-spectrum antibiotics in the near term, their usefulness is limited to bacterial pathogens, which account for only 29 percent of the Department of Health and Human Services’ select agent list. See <http://www.cdc.gov/od/sap/docs/salist.pdf>.

20. For a related discussion, see Paul Schulte, “The Uncertainly Horrifying Prospect of Biological Weapons: International Risks, Responses, and Dilemmas,” Harvard University, March 20, 2003.

21. National Research Council, *Making the Nation Safer*, p. 68.

22. Philip K. Russell, “Vaccines in Civilian Defense against Bioterrorism,” *Emerging Infectious Diseases*, Vol. 5, No. 4 (July/August 1999), p. 532.

first line of defense is impractical. Vaccines are invaluable, however, in several of the postattack scenarios described above. This would be particularly true in the event of an anthrax or a smallpox attack, because these vaccines can be used for postexposure prophylaxis.

#### VACCINE DEVELOPMENT AND SUPPLY PROBLEMS

Vaccines are vitally important in deterring and mitigating biological attacks, and security planners cannot take their availability for granted. Over the past thirty years, the rate of biodefense vaccine development has not kept pace with the growing number of biological threats facing the United States. Of the forty-nine biological threat agents identified by the Department of Health and Human Services (HHS), the Federal Drug Administration (FDA) has licensed vaccines to protect against only four agents on this list (anthrax, cholera, plague, and smallpox).<sup>23</sup> Each of these vaccines was developed in the 1970s or earlier, and none is proven to protect humans against weaponized versions of these pathogens. Furthermore, manufacturers have ceased producing FDA-licensed versions of all but one of these vaccines (anthrax).<sup>24</sup> Once development begins, new biodefense vaccines are not likely to reach licensure for another five to ten years.<sup>25</sup>

Although the need for new and improved biodefense vaccines is clear, the means for acquiring them is not. Commercial incentives for the pharmaceutical and biotechnology industries to develop biodefense vaccines are few in number because vaccines protect against diseases with low-to-no natural incidence in traditional markets, and the use of these vaccines is typically limited to military and laboratory settings.

Recent government attempts to procure biodefense vaccines have failed to compensate for poor commercial incentives. In 1994, the Department of Defense (DoD) established the Joint Vaccine Acquisition Program (JVAP) in an attempt to bring experimental biodefense vaccines to licensure. The JVAP has a

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23. For a list of biological threat agents, see <http://www.cdc.gov/od/sap/resource.html>.

24. A 1970s' version of the smallpox vaccine has recently been relicensed, but supplies are limited because the pharmaceutical industry no longer manufactures this version, which contains vaccinia virus cultured on calf bellies. Acambis, a U.K.-based firm, is developing a "cleaner" version of the smallpox vaccine containing cell-cultured vaccinia virus, which the FDA is expected to approve in 2004.

25. Dr. Anna Johnson-Winegar, deputy assistant to the U.S. defense secretary for chemical and biological defense, expects that the Department of Defense will have an improved smallpox vaccine by 2006 and a tularemia vaccine by 2012. One exception is the new cell-cultured smallpox vaccine under development at Acambis.

budget of \$747 million to develop eight vaccines. To date, this program has failed to license a single new biodefense vaccine. According to interviews conducted with a senior scientist and Centers for Disease Control (CDC) official, the pharmaceutical industry “guffaws” at the JVAP’s paltry contracts, citing \$500 million to \$1 billion as the average development cost for a new vaccine.<sup>26</sup> Without assistance from the commercial sector, the military has been unable to engineer and manufacture enough vaccine to conduct large clinical trials for FDA licensure.

Given the protracted and unpredictable nature of biological threats, there will be a long-term government demand for a range of commercially unattractive vaccines to build and maintain national pharmaceutical stockpiles. Recognizing the need to move quickly to develop new biodefense vaccines, the Bush administration has proposed making \$5.6 billion available to develop these vaccines over the next ten years through Project Bioshield.<sup>27</sup> Should Congress approve this level of funding, Project Bioshield may raise incentives for vaccine manufacturers.<sup>28</sup>

To fully capitalize on opportunities presented in proposals such as Project Bioshield, security planners must understand the dynamics of biomedical innovation in the commercial sector to ensure that effective and safe biodefense vaccines are developed as quickly as possible. The next section of this article argues that it is essential for U.S. policymakers concerned with bolstering biodefense capabilities in general, and vaccine development in particular, to understand how economic globalization has reshaped the nature of technological development in the biotechnology sector in recent decades. Unless this is recognized, policymakers risk taking counterproductive steps in the pursuit of enhanced biosecurity.

### *Globalization and the Changed Parameters of Vaccine Development*

A number of recent analyses have recognized the importance of preserving openness in the conduct and communication of scientific research, both do-

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26. Amy Smithson and Leslie Anne Levy, *Ataxia: The Chemical and Biological Terrorism Threat and the U.S. Response*, Report No. 35 (Washington, D.C.: Henry L. Stimson Center, 2001), p. 317.

27. “President Details Project Bioshield,” White House press release, February 3, 2003, <http://www.whitehouse.gov/news/releases/2003/02/20030203.html>.

28. Marilyn Chase, “Project Bioshield Is a Big Incentive to Vaccine Makers,” *Wall Street Journal*, February 3, 2003, p. D2. In addition to ensuring funds, Project Bioshield will give the National Institutes of Health authority to fast-track biodefense grants, and it will give the FDA authority to approve the use of investigational vaccines and drugs in an emergency.

mestically and internationally, in the face of the threat from bioterrorism.<sup>29</sup> Although collaboration among academic scientists across borders is essential, it is only one facet of globalization that is relevant to biodefense. What has not been sufficiently recognized is the significance of international collaboration among biotechnology and pharmaceutical firms. With respect to vaccine development, the commercial sector is indispensable: Not only is it the sole source of manufacturing expertise, but industry efforts to translate pilot lots into large-scale production require specialized research and bioengineering capabilities.

#### NEW GLOBALIZATION STRATEGIES FOR A NEW TECHNOLOGICAL ENVIRONMENT

Although firms have always collaborated in production activities across borders, the form and extent of globalization linkages that have emerged over the past three decades are historically unique. Two new globalization strategies that many firms have turned to during this period—international subcontracting and the pursuit of technological cooperation agreements—are particularly relevant to vaccine development.

The first is international subcontracting. Of course, there has always been subcontracting—that is, contracting out to other firms for the production of components, supplies, and sometimes entire products. What is new is the international component of this strategy. As Peter Dicken stresses, “An important development of the past thirty years has been the extension of subcontracting across national boundaries: the emergence of *international subcontracting* as an important global activity. The revolution in transport and communications technology, together with developments in the production process itself, have created the potential for firms to establish subcontracting networks over vast geographical distances.”<sup>30</sup>

Most significant for vaccine development, however, is a second new globalization strategy: pursuing technological cooperation agreements with firms in other countries. These cooperation agreements, which can focus on production, R&D, or both simultaneously, are attractive to firms because many of the same benefits of collaboration usually associated with mergers can be achieved without having to deal with any of the complicated and contentious issues associated with changes in long-term ownership. Although comprehensive data

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29. See Skolnikoff, “Research Universities and National Security”; Chan et al., *In the Public Interest*; and Stern, “Dreaded Risks and the Control of Biological Weapons.”

30. Peter Dicken, *Global Shift: Transforming the World Economy* (New York: Guilford, 1998), p. 233 (emphasis in original).

on technological cooperation agreements do not exist, the number of such agreements has risen dramatically from near zero since the mid-1970s.<sup>31</sup>

Why have so many firms recently turned to international subcontracting and technological cooperation agreements? A key reason is that both of these strategies help firms cope with the rapid increase in the cost, risk, complexity, and scale of technological development that has occurred in the last several decades.<sup>32</sup> In this technological environment, international subcontracting is attractive because it allows firms to specialize in those aspects of production that use resources and capabilities in which the firm has a perceived competitive advantage.<sup>33</sup> In turn, technological cooperation agreements make it easier for firms to minimize the risk/cost of engaging in R&D and enhance the potential for innovation. As François Chesnais points out, in a world of “rapid and radical technological change, the new forms of agreements offer firms a way of ensuring, in a wide variety of situations, a high degree of flexibility in their operations. When technology is moving rapidly, the flexible and risk-sharing (or indeed risk-displacing) features of inter-firm agreements offer firms a wide range of opportunities for acquiring key scientific and technical assets from outside their own walls. . . . Inter-firm agreements can likewise provide firms with a possibility of pooling limited resources in the face of rising R&D costs.”<sup>34</sup>

The cost, risk, complexity, and scale of technological development have greatly increased in recent decades in the area of biopharmaceutical drug development. During the 1990s alone, R&D budgets in the pharmaceutical industry increased threefold.<sup>35</sup> To cope with the changed parameters of technological development, firms in this sector have strongly turned to greater international collaboration. Since 1970 the number of technological cooperation agreements has exploded (see Figure 1). Given the historical strength of

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31. Stephen Kobrin, “The Architecture of Globalization: State Sovereignty in a Networked Global Economy,” in John H. Dunning, ed., *Governments, Globalization, and International Business* (Oxford: Oxford University Press, 1997), p. 150.

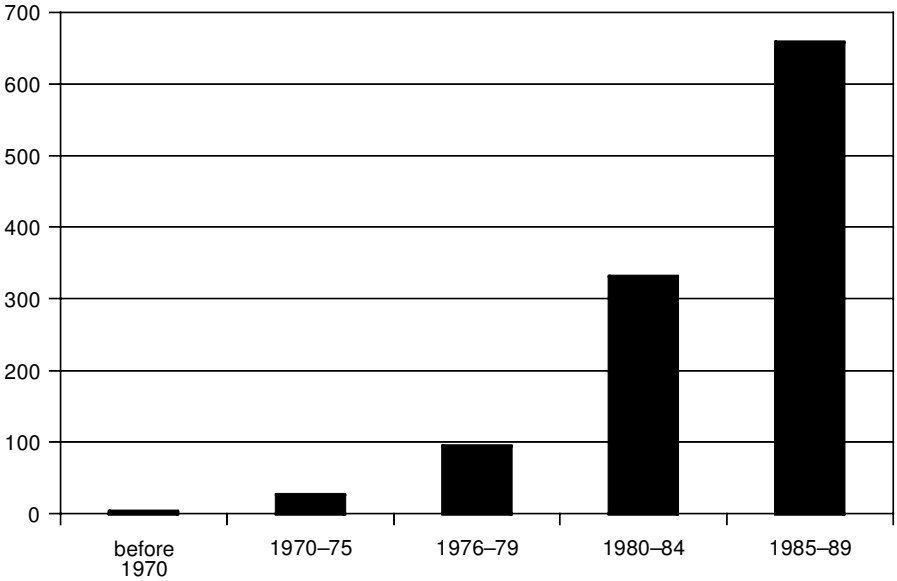
32. See, for example, *ibid.*, pp. 149–150; and Lynn Krieger Mytelka, “Crisis, Technological Change, and the Strategic Alliance,” in Mytelka, ed., *Strategic Partnerships: States, Firms, and International Competition* (Rutherford, N.J.: Fairleigh Dickinson University Press, 1991), pp. 16–21, and the sources cited therein.

33. See, for example, Geoffrey Jones, *The Evolution of International Business: An Introduction* (London: Routledge, 1996), p. 142.

34. François Chesnais, “Preface,” in Mytelka, *Strategic Partnerships*, p. x.

35. Sarah C. Stallings, Robert H. Rubin, Thomas J. Allen, Charles M. Cooney, Anthony J. Sinskey, and Stan N. Finkelstein, “Technological Innovation in Pharmaceuticals,” Working Paper No. 59-01 (Cambridge, Mass.: MIT Program on the Pharmaceutical Industry, 2001), p. 2.

**Figure 1. Number of Technological Cooperation Agreements Formed in Biotechnology from the Early 1950s to 1989.**

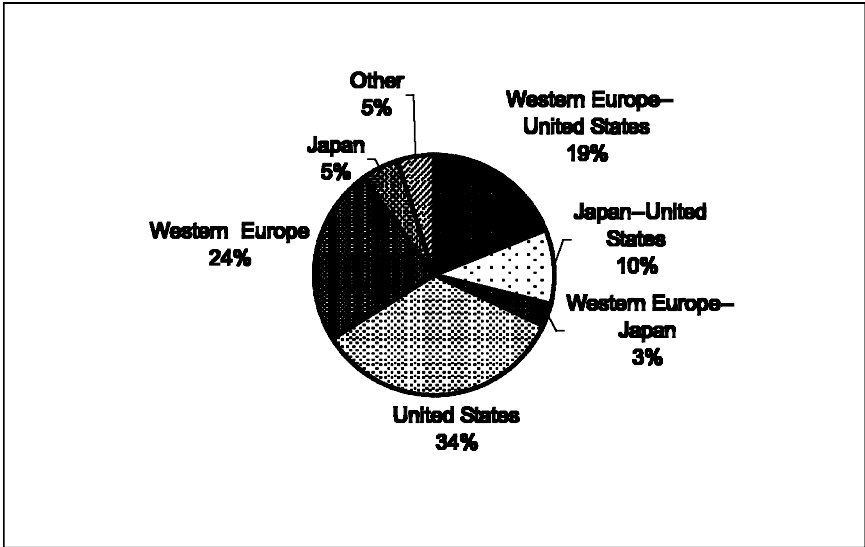


SOURCE: John Hagedoorn and Jos Schakenraad, "Strategic Partnering and Technological Co-Operation," in Ben Dankbaar and John Groenewegen, eds., *Perspectives in Industrial Organization* (Dordrecht, Netherlands: Kluwer, 1990), p. 176.

U.S. firms in the biotechnology sector and the size of the U.S. economy, one might suppose that a large number of the technological cooperation agreements in this sector would be limited to U.S.-based firms. This is indeed the case (see Figure 2). Figure 2 also reveals, however, that the level of collaboration by U.S. firms in this sector with both Japanese and West European firms is almost equal in significance to that between U.S.-based firms. The bottom line is that starting from a base of essentially zero, several hundred technological cooperation agreements between U.S.-based firms and biotechnology firms in other countries were formed during the 1970-89 period.

**THE INCREASED IMPORTANCE OF COLLABORATION IN VACCINE DEVELOPMENT**  
 Recent advances in molecular biology and genetic engineering have led to new vaccine development strategies. At the same time, this explosion of technologi-

Figure 2. Geographic Nature of Technological Cooperation Agreements Formed in Biotechnology from the Early 1950s to 1989.



SOURCE: John Hagedoorn and Jos Schakenraad, "Strategic Partnering and Technological Cooperation," in Ben Dankbaar and John Groenewegen, eds., *Perspectives in Industrial Organization* (Dordrecht, Netherlands: Kluwer, 1990), p. 177.

cal opportunity has made it progressively more difficult for any one firm to assemble the optimal array of in-house development expertise. Expertise relevant to early-stage vaccine development has become increasingly specialized and more widely distributed. This trend is reflected in the number of small, dedicated biotechnology firms, which grew from just a handful in the 1970s to 1,457 in 2001.<sup>36</sup>

As the scientific and technological base for vaccine development has expanded, so too have the costs. Although there is little publicly available data on vaccine industry investments in biotechnology, one study was able to determine that overall levels of R&D devoted to vaccine development within the pharmaceutical industry increased from 2 percent in the early 1980s to an aver-

36. For this statistic, see Biotechnology Industry Organization, "No. of Biotech Companies, 1999–2000," <http://www.bio.org/investor/signs/200210num.asp>.

age of 4 percent during the 1990s.<sup>37</sup> Furthermore, it takes \$300 million to \$1 billion and seven to ten years to bring a single vaccine to market.<sup>38</sup>

Commercial vaccine developers have responded to the changed parameters of technological development by expanding their reliance on outsourcing and technological cooperation agreements. Increasingly, vaccines and other biopharmaceuticals are being developed under collaborative R&D and production efforts between large pharmaceutical companies and smaller biotechnology start-ups and academic and government research institutions.<sup>39</sup>

Pursuing collaboration is not only an efficient solution to the growing cost and complexity of vaccine production; it is also a valuable source of innovation.<sup>40</sup> Vaccine development is a highly interdisciplinary endeavor that requires a wide range of expertise to bring an effective product to market. Firms in the vaccine industry, therefore, have much to gain from close working relationships with partners that share heterogeneous, yet complementary, R&D capabilities. As three analysts note, these dense networks of collaborative relationships serve as "organizational devices for the coordination of heterogeneous learning processes by agents characterized by different skills, competencies, access to information and assets."<sup>41</sup>

In the area of vaccine development, the advantages of partnerships between large pharmaceutical companies and smaller biotechnology firms are particularly apparent. Small biotechnology firms that are on the cutting edge of the most recent scientific developments are often ideally suited to introduce promising new biodefense vaccine candidates. For example, Acambis, a small British biotechnology company, is producing the first cell-culture version of the smallpox vaccine for the U.S. government. Because of its experience with an

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37. Henry G. Grabowski and John Vernon, *The Search for New Vaccines: The Effects of the Vaccines for Children Program* (Washington, D.C.: AEI Press, 1997), p. 10.

38. When associated facility cost investments are excluded, the estimated cost of bringing a vaccine to market is \$300 to \$500 million. Changes in FDA licensing requirements for biodefense vaccines and manufacturing process improvements may also reduce development times. Department of Defense, *Report on Biological Warfare Defense Vaccine Research and Development Programs* (Washington, D.C.: Department of Defense, 2001); and Institute of Medicine, *The Children's Vaccine Initiative: Achieving the Vision* (Washington, D.C.: National Academy Press, 1993).

39. Ashish Arora and Alfonso Gambardella, "Complementarity and External Linkage: The Strategies of Large Firms in Biotechnology," *Journal of Industrial Economics*, Vol. 38, No. 4 (June 1990), p. 361; and Gary P. Pisano, "The Governance of Innovation: Vertical Integration and Collaborative Arrangements in the Biotechnology Industry," *Research Policy*, Vol. 20, No. 3 (June 1991), p. 237.

40. Luigi Orsenigo, Fabio Pammoli, and Massimo Riccaboni, "Technological Change and Network Dynamics: Lessons from the Pharmaceutical Industry," *Research Policy*, Vol. 30, No. 3 (March 2001), pp. 485-508.

41. *Ibid.*, pp. 485-486.

array of genetic engineering techniques, Acambis is able to engineer immunogens apart from the entire pathogen and thereby develop safer vaccines according to FDA-recommended manufacturing practices.<sup>42</sup> Unlike large pharmaceutical companies, however, small biotechnology firms such as Acambis generally do not have the expertise or facilities to perform late-stage vaccine development and manufacturing.<sup>43</sup> To produce the smallpox vaccine, Acambis has partnered with Baxter International, a large, U.S.-based, medical supply and manufacturing company. In short, small biotechnology firms and large pharmaceutical companies have different strengths that, when combined, can more effectively develop biodefense vaccines.

#### THE GLOBALIZATION OF U.S. BIODEFENSE VACCINE EFFORTS

The need to pursue partnerships to maintain high rates of innovation for vaccine development has grown rapidly in recent years. In early 2003 President Bush observed, "Right now America must go beyond our borders to find companies willing to make vaccines to combat biological weapons."<sup>44</sup> As the need for international collaboration has grown, the ability of companies and research institutes to work with international partners has also greatly increased. Of particular importance in this regard are recent advances in communications technology that have made it possible to share specifications, plans, data, and so on in real time.<sup>45</sup> In light of these trends, it is not surprising that international biotechnology companies now play an important role in U.S. biodefense vaccine research. Of the top-six Class A biological threat agents identified by the HHS (anthrax, Botulinum toxin, plague, smallpox, tularemia, and viral hemorrhagic fevers such as Ebola), vaccines for all but one (Botulinum toxin) are being developed in cooperation with international biotechnology companies.<sup>46</sup>

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42. Companies such as Bioport, the beleaguered manufacturer of the DoD's anthrax vaccine, have struggled to obtain FDA approval for the manufacture of this vaccine partly because of their reliance on older and less precise manufacturing techniques.

43. Alfonso Gambardella, *Science and Innovation: The U.S. Pharmaceutical Industry in the 1980s* (Cambridge: Cambridge University Press, 1995), p. 147.

44. "President Discusses Measures to Protect the Homeland from Bioterrorism," remarks by President George W. Bush on the Bioshield Initiative, National Institutes of Health, February 3, 2003, <http://www.whitehouse.gov/news/releases/2003/02/20030203-13.html>.

45. See the discussion in Thomas Malone and John Rockhart, "How Will Information Technology Reshape Organizations?" in Stephen P. Bradley, Jerry A. Hausman, and Richard L. Nolan, eds., *Globalization, Technology, and Competition: The Fusion of Computers and Telecommunications in the 1990s* (Boston: Harvard Business School Press, 1993).

46. The U.S. Army Medical Research Institute of Infectious Diseases has applied to NIAID to develop a pentavalent vaccine (covering types A, B, C, E, and F) using recombinant DNA technology

Finding a safer alternative to the current smallpox vaccine is a major priority for the biodefense community, and international collaborative ventures are responsible for many alternatives under investigation. As noted above, Acambis and Baxter are in the late stages of developing a cell-cultured version of the smallpox vaccine, and one of Baxter's overseas affiliates in Austria will produce the vaccine.<sup>47</sup> In addition to this project, Bavarian Nordic, a German-Danish company based in Copenhagen, is developing a promising alternative with the modified vaccinia Ankara strain of the vaccinia virus for which the National Institute of Allergy and Infectious Diseases (NIAID) is considering a contract for 30 million doses.<sup>48</sup> Similarly, VaxGen, a California company, has been working with Kaketsuken, a Japanese company, to begin clinical trials on a vaccine with the Japanese-developed LC16-Kaketsuken strain.<sup>49</sup> And most recently, NIAID awarded Omrix Biopharmaceuticals, a Brussels-based company with research and production facilities in Israel, a two-year grant of more than \$3 million to develop vaccinia immunoglobulin first-aid kits that individuals can self-administer in an emergency.<sup>50</sup>

In October 2002, NIAID issued contracts to VaxGen and Avecia of Manchester, England, to develop a civilian anthrax vaccine based on an experimental vaccine developed by research scientists at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID).<sup>51</sup> Similarly, biotechnology companies in two countries are cooperating on a NIAID contract to develop a vaccine for Ebola. Vical, a California company, is developing the DNA component of the vaccine, while Crucell, located in the Netherlands, is engineering a recombinant adenovirus vector for the vaccine.<sup>52</sup>

The search for a plague vaccine has an international element as well. Military research laboratories in the United States and the United Kingdom

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being developed for the DoD under a grant from the National Institute of Allergy and Infectious Diseases.

47. Andrew Pollack and Melody Petersen, "Untested Companies Enlist in U.S. Biodefense," *New York Times*, March 23, 2003, sec. 3, p. 1.

48. The NIAID, a division of the National Institutes of Health, contracts for and conducts the majority of federally funded biodefense vaccine research.

49. Jon Cohen, "Looking for Vaccines That Pack a Wallop without the Side Effects," *Science*, December 20, 2002, p. 2314.

50. Israel21c staff, "Israelis Win U.S. Grant to Develop Anti-smallpox First Aid Treatment," *Israel21c*, August 17, 2003, <http://www.israel21c.org>.

51. The civilian vaccine will require fewer doses than the DoD-licensed vaccine and, because it will be produced with recombinant DNA technology, it is expected to produce fewer side effects.

52. Douglas Steinberg, "Antiterror Agenda Promotes Ebola Vaccine and Immunotherapy," *Scientist*, July 8, 2002, p. 32.

(USAMRIID, and Porton Down, respectively) are following two promising leads in parallel for a recombinant plague vaccine to protect humans against aerosolized versions of the bacterium *Yersinia pestis*.<sup>53</sup> DynPort Vaccine Company—a joint venture between DynCorp, based in Reston, Virginia, and Porton International, a subsidiary of the French pharmaceutical company Beaufour-Ipsen—is also developing a plague vaccine.

Finally, efforts to develop a tularemia vaccine also have a strong global component. NIAID is pursuing the development of a civilian tularemia vaccine through a number of early development grants to institutions in Canada, Russia, Sweden, and the United Kingdom.<sup>54</sup> At the same time, the DoD has contracted the DynPort Vaccine Company to develop another version of this vaccine for the military.

### *Regulating toward Autarky*

In response to the September 2001 terrorist attacks, federal agencies and lawmakers in the United States constructed a new regulatory framework to make it more difficult for terrorists to obtain dangerous biological agents and sensitive research information. Though this framework is designed to enhance U.S. security, it is likely to have the unintended and counterproductive effect of encouraging a shift away from globalization; this is the case with respect to vaccine development, in particular, and U.S. biodefense efforts, more generally.

#### A NEW REGULATORY FRAMEWORK

The U.S. biosecurity regulatory framework delineates new restrictions on the use of select agents, the activities of select foreign research scientists and students, and the communication of sensitive research.<sup>55</sup> Its primary objective is to make it more difficult for potential adversaries to exploit open systems of research, education, and commerce in the biological sciences to develop biological weapons.

Select agent restrictions are outlined in the USA Patriot Act of 2001 and the Public Health Security and Bioterrorism Preparedness Act of 2002, which

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53. Mary Beth Nierengarten and Larry Lutwick, "Vaccine Development for Plague," *Medscape Infectious Diseases*, Vol. 4, No. 2 (2002).

54. Mary Beth Nierengarten and Larry Lutwick, "Developing New Tularemia Vaccines," *Medscape Infectious Diseases*, Vol. 4, No. 1 (2002).

55. Regulations affecting the first two categories are already in effect, and individual scientific journal editors administer prepublication review at their own discretion.

criminalize the unauthorized possession, use, or transfer of the forty-nine biological agents or toxins listed by HHS. Individuals working with these agents must register with HHS and institute access controls, handling and reporting requirements, and personnel screening for their labs. HHS must also develop a national database of registered individuals and institutions as well as information about the pathogens they possess.

These acts introduce numerous personnel restrictions as well. Both acts prohibit universities from employing individuals from several foreign countries (currently seven) to work with select biological agents and toxins listed by HHS.<sup>56</sup> All other employees in these laboratories—from principal investigators to janitors—are subject to extensive background checks to determine if they are security risks. In May 2002, the DoD restricted access to research data and facilities among foreign citizens as well. New visa regulations, as well as new approaches to scrutinizing applications, have introduced another layer of personnel restrictions.<sup>57</sup> As a result, numerous foreign researchers were barred from the United States in the first half of 2003, leading to the disruption of more than two dozen research projects related to biodefense at twenty universities.<sup>58</sup> New visa regulations have also increased the ability of the federal government to monitor the activities of foreign students and researchers as well as educational institutions to ensure compliance with the new guidelines.

Given the links between biological research and commerce and weapons development, other regulations are now likely to be applied more broadly as well. The International Traffic in Arms Regulations (ITAR), for example, regulate the export of all weapons-related knowledge. Although these regulations have traditionally applied to space research and munitions development,

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56. These seven countries are Cuba, Iran, Iraq, Libya, North Korea, Sudan, and Syria. This regulation also applies to non-U.S. citizens who have become permanent U.S. residents. In addition, student and researcher visa applications from twenty-six primarily Muslim countries have been held up for special review by the U.S. government through the Visas Condor program, initiated in November 2001. This review is conducted by the Foreign Terrorist Tracking Task Force, which is led by Attorney General John Ashcroft and comprises experts from a variety of U.S. federal agencies, including the State Department, Federal Bureau of Investigation, Immigration and Naturalization Service, Secret Service, and Customs.

57. Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism (USA Patriot) Act of 2001, Public Law 107-56, 107th Cong., 1st sess.; and Enhanced Border Security and Visa Entry Reform Act of 2002, Public Law 107-173, 107th Cong., 2d sess.

58. Lisa Chedekel, Kim Martineau, and Janice D'Arcy, "Stalling Science: New Visa Rules Are Stranding Foreign Scientists Abroad and Leaving Their U.S. Research to Languish or Die," *Hartford Courant*, March 23, 2003, p. A1.

Eugene Skolnikoff notes that the life sciences may not be exempt.<sup>59</sup> Under ITAR, U.S. researchers must obtain an export license before sharing information with non-NATO foreign students and scientists. Violators of these regulations, which cover not just formal collaborations but also informal interactions such as meetings and emails, may be fined or imprisoned.

Meanwhile, the research community is receiving mixed messages regarding future policy on the communication of sensitive biological research in the United States. The White House declared that it intends to uphold a nearly twenty-year-old policy of not placing restrictions on the conduct and communication of unclassified federally funded fundamental research, and yet the administration has taken several measures that suggest otherwise.<sup>60</sup> After September 11, for example, the White House asked federal agencies to remove “sensitive but unclassified,” material from their websites, thereby creating a new, if poorly defined, category of restricted information.<sup>61</sup> It also encouraged the American Society of Microbiology (ASM, publisher of eleven scientific journals) to restrict the publication of sensitive research papers. While the presidents of the National Academy of Sciences (NAS) warned that vague categories such as “sensitive but unclassified” would “generate deep uncertainties . . . [and] stifle scientific creativity,” the NAS, together with the ASM, announced in January 2003 that the editors of more than thirty leading scientific journals had agreed to screen potentially dangerous research from their publications.<sup>62</sup> In addition, the Department of Defense has indicated that unclassified DoD-funded research may be subject to prepublication review. It has not, however, issued an explicit policy to this effect.

#### INCENTIVES TO SHIFT AWAY FROM GLOBALIZATION

Although this new regulatory framework is intended to reduce the threat of bioterrorism, it could undercut the development of biodefenses. Some analysts and researchers have argued that it will discourage scientific progress by U.S. researchers in areas that require working with select pathogens and will make

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59. Skolnikoff, “Research Universities and National Security,” p. 67.

60. This policy is outlined in National Security Decision Directive 189, 1985.

61. White House memorandum from Chief of Staff Andrew Card to the heads of executive departments, March 19, 2002.

62. “Statement on Science and Security in an Age of Terrorism from Bruce Alberts, Wm. A. Wulf, and Harvey Fineberg,” presidents of the National Academies, October 18, 2002, <http://www4.nas.edu/news.nsf/isbn/s10182002b?OpenDocument>; and Journal Editors and Authors Group, “PNAS Policy on Publication of Sensitive Material in the Life Sciences,” *Proceedings of the National Academies of Sciences*, Vol. 100 (February 2003), p. 1464.

continuing research much less effective by restricting scientific openness.<sup>63</sup> Although these concerns are valid, they reflect only part of the problem.

The ability to innovate and manufacture safe and effective biodefense technologies depends on the strength of three system components: the biodefense research and commercial base in the United States; the biodefense research and commercial base in other countries; and the interaction between them—that is, the globalization of research and commerce in this area. Given that the pursuit of globalization has an independent contribution to make in the development of effective biodefense capabilities, an important unresolved question is whether the new U.S. regulatory framework is likely to have a disproportionately negative influence on the scope of international collaboration in this area.

Although this framework will generally reduce the willingness of researchers and firms to participate in biodefense research, there are a number of reasons to expect that it will be especially damaging to international collaboration. One issue concerns the added bureaucratic and financial costs associated with conducting research on select pathogens. Dr. Michael Donneberg, head of infectious disease research at the University of Maryland School of Medicine asks, “Will all these forms we have to fill out impede our ability to do research? It weighs into the question of whether to work with these agents.”<sup>64</sup> Those who cannot shoulder the new bureaucratic, financial, and other burdens associated with doing research on select pathogens will be driven out of the field. Foreign firms and researchers not subject to U.S. law also suffer from the uncertainty and delays that these regulations generate. Rick Smith, director of regulatory affairs at Aventis Pasteur, observes that the new select pathogen rules have already slowed the pace of international collaboration. He notes that whereas international collaboration was once relatively effortless, routine

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63. The Institute of Medicine noted that the current biodefense effort suffers from a shrinking talent base for vaccine development. Institute of Medicine, *Protecting Our Forces: Improving Vaccine Acquisition and Availability in the U.S. Military* (Washington, D.C.: National Academies Press, 2002). See also statement by Ronald Atlas, president of the American Society for Microbiology, before the House Committee on Science, “Conducting Research during the War on Terrorism: Balancing Openness and Security,” 107th Cong., 2d sess, October 10, 2002; Ronald M. Atlas, “National Security and the Biological Research Community,” *Science*, October 25, 2002, pp. 753–754; Nils Hasselmo, C. Peter Magrath, and Katharina Phillips, “Association of American Universities, Council on Governmental Relations, and National Association of State Universities and Land-Grant Colleges Letter to the Office of Science and Technology Policy Director on Scientific Openness,” January 31, 2003, <http://www.aau.edu/research/Ltr1.31.03.html>; Stern, “Dreaded Risks and the Control of Biological Weapons,” pp. 114–118; and Anne Marie Borrego, “Regulatory Overkill?” *Chronicle of Higher Education*, January 31, 2003, pp. A25–A26.

64. Quoted in Scott Shane, “Terror Threat Casts Chill over World of Biological Research,” *Baltimore Sun*, January 26, 2003.

attempts to exchange seed strains between the United States, France, and Canada are now bogged down for weeks in paperwork and delays.<sup>65</sup> Moreover, if foreign researchers and firms believe that major constraints could at some point be placed on the way they conduct or disseminate research, they are likely to choose to work with non-U.S. partners. In light of recent regulatory changes, foreign firms and researchers working in areas relating to biodefense have reason to expect that these restrictions will only become more stringent in the years ahead.<sup>66</sup>

The new regulatory framework also raises the professional risk of working with select pathogens. Research scientists took note when Dr. Thomas Butler, chief of infectious diseases at Texas Tech University Medical School, ran afoul of these regulations in January of 2003 by failing to document the destruction of thirty vials of plague. Unable to account for the vials, Dr. Butler suggested that they might have been misplaced or stolen. More than sixty federal, state, and local law enforcement agents descended on the university; the media splashed his name across the news; and he was charged and tried in a federal court on sixty-nine counts of misconduct. Although acquitted of the most serious charges relating to the incident, Dr. Butler was convicted on forty-four counts. Apart from the specifics of this case, the manner in which scientists who work with select pathogens will respond to these events is at issue. Predicting the reaction of the biomedical research community, Ronald Atlas, president of the American Society for Microbiology, stated, "If I had select agents in my lab, I think I'd give serious consideration in the morning as to whether I really want to do this or not."<sup>67</sup>

These professional risks extend beyond the U.S. research community to threaten international collaboration. In the Butler case, his arrest has interrupted important collaborative efforts with the Tanzanian government to test a potentially valuable plague therapy in areas of that country where plague is endemic.<sup>68</sup> More generally, foreign firms and researchers based outside the

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65. Interview with Rick Smith, director of regulatory affairs, Aventis Pasteur, Swiftwater, Pennsylvania, March 6, 2003.

66. Referring to the new personnel restrictions on foreign researchers, Kevin Casey, director of federal and state relations for Harvard University, declared, "I'm anticipating we're going to experience more, rather than fewer, problems. . . . It's a situation where the Homeland Security agencies are feeling on the hot seat. Nobody wants to be the one who makes the wrong call." Quoted in Chedekel, Martineau, and D'Arcy, "Stalling Science," p. A1.

67. Quoted in David Ruppe, "New Regulations on Biological Materials Get Mixed Reviews," *Global Security Newswire*, December 12, 2002, [http://www.nti.org/d\\_newswire/issues/newswires/2002\\_12\\_12.html](http://www.nti.org/d_newswire/issues/newswires/2002_12_12.html).

68. Russell Gold, "Research Questions: With Plague Fears on Rise, an Expert Ends Up on Trial," *Wall Street Journal*, April 14, 2003, p. A1.

United States will likely think twice before assuming the added cost and risk of choosing a U.S.-based partner as opposed to working with a partner located in a country with less stringent standards. Moreover, foreign researchers and the affiliates of foreign companies located in the United States and interested in doing work in this area may become less inclined to do so because of rapidly evolving and unpredictable regulatory standards, particularly those concerning visas and research rules.

For the above reasons, the new regulatory framework produces particularly strong incentives for foreign firms and researchers to avoid or reduce their participation in U.S. biodefense efforts. At the same time, the willingness and ability of U.S. firms and researchers to pursue international collaboration will also be constrained given the difficulties of working with foreign partners that are not subject to the same set of pathogen, personnel, and publication regulations. Long-term international collaboration becomes an increasingly risky proposition for firms and researchers operating in rapidly evolving and disparate regulatory environments for biosecurity. Indeed, the U.S. government could decide at some point that these foreign partners are a security risk and move to constrain their projects. Looking forward, many U.S. firms and researchers working in biodefense may decide that the risk of having a long-term project interrupted has become too great relative to the advantages of working with foreign partners.

### *Future Policy Directions*

The new U.S. biosecurity regulatory framework encourages a shift away from globalization in research and production related to biodefense. Given the trajectory of U.S. biosecurity regulations since September 2001, restrictions on the conduct and communication of biological research and commerce are likely to grow. Although the current regulations encourage a move away from globalization in biodefense efforts indirectly, the next round of regulations may do so directly, especially in light of the view held among many analysts and policymakers that globalization serves to facilitate terrorism.

U.S. policymakers faced a similar set of decisions during the 1980s. At that time, the increasing tendency of U.S. firms involved in defense-related production to pursue globalization strategies troubled many American defense analysts. Some of these analysts argued for dramatically scaling back the globalization of U.S. weapons production.<sup>69</sup> Congress did, in fact, initiate a

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69. For a discussion of the concerns in the 1980s about the globalization of U.S. defense production

sharp increase in the number of "Buy American" restrictions in weapons production during the 1980s.<sup>70</sup> The practical effect of these restrictive policies, however, was essentially nil: In response to lobbying by the DoD, Congress allowed for a variety of exceptions to these Buy American restrictions, which the DoD then rigorously exploited.<sup>71</sup> In the end, the globalization of U.S. weapons production proceeded largely unchecked. The decision to embrace globalization in U.S. defense production was clearly the right one. The Soviet Union fell significantly behind the United States in military technology during the 1980s, and a key reason why is that the U.S. government pursued globalization in its defense-related production during this period while the Soviets did not.<sup>72</sup> In short, Washington successfully leveraged economic globalization to help the United States rapidly outpace its adversary during the final phase of the Cold War.

Our analysis indicates that national policymakers should refrain from initiating any direct restrictions on the globalization of U.S. biodefense efforts. But what about the current U.S. biosecurity regulatory framework, which works against the pursuit of globalization in biodefense only indirectly? Should all recently enacted biosecurity regulations be eliminated? Some might conclude yes, not just because these regulations constrain globalization in biodefense but also because they may not be especially effective. In particular, some analysts have suggested that efforts to regulate access to materials and knowledge relevant to the development of biological weapons will have limited success.<sup>73</sup> With an estimated 800 laboratories in the United States working with any one of the forty-nine pathogens and toxins controlled under the CDC's select agent program, federal officials have acknowledged the difficulty of their task.<sup>74</sup> In

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and the numerous calls to restrict the extent of globalization that were voiced at this time, see Theodore H. Moran, "The Globalization of America's Defense Industries: Managing the Threat of Foreign Dependence," *International Security*, Vol. 15, No. 1 (Summer 1990), pp. 57–99.

70. See U.S. Department of Defense, *The Impact of Buy-American Restrictions Affecting Defense Procurement*, report to the U.S. Congress by the secretary of defense, July 1989, pp. 15–22.

71. See John Blackwell, "The Defense Industrial Base," *Washington Quarterly*, Vol. 15, No. 4 (Autumn 1992), p. 197.

72. Stephen G. Brooks, "The Globalization of Production and International Security," Ph.D. dissertation, Yale University, 2001, chap. 5; see also Stephen G. Brooks and William C. Wohlforth, "Power, Globalization, and the End of the Cold War: Reevaluating a Landmark Case for Ideas," *International Security*, Vol. 25, No. 3 (Winter 2000/01), pp. 34–37.

73. See Gerald Epstein, "Controlling Biological Warfare Threats: Resolving Potential Tensions among the Research Community, Industry, and the National Security Community," *Critical Reviews in Microbiology*, Vol. 27, No. 4 (January 2001), pp. 321–354; Skolnikoff, "Research Universities and National Security," p. 72; and Stern, "Dreaded Risks and the Control of Biological Weapons," pp. 95, 119–120.

74. Gold, "Research Questions: With Plague Fears on Rise, an Expert Ends Up on Trial."

addition to efforts to control select agents, M.R.C. Greenwood (chancellor of the University of California, Santa Cruz) notes that attempts to stem the proliferation of biological tools and expertise will be even more difficult. She likens this situation to “a modern version of closing the barn door after the horse has left.”<sup>75</sup> The spread of nuclear weapons technology after World War II underscores this point, demonstrating that even under a strict classification regime, forming a hermetic seal around “sensitive” knowledge is impossible. In comparison, containing the spread of biological weapons poses a far greater challenge due, in part, to the dispersion of technologies and knowledge through the growth of the international biotechnology industry.

Against this line of argument is a stark reality: The biological proliferation threat is real, and the world cannot ignore highly dangerous activities in the biological sciences and in the biotechnology and pharmaceutical industry.<sup>76</sup> The issue is not whether regulations are needed, but the form they should take. How is it possible to reduce the biological proliferation threat without compromising the ability to develop adequate biodefenses?

We argue that an international regime that establishes a uniform set of biosecurity regulations may offer the best solution. On its face, an international biosecurity regime would seem to exacerbate the regulatory burden on bio-defense research. Policymakers searching for a moderate solution to the threat of biological banditry are therefore more likely to opt for a series of stopgap domestic regulations. As demonstrated above, however, this strategy solves some problems but unintentionally creates others.

Various proposals for an international biosecurity governance regime are already on the table.<sup>77</sup> Two are notable in their call for uniform, enforceable biosecurity standards across countries. Michael Barletta, Amy Sands, and Jonathan Tucker advocate the development of a biosecurity convention that would provide a legally binding, multilateral mechanism for participant countries to negotiate and enforce biosecurity standards akin to those of the CDC select

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75. Quoted in David Malakoff, “Researchers See Progress in Finding the Right Balance” *Science*, October 18, 2002, p. 529.

76. John Steinbruner and his group at CISSM are working to define “highly dangerous” activities. Examples include research efforts to increase the virulence, stability, or communicability of pathogens and the indiscriminate transfer of category A agents to unknown parties. Steinbruner et al., *Controlling Dangerous Pathogens*.

77. In addition to these proposals, a smaller-scale international effort is also under way. To create industrywide standards that will eliminate the competitive disadvantages of biosecurity compliance, Interpharma (a consortium of Swiss pharmaceutical companies) has devised a collection of best practices for preventing the hostile use of biotechnology. See Interpharma, “Biosafety and Biosecurity—Industry Best Practices to Prevent Misuse of Biohazardous Material,” Basel, Switzerland, May 2002.

agent program.<sup>78</sup> Similarly, John Steinbruner and his group at the Center for International Security Studies at Maryland have proposed a protective oversight system for sensitive biological research on an international scale. This system takes the idea of a biosecurity convention a step further by calling for a biological research security system that would not only track the pathogens themselves but would also oversee particularly dangerous categories of research.<sup>79</sup> Steinbruner advocates a tiered system in which “potentially dangerous” research activities would be monitored locally, “moderately dangerous” activities nationally, and “extremely dangerous activities” internationally.<sup>80</sup> Although oversight jurisdiction would be tiered, all research activities would abide by legally binding uniform international standards. Most significantly, this proposal provides a mechanism for the independent evaluation of research projects before the work begins.

Neither of these proposals was expressly designed to facilitate international collaboration, and they would ostensibly appear to threaten biodefense research and development initiatives through excessive regulation. They do, however, ameliorate the much larger problems introduced by balkanized biosecurity regulatory regimes. In part for this reason, an international regulatory regime is likely to receive the support of U.S.-based industry leaders. As Tucker explains, “Because the U.S. pharmaceutical and biotechnology companies that work with select agents already face strengthened domestic regulations, they would benefit from a level regulatory playing-field vis-à-vis competitors in Europe and Japan.”<sup>81</sup> From a business perspective, an international regime would not only level the playing field but would also reduce uncertainty—a key factor that currently discourages long-term commitment to cross-national collaboration. Under a protective oversight regime, for example,

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78. Michael Barletta, Amy Sands, and Jonathan B. Tucker, “Keeping Track of Anthrax: The Case for a Biosecurity Convention,” *Bulletin of the Atomic Scientists*, Vol. 58, No. 3 (May/June 2002), pp. 57–62; and Jonathan B. Tucker, “Preventing Terrorist Access to Dangerous Pathogens: The Need for International Standards,” *Disarmament Diplomacy*, No. 66 (September 2002), <http://www.acronym.org.uk/dd/dd66/66op2.htm>.

79. Steinbruner et al., *Controlling Dangerous Pathogens*.

80. “Extremely dangerous” research is currently defined as projects that may create pathogens significantly more dangerous (i.e., lethal, infective, or transmissible) than existing pathogens. *Ibid.*

81. Tucker, “Preventing Terrorist Access to Dangerous Pathogens.” A recent Stimson Center study also found that pharmaceutical and biotechnology industry leaders agreed to the need for an international biosafety standard for biosecurity. See *Compliance through Science: U.S. Pharmaceutical Industry Experts on a Strengthened Bioweapons Nonproliferation Regime—A Collaborative Research Report of Experts from the U.S. Pharmaceutical and Biotechnology Industries*, Report No. 48 (Washington, D.C.: Henry L. Stimson Center, September 2002), p. 49.

a research team could receive official assurance that its project complied with international biosecurity standards, thereby significantly reducing the long-term regulatory risks of undertaking an international collaborative project. Over time, the bureaucratic hassles associated with biosecurity compliance would diminish as reporting requirements are standardized and harmonized across borders. Moreover, it will likely be possible to reduce the number of nationality-based personnel restrictions in direct proportion to the number of countries that comply with the international regulatory regime.

In sum, internationally enforced biosecurity regulations would, at a minimum, harmonize biosecurity regulations and thereby eliminate the indirect incentives for autarky in biodefense research and production that are generated by an exclusively domestic regulatory regime. At best, an international regime will both facilitate international collaboration and provide a more effective means of preventing the hostile use of biology. Although a biosecurity regime that covers a broad range of countries would be preferable, even one limited to countries in North America, Western Europe, and Japan would be extremely beneficial because international collaboration in this area is largely limited to these regions. This is reflected in Figure 2, which shows that more than 90 percent of all technological cooperation agreements in the biotechnology sector involve companies from North America, Western Europe, and Japan. Encouraging a coalition of countries from these regions to adopt international biosecurity standards would be both practical and useful.

### *Conclusion*

After the terrorist attacks of September 2001, many scholars and policymakers began to argue that economic globalization facilitates terrorism. This is only half right. While economic globalization does enhance the threat of terrorism, it also facilitates the effort to respond to this threat. Our examination reveals that to reduce the bioterrorist threat, it is crucial to make rapid progress in vaccine development and that one of the best ways to do this is to preserve international systems of collaboration, especially among commercial firms. In short, all aspects of the globalization trade-off must be considered in the ongoing effort to reduce the threat of terrorism in general and bioterrorism in particular.

To date, U.S. biosecurity policy has not adequately factored in the significance of globalization. Focusing on the threat that sensitive materials and knowledge will fall into the hands of a would-be bioterrorist, the U.S. government recently adopted an exclusively domestic regulatory framework. One

unintended consequence of this policy shift is that it encourages a move toward more autarkic research and production strategies in the biodefense sector. To avoid this problem and ensure that the globalization of biodefense continues, it is necessary to harmonize regulations in this area through the creation of an international biosecurity regime. Taking this route will not only eliminate the incentives for autarky in the development of biodefense technologies, but it also promises a more effective means to guard against the hostile use of biology.