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Dockets Management Branch (HFA-305)
Food and Drug Administration
5600 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. 2008N-0120: Standards for Standardized Numerical Identifier, Validation, Track and Trace, and Authentication for Prescription Drugs; Request for Comments

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments and provide requested information with respect to *Standards for Standardized Numerical Identifier, Validation, Track and Trace, and Authentication for Prescription Drugs*.

BIO welcomes FDA's request for information as a promising step towards establishing a uniform national standard for product serialization and electronic track-and-trace for prescription drugs. BIO represents more than 1,200 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology technologies, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, and a cleaner and safer environment.

STRONG, UNIFORM NATIONAL PEDIGREE AND SERIALIZATION STANDARDS SHOULD BE ESTABLISHED:

Due to the nature of the United States' closed and highly regulated pharmaceutical supply chain, American patients have high confidence in the integrity of the drugs and biologics they are prescribed. However, pharmaceutical counterfeiting, adulteration, and diversion remain a persistent threat in the global marketplace. The actual prevalence of criminal counterfeiting is difficult to quantify, but the World Health Organization estimates that less than 1% of sales in developed countries and more than 10% in developing countries are counterfeit or adulterated. Biopharmaceutical manufacturers currently deploy a wide variety of sophisticated, multilayered anti-counterfeiting strategies, but also recognize that there are additional ongoing steps that can be taken to further secure the supply chain and enhance inventory management.

One such tactic is the development and deployment of standards-based e-pedigree and track-and-trace technology to validate a medical product's transaction history and confirm its authenticity. BIO is encouraged that FDA is reasserting its leadership in this area, consistent with the agency's authority under Section 913 of *The Food and Drug Administration Amendments Act of 2007* (FDAAA, P.L. 107-085) BIO supports the establishment of strong, uniform national pedigree and serialization standards, rather than the emerging patchwork of individual state mandates. A comprehensive federal regulatory scheme will not only ensure compatibility of systems and operational efficiencies but more importantly, be more effective in deterring counterfeiting.

Without federal leadership in this area, biologics manufacturers will be subject to up to 50 separate and potentially inconsistent statutory schemes which would introduce significant inefficiencies into the national drug distribution system, erect barriers to interstate commerce and create confusion which counterfeiters may seize upon. Additionally, a heterogeneous system of state-by-state pedigree laws will encourage counterfeiters to establish criminal enterprises in those states with the most lenient pedigree standards. This has been a problem in the past in regards to paper pedigrees. If supply chain stakeholders can work towards the implementation of a single uniform national standard for product serialization, they will be able to more efficiently and effectively establish new track-and-trace systems that can serve as a cornerstone of a uniform federal track-and-trace program.

BIO believes that such a program should in turn be implemented using a risk based approach that is part of an overall risk based anti-counterfeiting strategy. Through a more focused implementation effort, there will be greater assurance that the complexities of such a program can be addressed. This will ultimately serve to ensure the success of track-and-trace implementation.

FEDERAL EFFORTS SHOULD BUILD UPON ONGOING INITIATIVES:

BIO is pleased that the agency notes that “it is FDA’s preference that such standards be the result of existing private and public sector collaborative standards processes.” (p.3) Indeed, the private sector has made significant progress towards developing, piloting, and adopting interoperable electronic standards for track-and-trace. Under California’s e-pedigree laws (SB 1307, SB 1476), drug and biologics manufacturers made significant efforts towards meeting the January 1, 2009 goal for implementing serialized, interoperable e-pedigree systems. Although supply chain stakeholders were unable to meet that targeted implementation date and the effective date of the law has been postponed to 2011, any federal initiatives should complement and build upon the progress made under the California initiative. Additionally, any federal standard should not become effective prior to 2011. Manufacturers have already invested a considerable manpower and resources piloting and learning about which approaches are the most effective and federal efforts should capitalize on that accumulated knowledge base to leverage the infrastructure enhancements already implemented to date.

ADDITIONAL KEY ISSUES SHOULD BE ADDRESSED:

If a uniform standard for e-pedigree and track-and-trace is to be successfully implemented, FDA should provide additional guidance to industry on several key issues that remain to be addressed under various state pedigree laws. BIO notes, however, that additional statutory authority may be necessary for FDA to successfully implement a uniform national pedigree and track-and-trace system that fully addresses the key issues described below:

- *Level of Serialization:* FDAAA § 913 requires that FDA develop a standardized numerical identifier to be applied at the point of manufacturing “at the unit or pallet level.” Manufacturers will require additional guidance on the level of required serialization and the definition of “unit” well in advance of any implementation date in order to retrofit product lines to integrate the standardized numerical identifier on pallets or units. The universe of prescription drugs, which these regulations will apply to, is broad. These prescription drugs are made in different forms (i.e. liquids, solids), and are sold in different packages (i.e. bottles of 100 pills, case of 10 IV bags). For example, one dose of antibiotics could be one pill within a bottle, or one bag of intravenous solution within a case. Therefore, compliant standards and technologies under the law must account for these differences in both the technology used and the level of serialization. With respect to many biological products, packages include multiple vials or ampoules in a single carton which constitutes the smallest unit of sale. Tracking each vial in such a carton would be operationally challenging and due to space constraints on vials and ampoules, may not even be feasible. For this reason BIO urges FDA to recognize that the smallest unit eligible for serialization is the smallest unit made by the manufacturer for sale to the pharmacy or other person furnishing, administering, or dispensing the drug.

- *Inference:* Supply chain stakeholders will require additional guidance on the principle of inference, and the extent to which an individual authenticating a pallet or unit of packaging can infer the identity of the sub-units of product contained therein. BIO believes that inference is appropriate with respect to the contents of a sealed container from the manufacturer. Otherwise, in instances where 2-D bar codes are used, distributors would be required to open sealed boxes to verify contents – a requirement which would lead to operational inefficiencies and defeat any tamper evident seals or secure packaging features.
- *Authentication:* BIO also notes that there will be little public health value in a serialized track-and-trace system if it lacks a requirement that the end-user must authenticate the identity of the product.
- *Grandfathering:* Supply chain stakeholders will need guidance regarding the grandfathering of products and whether non-serialized packages already in the supply chain will be deemed saleable. In the interim period before serialization takes effect, manufactured-released products in commercial distribution should continue to be ready for sale without a serialized identifier if supply chain stakeholders take reasonable steps to authenticate the source of the product. Furthermore, depending on the implementation schedule, manufacturers may not have sufficient time to “flush” inventory, thus highlighting the need for grandfathering finished product which is in manufacturers’ inventory at the time of the effective date.
- *Sealed Packs:* One of the key issues of importance in the larger context of anti-counterfeiting efforts is to make sure that manufacturer’s serialized packs are sealed to prevent tampering, adulteration, or the introduction of counterfeit product into the serialized package. Many biologics manufacturers currently use tamper evident Carton Closure Labels in the United States and are advocating their use in Europe. These manufacturers believe that it is inappropriate to intrude into the seal or sealed packs between their application by the manufacturer and use by the clinic or patient. The use of sealed packs and tamper resistant packaging from the manufacturer to the patient may help to complement and empower serialization, thereby ensuring the authenticity of the enclosed product.
- *Transfers to Affiliates, Co-Licensees, Contract Manufacturers Fill/Finish and Packaging Subcontractors, and/or Consignees:* Another aspect of pedigree and serialization relates to the point at which a transfer triggers reporting and authentication requirements. BIO believes that as long as ownership and/or control of product remains with the manufacturer, or one of its affiliates, or a co-licensee, transfers between such entities and/or contract manufacturers, filling, finishing and packaging subcontractors and/or consignees should not trigger pedigree or serialization requirements.

- *Returns:* Supply chain stakeholders will also require additional guidance on the circumstances when it is appropriate to return saleable products and controls to ensure the ability of manufacturers to accept and destroy non-saleable returns. BIO believes that saleable returns should be allowed if the product is returned on the same pedigree and the return should be considered non-saleable if it does not have an authorized pedigree.

STANDARD NUMERICAL IDENTIFIER:

In terms of specific numerical standards, BIO believes there are several elements that are appropriate to be included in a standard numerical identifier. However, there are additional data elements that may be required depending on the type of data carrier that is deployed. For example:

Numerical Identifier Characteristics	Data Element
BIO recommends that standard numerical identifier <u>should</u> include:	<ul style="list-style-type: none"> • The NDC code or The Global Trade Identification Number (GTIN), and • A unique identifier added in the form of a randomized or sequential number in addition to GTIN
BIO members believe that the amount of information in the numerical identifier should be minimized due to operational, capacity, and security considerations. For example, the standard numerical identifier <u>should not</u> include:	<ul style="list-style-type: none"> • Lot number • Batch number • Expiration date
When using a bar code, BIO believes the standardized numerical identifier <u>should only</u> include:	<ul style="list-style-type: none"> • The GS1 standard EAN.UCC: ECC 200 AI(01) + AI(21); and • A unique serial number AI(21) as above
When using RFID, the following elements <u>should</u> be included:	<ul style="list-style-type: none"> • GTIN • Serial number • Additional elements to ensure patient security and privacy

BIO understands that infrastructure will have to exist to manage the registry, assignment, ownership, access, and use of the numbers and other data created by the system. To accommodate this, organizational and legal issues need to be assessed and addressed. These underlying issues may be more complex than many of the technological issues confronting supply chain partners and government regulators. BIO would expect that the agency will undertake a formal notice-and-rulemaking process before any specific numerical identifier or data carrier would be required to be applied to products under FDA regulation.

STANDARDS SHOULD BE INTERNATIONALLY HARMONIZED:

BIO member companies conduct business in the global marketplace and wherever possible and appropriate, encourage the international harmonization of regulatory requirements. Counterfeiting and criminal tampering is a global problem, and as such, should be addressed from both a domestic and international perspective. FDAAA states that the standardized numerical identifier should “to the extent practicable, shall be harmonized with international consensus standards for such an identifier.” BIO is aware of several other international initiatives to develop and implement track-and-trace standards and technology, such as the European Federation of Pharmaceutical Industries and Associations (EFPIA) *Coding & Identification of Pharmaceuticals* initiative and the European Commission’s *Public Consultation in Preparation of a Legal Proposal to Combat Counterfeit Medicines for Human Use*. When identifying a standardized numerical identifier, BIO encourages the agency to work in close concert with these international bodies to ensure that track-and-trace standards can be harmonized across international borders.

PRIORITIZATION:

FDAAA § 913 requires the Secretary, after consultation with relevant supply chain stakeholders, to “*prioritize and develop* standards for the identification, validation, authentication and tracking and tracing of prescription drugs.” Prioritization, as used in this section, should be interpreted to mean that the standards development process must employ a defined, risk-based implementation methodology for such standards. Applying a risk-based prioritization process for implementation is consistent with FDA’s current view on risk-based regulation in other areas of pharmaceutical manufacture.¹ Risk-based standards are best suited to protect patient safety and supply chain integrity because they:

- Target the problem by focusing on drugs most vulnerable to counterfeiting and diversion.
- Prevent risk of market stock-out for commodity pharmaceutical product having no aftermarket popularity among counterfeiters/diverters.

- Prevent unnecessary dilution of enforcement resources, thereby providing an effective regulatory framework for all drugs, with the most at-risk drugs secured by more specific requirements and standards.

Consistent with the FDAAA § 913 language suggesting that the standardized numerical identifier be applied “at the point of manufacturing...at the package or pallet level,” the agency may consider phased piloting and implementation of track-and-trace systems beginning with product pallets before ultimately expanding the system to include package-level tracking-and-tracing.

CONCLUSION:

In conclusion, BIO believes that FDA should interpret the FDAAA as an indication of Congressional intent to establish a national pedigree standard which permits serialization technology to be implemented on a risk approach basis as part of an overall risk based anti-counterfeiting strategy. BIO appreciates this opportunity to comment on *Standards for Standardized Numerical Identifier, Validation, Track and Trace, and Authentication for Prescription Drugs*. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

Andrew J. Emmett
Director for Science and Regulatory Affairs
Biotechnology Industry Organization

ⁱ Refer for example to “FDA’s Pharmaceutical cGMPs for the 21st Century – A Risk-Based Approach” published in 2003.