FOLLOW-ON BIOLOGICS

A WHITE PAPER PRESENTED BY

THE COOPERATIVE NONPROLIFERATION PROGRAM
THE HENRY L. STIMSON CENTER
FEBRUARY 2007

AS THE BIOPHARMACEUTICAL INDUSTRY EXPANDS TO INCLUDE A FOLLOW-ON MARKET, CAREFUL ATTENTION SHOULD BE PAID TO ENSURE THAT NEW COMPANIES THAT HANDLE SELECT AGENTS, AND PRODUCE SELECT AGENT DERIVED PRODUCTS, ARE REQUIRED TO COME UNDER STRICT STANDARDS OF MANAGEMENT, USE, AND DISTRIBUTION OF RAW AGENTS AND FINISHED PRODUCT.

Seven days after the September 11 attacks on the World Trade Center and the Pentagon, anthrax spores were spread through the US Postal Service to a variety of news services and public officials. Within three months, eighteen people were known to have been infected, five of whom ultimately died. The personal tragedy was compounded by widespread economic and social disruption in the United States and around the world. Since then, the US Government has undergone a fundamental reordering of budgetary and institutional alignments to combat global weapons diffusion. Addressing the threat posed by biological weapons has focused almost exclusively on controlling access to the most hazardous pathogens, and monitoring research on a defined list of potentially dangerous agents. To date, little attention has focused on the movement of these dangerous pathogens beyond their collection and R&D stages. However, with an advancing life sciences industry and an evolving security environment, the unlicensed acquisition, proliferation and misuse of select agents and products, which are stored and distributed globally, may present new avenues through which bioterrorists could attack the United States.

In the current Congress, significant attention will be given to the issue of generic biopharmaceuticals, or 'follow-on' biologics. Biologics are the fastest growing and highest priced set of drugs in the US healthcare system. Sales for such drugs jumped 17.2% in 2005 to $32.8 billion.[1] In September 2006, a bill was introduced in the House and Senate that establishes a process for the FDA to approve lower-cost, follow-on biologics.[2] In January 2007, another bill was introduced that amends the Medicare program to exclude all brand-name drugs from coverage, unless a generic is not available.[3] These measures are clearly intended to create incentives for generic drug use and to reduce cost burdens on US consumers.

In September 2006, The Henry L. Stimson Center released the findings of a study that called upon federal and state governments to join private industry to enhance security surrounding bulk biological materials, develop common standards governing the chain-of-custody of pharmaceutical products that contain potentially dangerous biological agents and toxins, and tighten tracking mechanisms all in the interest of national security.[4]

THE HENRY L. STIMSON CENTER

1111 19th Street, NW | 12th Floor
Washington, DC 20036
P 202.223.5956 F 202.238.9604
www.stimson.org

While generics are common in many other types of drug products, there is no such market for biologics. **As the biopharmaceutical industry expands to include a follow-on market, careful attention should be paid to ensure that new companies that handle select agents, and produce select agent derived products, are required to come under strict standards of management, use and distribution of both raw agents and finished products.**

The CDC's Select Agent Program[5] has generated new intelligence on the uses, whereabouts and origins of over forty of the most high-consequence pathogens and toxins. However, it does not track the chain of custody of biological agents from their raw, research stage through their development into pharmaceutical products. More importantly, there are no standardized government or industry regulations that sufficiently prevent unlicensed persons or companies from obtaining access to raw biological agents.

With the certain emergence of a generic biopharmaceutical, or 'follow-on' biologics, industry, the FDA and Congress should work assiduously to require strict efficacy and safety trials for these new products—particularly those derived from select agents. As the industry and market develop, and more of these products move from R&D to full scale production, the number and quantity of select agents moving throughout the country will increase. Therefore, the risk of misuse, diversion or theft of select agents will also increase. **As this industry grows, any company that handles select agents must be required to abide by a standardized and stringent set of regulations to ensure public health and security.**

At present, financial and technical hurdles make existing products derived from select agents unattractive to terrorists intent on causing mass destruction. However, the potential use of a select product to incite panic within the United States and the potential harm that could come from counterfeit drugs should motivate government regulators to utilize all means available to track and trace the movement of both bulk agent and finished product. Under the existing Healthcare Common Procedure Codes (HCPCS) system, pharmaceuticals are given a J-code. The J-code system is generally used to process claims for higher-cost, injectable pharmaceuticals, the category under which existing select products fall. Regrettably, rather than basing that code on the unique properties of individual products, those codes are assigned based upon broad similarities. In addition, different brands of drugs which are manufactured from the same raw material are not differentiated—with either a unique nomenclature or unique J-codes. Rather they are identified based upon a common ingredient without regard for different dosages, applications or manufacturing processes. The likelihood of a new follow-on biologics market creates an added layer of risk and confusion to this issue.

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[1] IMS Health, *IMS National Sales Perspective*, February 2006.
[2] 'Access to Life-Saving Medicine Act', S. 4016 and H.R. 6257, introduced on 29 September 2007.
[3] 'Generics First Act of 2007', S. 28, introduced on 4 January 2007.
[4] A complete copy of the report, "Regulating Access to and Control of Dangerous Pathogens: Implications for the Pharmaceutical Industry," can be accessed online at: http://www.stimson.org/cnp/pdf/RegulatingAgentsReport.pdf
[5] See the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Public Law 107-188). There are also select agents and toxins which are overseen by the US Department of Agriculture for their potential to harm animals and agriculture, as well as a category of 'overlap' agents and toxins which have the potential to affect both humans and animals. 350 entities are registered with the CDC as possessing select agents with the capability to affect human health. They break down into the following categories: 105 academic/university; 104 state/local government; 61 federal government; 39 commercial; 35 private/non-profit/research institutions; 6 other. Federal Register, Vol. 70, no. 52, Friday March 18, 2005, Rules and Regulations, 13315.

RECOMMENDATION

When considering threats to the supply chain, including diversion and counterfeiting, relevant authorities must consider comparable products—particularly follow-on biologics, or generic biopharmaceuaticals. **In the interest of public health and security, as a generic biopharmaceutical industry expands alongside its brand-name counterpart, and with an ever-increasing consumer appetite for such products, the Cooperative Nonproliferation Program at the Henry L. Stimson Center recommends that these products are appropriately tracked and coded—particularly those derived from select agents.** An increase in the number of comparable products which are manufactured from the same raw material, but which do not have without proper identifying and tracking mechanisms, complicates the ability to identify and prevent a public health crisis, whether caused intentionally or unintentionally.