1225 Eye Street NW, Suite 400
Washington, D.C. 20006

February 8, 2006

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2005N-0510.
Anti-Counterfeit Drug Initiative Workshop and Vendor Display

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) appreciates the opportunity to comment on the Food and Drug Administration's (FDA's) "Anti-Counterfeit Drug Initiative Workshop and Vendor Display." BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations in all 50 U.S. States and 33 other nations. BIO members are involved in the research and development of health care, agricultural, industrial and environmental biotechnology products.

Counterfeit Pharmaceuticals are a Threat to the Public Health:

BIO commends FDA for its continued commitment to securing the nation's drug supply against counterfeit drugs and biologics. The American drug distribution system is the most secure in the world and, thanks to the efforts of the FDA, drug manufacturers and distributors, patients have high confidence that the drugs that they are prescribed are safe and efficacious. Some estimates place the proportion of counterfeit drugs in foreign markets as high as 10 percent, while counterfeit products in the U.S. distribution system are rare.

Nevertheless, the presence of any amount of fake, adulterated, sub-potent, or super-potent drugs in the American pharmaceutical distribution system poses a threat to the public health. These dangers can be even greater with counterfeit or adulterated biologic drugs, which must be injected or infused directly into a patient's bloodstream.

In recent years, there has been a proliferation of counterfeiting and the number of criminal cases opened by FDA has risen from six in 2000 to 58 in 2004 and 32 in 2005. In addition, counterfeiters have become increasingly sophisticated at mimicking pharmaceutical packaging and labels as well as overt and covert anti-counterfeiting technologies. Pharmaceutical supply experts are in a technological "arms race" to stay a step ahead of counterfeiters and industry has taken productive steps to secure drug products with holograms, color shifting dyes, and numerous other anti-counterfeiting technologies. However, there is more that government and industry can address to secure the drug supply and ensure patient safety.

Track-and-Trace Technology Offers Tangible Benefits:

In 2004, FDA strongly endorsed track-and-trace technology for pharmaceutical products to meet the pedigree requirements established under the Prescription Drug Marketing Act (PDMA). FDA endorsed a promising technology, Radio Frequency Identification (RFID), and set the goal of implementing RFID technology throughout the drug distribution system by 2007. EPC Global and its partners have made progress in setting standards for RFID and mass serialization, and individual drug manufacturers have taken concrete steps to implement RFID technology. Several BIO member companies have implemented RFID tags on at least one solid dose pharmaceutical product.

Pharmaceutical Product Verification: Because the U.S. drug distribution system is comprised of multiple points of entry for pharmaceutical products before they reach the patient (including sellers and purchasers, repackers, distributors, etc), there also are multiple opportunities for bad actors to introduce counterfeit drugs that then are passed down the supply chain to patients. Biopharmaceutical companies neither produce counterfeit drugs, nor do we have control over the entry points in secondary supply chain. However, we recognize that these vulnerabilities can be reduced by either shortening the supply chain or making it transparent.

Electronic track-and-trace technology, including RFID, could help create this transparency, disclosing the origin and distribution history of drug products. BIO supports its use within the drug distribution system in a responsible manner. First, and of foremost importance to the patients that the biotechnology industry ultimately serves, BIO believes that fully implemented electronic tracking from the manufacturer to the pharmacist will reduce the number of counterfeit drugs that enter the distribution system. If products carry serialized machine-readable tags, their authenticity can be verified through the electronic pedigree at every node of distribution. Patients are protected by these multiple verification steps.

Improved Supply Chain Management: RFID or similar technology may create more efficient supply chain management. In theory, with RFID tags and scanners deployed throughout the distribution channel, a company can track its products more effectively and efficiently, with fewer lost, diverted, or stolen products. Through real-time inventory

tracking, manufacturers can improve product forecasting and demand predictions and adjust shipments accordingly. In the event of a recall, products could be quickly located and returned.

Public Health Emergency Response: Improved product tracking capability would allow greater ability to trace biopharmaceutical products during distribution, so they can be diverted to meet emerging medical needs during a public health emergency or product shortage.

Obstacles Have Slowed RFID Adoption:

Industry has moved with due caution to adopt RFID due to a number of uncertainties, technological obstacles, business process limitations, and other barriers.

Technological Limitations and Business Process Integration: RFID technology is promising and the tags and readers are improving, but physical, technological, and business practice limitations persist. Materials to which the tag is affixed or those in proximity to the tag, such as liquids or metals, can affect readability and negate the advantage of not requiring line-of-sight for readings. Further, poor reliability of tags and inaccuracy of scanning can hamper product handling efficiencies and security. We also are concerned about methods that can be used to mask or disable the RFID tag, such as copper, aluminum foil, or static discharge.

Further, it is presently unclear how RFID technology will be integrated in individual companies' business processes. Many technical and business process issues are not adequately settled and there are additional uncertainties regarding implementation complexity and the potential for distribution disruptions.

While FDA should encourage the use of RFID technology, BIO believes a full complement of product-appropriate technologies must be deployed for full security of the drug supply; the door should be left open for alternative technologies to RFID.

Uniform Adoption among Distribution Partners: BIO also is concerned about uniform adoption of RFID technology among all of the partners in the drug distribution channel. Unless all parts of the distribution chain, including pharmacies, use track-and-trace technology, the system will not succeed in counteracting counterfeit products. Much of the upfront burden and responsibility regarding counterfeiting is being placed on the manufacturers rather than the distributors. While partial implementation might confer some benefit to patients and the distribution system as a whole, BIO believes that a reasonably evolved track-and-trace infrastructure should be established along the supply chain before manufacturers are expected to affix machine-readable tags to their products.

Concerns Regarding Biological Stability: Most biotechnology products are complex, protein-based biologics that are produced by living systems and are particularly vulnerable to changes in their environment. For instance, most biopharmaceuticals must

be refrigerated at all times before being administered to prevent fundamental changes that can render the drug ineffective or unsafe. Some products also must be kept at a certain pH level; others must be kept out of direct sunlight. To date, there is not a complete understanding of how RFID tags and readers may affect the stability of biological product during distribution; many companies have been hesitant to adopt the technology until these questions are answered. Recognizing these unique concerns, FDA has begun research, with the Center for Devices and Radiological Health, the Product Quality Research Institute (PQRI), and the Auto-ID Laboratories, to evaluate the effect of RFID tags on biological product stability, liquid temperatures, and storage conditions. BIO applauds FDA for initiating this research and looks forward to reviewing the results. BIO also encourages research to evaluate the use of RFID technology to monitor environmental exposures and integrity of the cold chain.

Repackaging: Although most biologic drugs are not regularly repackaged, repackaging does take place in the drug distribution chains and presents unique challenges for successful RFID implementation. No matter at what level of packaging the RFID tag is added, it is still tracking the package at best and may be discarded – intentionally or unintentionally – during routine repackaging. Additionally, without a clear mechanism for assuring that the RFID device is destroyed at its endpoint, the tag could be recycled and re-enter the supply chain. Reintroduction of enough tags into the system would undermine the integrity of the track and trace technology.

Cost: A significant barrier to adoption, particularly for smaller biotechnology companies, has been the upfront capital investment necessary to employ an RFID system. While the cost of implementing RFID appears to be dropping, wholesale investment in the technology is premature for many drug products, such as for products that rarely are counterfeited. Furthermore, unlike small molecule drugs, which are often distributed through large wholesale distributors, biopharmaceuticals are more frequently distributed through small specialty distribution channels that lack the economies of scale to maximize track-and-trace cost efficiency. Industry needs to conduct additional cost estimates so that a risk-based analysis can be developed.

Principles for Track-and-Trace Implementation:

As we move towards adopting track-and-trace technologies, the biotechnology industry suggests the following principles to help guide future implementation:

- *Patient Safety Is the First Priority:* The biotechnology industry has developed more than 200 drugs and vaccines that have helped millions of people worldwide. Improving the lives and well-being of patients is our first priority. The adoption of electronic track-and-trace technology should be supported in a way that enhances patient safety and public health.

- *High Standards for Supply Chain Integrity Must Be Preserved:* BIO agrees that a truly closed system would be the primary deterrent to counterfeit medicines

entering the distribution system. Like the discovery and manufacturing of biotech products, the distribution of biologics is complex and technical. The industry, working with regulators, should use a high degree of care and planning in the introduction of any massive distribution changes, such as the adoption of RFID and/or serialization. BIO opposes any regulatory requirements that would force premature adoption of developing technologies or unproven systems.

- *There Is No Single Technological Solution to Counterfeits:* There are a number of technologies are currently available to secure the drug supply, and other promising technologies are under development. Offering the industry a multiplicity of approaches recognizes the variations among drug products and between drugs and biological products. Deploying product-appropriate technologies will best challenge those who want to counterfeit prescription drugs. BIO believes that the choice of specific anti-counterfeit technology should be left to the manufacturers, who have expertise in the development, manufacture and design of both products and packaging components.

- *Electronic Pedigrees Should Be Fully Implemented:* BIO has previously stated its support for the FDA's full implementation of 21 C.F.R. 203.50. This rule, which has been on hold for several years, would require "paper pedigrees" for pharmaceutical products, from which it would be possible to document the source of the product, the numbers and kinds of transactions between the initial sale by the manufacturer and the final purchase by the end user, and other key information. However, new information technologies can decrease the logistical and administrative burden created by paper pedigrees, and BIO supports harmonized electronic pedigree standards.

- *Role of FDA:* FDA can accelerate the use of track-and-trace technology by providing a forum for information sharing among industry stakeholders in order to highlight best practices and promising new technologies.

- *Prescription Drug Importation Invites Criminal Counterfeiting*: Finally, we support FDA's opposition to drug importation proposals that would open up America's borders to unsafe or illicit pharmaceutical products. We believe it is crucial for FDA not only to retain its authority to control the entry of pharmaceutical products into the United States, but also to receive the resources it needs to enforce the law. BIO believes that a number of national and state actions and statements are unfortunately signaling that the United States is willing to become a marketplace for illicit prescription drug traffickers. We recommend FDA continue its opposition to efforts that weaken our border controls and invite criminal elements into our pharmaceutical distribution system.

Conclusion:

We again thank FDA for the opportunity to provide our comments and look forward to continuing to work with the agency and other private partners to fight counterfeit drugs. If we may be of further assistance on any of the topics addressed above, please do not hesitate to contact us.

Sincerely,

/s/

Sara Radcliffe
Managing Director for Science and Regulatory Affairs
Biotechnology Industry Organization (BIO)