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

**Re: Docket No. FDA-2009-D-0001, OC 2008299**

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the *Draft Guidance for Industry on Standards for Securing the Drug Supply Chain--Standardized Numerical Identification for Prescription Drug Packages*. BIO supports the establishment of a uniform national e-pedigree/track-and-trace system and we believe that identification of a product serialization standard will lay the foundation for a successful system which will enhance supply chain management and deter criminal counterfeiting. BIO endorses GS1 standards for product serialization which can successfully meet those goals and facilitate the adoption of a national, integrated, and interoperable track-and-trace system.

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 products, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, and a cleaner and safer environment.

**I. SERIALIZATION WILL FACILITATE A UNIFORM NATIONAL E-PEDIGREE/TRACK-AND-TRACE SYSTEM:**

BIO welcomes this guidance as an important step towards establishing a uniform national standard for product serialization and electronic track-and-trace for prescription drugs. The

biotechnology industry has been proactive in combating counterfeiters through multi-layered approach of anti-counterfeiting technologies and supply chain security strategies. We recognize that a Standardized Numerical Identifier (SNI) affixed to prescription drug packages and coupled with e-pedigree and track-and-trace technologies can offer an additional layer of patient protection by facilitating authentication of a medical product's transaction history. It should be noted that the creation and implementation of new electronic technologies to track the distribution of drug and biologic products is a tremendous undertaking for large pharmaceutical companies and small biotech companies alike. These changes in business practice will have profound consequences for the highly complex operations of manufacturing facilities, packaging lines, distribution centers, and the operations of third-party partners and logistics providers. Nonetheless, BIO member companies are actively engaged in the process of working toward the development of an interoperable track-and-trace system that will benefit the industry, the supply chain, and all consumers of drug and biologic products.

BIO supports the establishment of strong, uniform national pedigree and serialization standards, rather than relying on the emerging patchwork of individual state mandates. Continued federal leadership in this area will help to minimize the potential for up to 50 separate and potentially inconsistent statutory e-pedigree/track-and-trace 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. Identifying and adopting a consensus standard for product serialization will establish the foundation for an effective federal track-and-trace system and allow stakeholders to more efficiently and effectively work towards the implementation of a single uniform national system for e-pedigree/track-and-trace systems.

## **II. DEFINITION OF PACKAGE-LEVEL SERIALIZATION:**

Under Section 913 of the Food and Drug Administration Amendment Act of 2007 (P.L. 110-085), FDA was directed to develop a standardized numerical identifier "to be applied to a prescription drug at the point of manufacturing and repackaging...at the package or pallet level." Under the proposed guidance, FDA opted to define a standard for package-level serialization. In doing so, it is critically important to have a standard definition of the applicable "package." In the guidance, FDA defines "the package to be the smallest saleable unit placed into interstate commerce by the manufacturer or the repackager for sale to the pharmacy or other dispenser of the drug product." (lines 60-62)

In order to further strengthen the definition of "package" and minimize the potential for any confusion between the package and its individual sub-units, we recommend that the "package level" be defined as "the smallest saleable unit [with its own package insert](#) placed into interstate commerce..." Often, biologic products are sold to the pharmacist or dispenser in packages that may contain several individual vials of product or pre-filled syringes that are not introduced into interstate commerce or sold independently. While it may be appropriate to place the SNI on the larger packaging sold to the pharmacist, diminutive label sizes may limit a manufacturer's ability to place an SNI on the individual sub-units within the packaging and these sub-units should not be subject to the serialization requirements.

BIO also recommends that the term “*smallest saleable unit*” be used consistently throughout the guidance, rather than other terms such as “*individual prescription drug package*” (lines 107 & 112), which may lend themselves to confusion.

### **III. THE sNDC MAY NOT GENERATE ADEQUATE NUMERICAL SEQUENCES FOR HIGH VOLUME PRODUCTS:**

In the Federal Register notice accompanying the draft guidance, FDA requested feedback on several questions, including the use of alpha-numeric numbering to facilitate additional unique number sequences:

*“Some comments recommended that the SNI allow for alpha-numeric serial numbers in order to increase the choices for the numbers. FDA’s draft guidance recommends that the SNI for most prescription drug packages be an sNDC, consisting of the NDC plus a unique 8- digit numerical serial number. Given the FDA recommendation for SNI, please comment on the necessity of having the serial number allow for alpha-numeric possibilities and under what standards this might be achieved.”*

BIO believes that the proposed Serialized National Drug Code (sNDC) standard, which incorporates the product’s 10-digit NDC number and a unique 8-digit serial number, will be sufficient for many prescription drug products, but may not provide adequate capacity for high volume products and/or products with long expiration dating. This may not be an issue in the near term, but could have a future impact, particularly for manufacturers that could potentially produce in excess of one billion units over an extended time period.

Industry experience suggests that a serial number for healthcare purposes should be alphanumeric, left-justified, of variable length (up to 20 digits long), and maintain uniqueness for 100 years. We recommend the GS1 serial number AI (21) specifications as an acceptable option to successfully meet these criteria.

BIO has been supportive of the work of GS1 and EPCGlobal standards development teams and many biopharmaceutical companies have utilized these standards to meet state and international track-and-trace requirements. To the extent possible, we suggest that the FDA-endorsed serialization standard should build upon existing GS1 standards and leverage the infrastructure already implemented to date rather than establishing a separate, divergent standard.

### **IV. STANDARDS SHOULD SUPPORT CASE AND PALLET IDENTIFICATION:**

In the Federal Register notice, FDA also solicited feedback on case and pallet level identification:

*“We believe that the serialized National Drug Code (sNDC) described in the draft guidance is appropriate for package level identification for most prescription drugs; however, it might not be useful at the pallet or other intermediate level, such as the case. We did not receive many comments related to standards for numerical*

*identification at the case or pallet level and would like broader input on this subject. Please comment on whether there are any standards that would be appropriate for serialization or other numerical identification at the case or pallet level.”*

In order to optimize information across the supply chain, all levels of packaging from individual unit to pallet should be marked with a unique identifier. Experience has shown that identifying and marking all levels of packaging provides a much greater level of information, which is especially useful for recalls and tracking. Thus, BIO recommends that all levels of packaging from saleable unit to pallet should be marked with a unique numerical identifier in order to maximize the efficiency of the prescription drug supply chain.

BIO agrees that the serialized National Drug Code described in the draft guidance may not be appropriate at the pallet or other intermediate level. GS1 standards allow items and cases to use homogenous or heterogeneous Global Trade Item Numbers (GTINs) as long as the identification of each is well defined. These standards for intermediate packaging levels and pallets are well recognized and can be applied to prescription drug packaging as well.

Supply chain stakeholders will also 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.

## **V. MACHINE READABLE FORMS OF THE SNI:**

The guidance suggests that “The SNI identified in this guidance is compatible with, and flexible for, encoding into a variety of machine readable forms of data carriers, such as 2-dimensional bar codes and RFID, leaving options open as technologies useful for securing the supply chain continue to be identified, and standards making use of SNI are developed.” (Lines 119-120) BIO is pleased that the guidance does not mandate any specific data carrier, as some current technologies such as 2-D barcodes may be better suited for large molecule biologic products.

BIO agrees with GS1’s view on how to implement standardized numerical identifiers of prescription drugs in the U.S. supply chain and we request additional clarification around the implementation of machine readable data carrier to ensure consistency with the GS1 approach. For example, it is unclear if the guidance requires that the NDC (GTIN) and Serial Number be contained in the same machine-readable symbol. If so, we believe that it would be appropriate to relax the requirement for linear bar code of the NDC on the package that touches the product assuming FDA allows use of serialized GTIN. We recommend that the FDA allow the use of 2D data matrix in replacement for linear bar code.

## VI. HUMAN READABLE FORMS OF THE SNI:

The guidance states that the SNI “will be applied to the package in both human readable and machine readable forms. A redundant human readable SNI on the package will provide the ability to identify the package when electronic means are unavailable (e.g., in the event of hardware/software failure).” (Lines 122-125) As the FDA moves toward serialized numbers for prescription drugs, printing of the serial number will present a challenge in light of space limitations on small items to which they are attached. Does this mean that the SNI must also appear in its numeric (or alpha numeric) form on the label also? Some biologic product vials and vial cartons are very small and we would likely have difficulty including an 8 digit number in addition to a 2D barcode (assuming the current NDC barcode must remain on the packaging).

Therefore we recognize in certain circumstances the numerical identifier should be machine readable only. Human readable requires additional space that is problematic for item level serialization and also lends itself to human error. Where human readable markings are not possible, standards should be developed for how to convey the information.

Additionally, we recommend that the provision specify that the human readable and bar-code form of the SNI be applied the outer-most package of each saleable unit to avoid confusion with respect to vials that are packaged within individual, saleable cartons.

We offer the following suggested edits to lines 122-127:

“FDA expects that SNI generally will be applied to [the outer-most package of each saleable unit](#) ~~each package~~ in both human readable and machine-readable forms [where technically practical and when it will not lend itself to human error](#). A redundant human readable SNI on the package will provide the ability to identify the package when electronic means are unavailable (e.g., in the event of hardware/software failure). FDA is also not specifying a location on the package where an SNI should be placed, although any SNI would need to be placed on the [outer-most package of the smallest saleable unit](#) in a manner that does not obstruct FDA required labeling information.”

## VII. CO-LOCATION OF THE SNI FORMS:

The guidance adds that “FDA also is not specifying a location on the package where an SNI should be placed, although any SNI would need to be placed on the package in a manner that does not obstruct FDA required labeling information.” (line 125-127) BIO interprets this provision to mean that the machine-readable and human readable information need not be co-located. On certain small carton panels, it may be difficult to co-locate or physically fit the 2-D barcode the human-readable serial number and the human-readable NDC number. On high speed packaging machinery the barcode and human-readable text must be of sufficient size and in unique location to be reliably processed, which may prohibit the barcode and human-readable serial number from being located together on the same end of the carton. Additionally, it is unclear if the 10 digit NDC number and the 8 digit Serial Number can be placed in two separate places on a package and we request clarification.

## **VIII. REPACKAGED PRODUCTS SHOULD CARRY A UNIQUE SERIAL NUMBER:**

The document states that “This guidance addresses only package-level SNI. For this purpose, FDA considers the package to be the smallest saleable unit placed into interstate commerce by the manufacturer or the repackager for sale to the pharmacy or other dispenser of the drug product” and that “linking of a repackager SNI to a manufacturer SNI is also addressed in this guidance, or a future guidance.” (lines 60-65) While BIO recognizes that the FDAAA statute includes repackaging in the scope of the SNI, we must underscore that the practice of repackaging introduces substantial vulnerabilities into the biopharmaceutical supply chain. This guidance is intended to enhance patient safety through a more secure supply chain, yet repackaging continues to undermine patient safety as inadvertent mistakes or deliberate substitution of products during repackaging could put individual patients at risk.

BIO believes that FDA should prohibit the use of the same number on the repackaged product that was applied to the original pack. Rather FDA should establish requirements that the repackager apply a different number to the repackaged item that links back to the original serial number. We suggest that FDA add the following direction where appropriate: [“If a repackager breaks down a manufacturer’s smallest unit of sale \(carton\) into individual units, then repackager must assign a unique number to each individual unit and aggregate the numbers with the carton number.”](#) We also request that FDA clarify what “other dispenser of the drug product” means.

## **IX. INTERNATIONAL HARMONIZATION:**

FDAAA requires that “to the extent practicable, shall be harmonized with international consensus standards for such an identifier” and BIO is pleased that the guidance specifically addresses efforts to prevent the divergence of track-and-trace standards internationally. While this guidance serves as the “initial step to facilitating other measures for securing the drug supply chain,” (line 21) it is imperative that both FDA and the pharmaceutical industry adopt a standard (e.g. GS1), which can support future growth. The most widely used international consensus standards are the GS1 standards for product identification and serial numbers, currently required as part of the “*FDA 2004 Barcoding Act*”.

Additionally, although the use of GS1 Standards GTINs is mentioned as a potential platform to achieve international harmonization, (lines 129-141) we suggest that GTIN’s use be more firmly stated in the guidance.

## **X. IMPLEMENTATION OF THE STANDARDIZED NUMERICAL IDENTIFIER:**

The guidance clearly identifies the use of package-level SNIs as an initial step to facilitating other measures for securing the drug supply chain. However, it offers very limited information about the SNI implementation process and does not provide a clear view on the direction the Agency is taking to ensure harmonization with international standards. In order to ensure that the industry efforts, developing technologies and control systems are aligned with the Agency’s practices and views on this topic, we encourage FDA to provide the industry with

more detailed information regarding the plans and timelines that will be followed to implement SNIs. While the Agency's Guidelines are a welcome step, they do not represent a complete description of its expectations; indeed, it states, "This guidance is intended to be the first of several guidances and regulations that FDA may issue to implement section 505D of the act..." (lines 66-67) We encourage the Agency to expedite the issuance of its further guidance. It is important for the full supply chain to understand and be able to comment on the overall expectations of the Agency. Additionally, it is important that the industry receives more clear guidance regarding the application of GS1 standards as this will help drive consistency across the industry.

BIO believes that track-and-trace systems should be implemented using a risk-based approach that is an element of a comprehensive, risk-based anti-counterfeiting strategy. Congress' requirements and the FDA's guidance are motivated in large part to protect the safety of patients against counterfeit in the medicine supply, which BIO fully endorses. We urge the Agency to be aggressive in its requirements where the guidance is directly linked to a safety issue, but to show flexibility for the industry to adopt the most efficient approaches where the specific guidance would not affect safety.

Relative to the risk-based approach that FDA suggests, we request that FDA identify how this will be established. We are concerned that this will be applied first to those companies whose products have been the subject of counterfeiting without consideration of other products which might best be included. BIO respectfully requests the opportunity to further discuss proposed criteria for risk-based implementation of track-and-trace standards and we encourage FDA to initiate a public process to further consult with supply chain stakeholders.

## **XI. GLOSSARY OF TERMINOLOGY:**

Since several key terms were not defined in statute, BIO encourages FDA to define these terms in this or a subsequent guidance. By more clearly defining key terms, supply chain stakeholders can develop a common understanding of future capabilities and expectations, which can help facilitate the adoption of appropriate standards and systems. For example, it is not always clear exactly what "package or pallet level" means for pharmaceuticals. Does this refer to the case level, the individual unit of use, or a saleable unit? Many pharmaceutical products do not ship in pallet quantities making it impossible to identify them at a pallet level. However, many pharmaceuticals are shipped as cases.

Additionally, please explain the implications of "tracking and tracing." While those terms are used frequently, they can mean different things. Must the tracing go back to manufacturing of finished or raw materials? "Identification, validation, authentication AND tracking and tracing" are treated as one idea; thus appearing to require that manufacturers must satisfy all of these with a comprehensive solution. Many of these terms have been defined in other venues, such as by GS1, and we suggest that FDA adopt commonly accepted descriptions rather than establish new definitions.

**CONCLUSION:**

BIO appreciates this opportunity to comment on *Standardized Numerical Identification for Prescription Drug Packages*. 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 (BIO)

**PREVIOUS BIO TRACK-AND-TRACE COMMENTS:**

BIO's comments to the FDA on *Standards for Standardized Numerical Identifier, Validation, Track and Trace, and Authentication for Prescription Drugs; Request for Information*, May 19, 2008, [http://bio.org/reg/20080519\\_standard\\_numerical\\_id.pdf](http://bio.org/reg/20080519_standard_numerical_id.pdf)

BIO's comments to the FDA on *Technologies for Prescription Drug Identification, Validation, Track and Trace, or Authentication; Request for Information*, May 19, 2008, [http://bio.org/reg/20080519\\_trackntrace.pdf](http://bio.org/reg/20080519_trackntrace.pdf)

BIO statement before the FDA *Anti-Counterfeit Drug Initiative Workshop and Vendor Display*, February 8, 2006, <http://bio.org/reg/20060208.pdf>