Guidance for Industry

Standards for Securing the Drug Supply Chain - Standardized Numerical Identification for Prescription Drug Packages

FINAL GUIDANCE

U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner (OC)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Office of Regulatory Affairs (ORA)
March 2010

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Contains Nonbinding Recommendations

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I. INTRODUCTION

This guidance is intended to address provisions set forth in Section 505D of the Federal Food, Drug, and Cosmetic Act (the Act) regarding development of standardized numerical identifiers (SNIs) for prescription drug packages. In this guidance, FDA is identifying package-level SNIs, as an initial step in FDA's development and implementation of additional measures to secure the drug supply chain.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Office of the Commissioner (OC), the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Office of Regulatory Affairs (ORA) at the Food and Drug Administration.

II. BACKGROUND

A. Food and Drug Administration Amendments Act of 2007

On September 27, 2007, the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85) was signed into law. Section 913 of this legislation created section 505D of the Federal Food, Drug, and Cosmetic Act, which requires the Secretary of Health and Human Services (the Secretary) to develop standards and identify and validate effective technologies for the purpose of securing the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs. Section 505D directs the Secretary to consult with specific entities to prioritize and develop standards for identification, validation, authentication, and tracking and tracing of prescription drugs. The statute also directs that, no later than 30 months after the date of enactment of FDAAA, the Secretary shall develop an SNI to be applied to a prescription drug at the point of manufacturing and repackaging at the package- or pallet-level, sufficient to facilitate the identification, validation, authentication, and tracking and tracing of the prescription drug. An SNI applied at the point of repackaging is to be linked to the SNI applied at the point of manufacturing and, to the extent practicable, the SNI should be harmonized with international consensus standards for such an identifier. (See Section 505D(b)(2)). The provisions in section 505D(b) of the act complement and build upon FDA's longstanding efforts to further secure the U.S. drug supply. This guidance finalizes the draft guidance of the same title dated January 16, 2009 (74 FR 3054).

B. Scope of this Guidance

This guidance is intended to be the first of several guidances and regulations that FDA may issue to implement section 505D of the Act, and its issuance is intended to assist with the development of standards and systems for identification, validation, authentication, and tracking and tracing of

prescription drugs.[2] This guidance defines SNI for package-level identification only. For the purpose of this guidance, FDA considers the prescription drug package to be the smallest unit placed into interstate commerce by the manufacturer or the repackager that is intended by that manufacturer or repackager, as applicable, for individual sale to the pharmacy or other dispenser of the drug product. Evidence that a unit is intended for individual sale, and thus constitutes a separate "package" for purposes of this guidance, would include the package being accompanied by labeling intended to be sufficient to permit its individual distribution. For example, if a manufacturer's smallest unit of sale package is a container holding six drug-filled syringes, a single SNI would be the package-level identifier for the container holding the six drug-filled syringes; there would be no SNIs for the individual syringes, not intended by the manufacturer for individual sale. If a repackager then breaks that container down and repackages each syringe for individual sale, then the repackager must ensure that appropriate labeling accompanies each individual syringe[3] and a new and unique SNI would be the package-level identifier for each new package (e.g., each individual drug-filled syringe). SNIs applied to each new package by the repackager are to be linked back to the manufacturer's SNI for the container of six drug-filled syringes (505D(b)(2)).

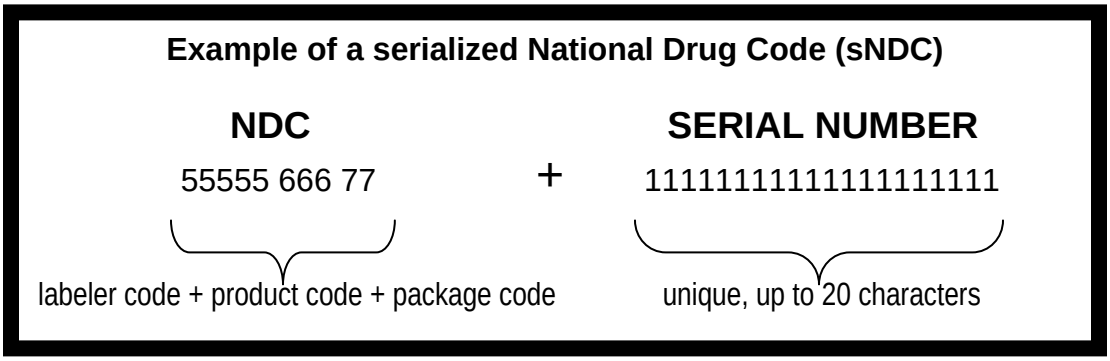
This guidance does not address how to link a repackager SNI to a manufacturer SNI, nor does it address standards for prescription drug SNI at levels other than the package-level including, for example, the case- and pallet-levels. Standards for track and trace, authentication, and validation are also not addressed in this guidance because this guidance only addresses the standardized numerical identifier itself and not implementation or application issues.

[2] Prescription drugs as defined in section 503(b)(1) of the act.
[3] See, e.g., Sections 502 (b) and (f).

III. STANDARDIZED NUMERICAL IDENTIFIERS

A. What should be a package-level SNI for most prescription drugs?

The SNI for most prescription drug packages should be a serialized National Drug Code (sNDC). The sNDC is composed of the National Drug Code (NDC) (as set forth in 21 CFR Part 207) that corresponds to the specific drug product (including the particular package configuration)[4] combined with a unique serial number, generated by the manufacturer or repackager for each individual package. Serial numbers should be numeric (numbers) or alphanumeric (include letters and/or numbers) and should have no more than 20 characters (letters and/or numbers). An example is shown below with a 10-character NDC.



B. What should be the package-level SNI for certain biological products that do not use NDC numbers?

Some prescription drugs approved under Section 351 of the Public Health Service Act, such as blood and blood components and certain minimally manipulated human cells, tissues, and cellular and tissue-based products (HCT/Ps), do not currently use NDC numbers. Examples of HCT/Ps that do not use NDC numbers include allogeneic placental/umbilical cord blood, peripheral blood progenitor cells, and donor lymphocytes for infusion. Instead, such products

[4]In the case of repackaged drugs, each package type should have an NDC that corresponds to the repacker or private label distributor for whom the drug is repacked and to the new package configuration.

currently use other recognized standards for identification and labeling, such as ISBT 128, which creates a unique identification number for each product package. See http://iccbba.org/about_gettoknowisbt128.html, "Guidance for Industry: Recognition and Use of a Standard for Uniform Blood and Blood Component Container Labels," (http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm073362.htm.) The SNI for these products should be the unique identification number created for each package under these other recognized standards, such as ISBT 128.[5]

C. Does the SNI include expiration date and/or lot or batch number?

Expiration date and/or lot or batch numbers are not part of the recommended SNI. Expiration date and/or lot or batch numbers are already accessible because FDA regulations require the inclusion of this information on the label of each drug product. (See 21 CFR §§ 201.17, 201.18, 211.130, 211.137, 610.60, and 610.61.) In addition, the SNI can be linked to databases containing this and other information. Addition of this information within the SNI will unnecessarily increase the length of, and introduce complexity into, the SNI. However, if a manufacturer or repackager chooses to include expiration date and/or lot or batch number with the SNI, it should ensure that the resulting number still permits users to distinguish and make use of the SNI. For example, expiration date and lot or batch number may be incorporated in accordance with the GS1 standards for use of Global Trade Item Numbers (GTIN)[6] (discussed below in Section F).

[5] FDA currently also recognizes Codabar as a standard for blood and blood component container labels. We note that ISBT 128 is becoming the more widely-used industry standard.

[6] See www.GS1.org -- Healthcare GTIN Allocation Rules (http://www.gs1.org/docs/gsmp/healthcare/GS1_Healthcare_GTIN_Allocation_Rules.pdf).

D. Why did FDA select the serialized NDC for package-level SNI for most prescription drugs?

FDA chose the sNDC as the package-level SNI for most prescription drugs because we believe that it serves the needs of the drug supply chain as a means of identifying individual prescription drug packages,[7] which in turn should facilitate authentication and tracking and tracing of those drugs. Most prescription drug product packages already have an NDC on them. By combining a serial number of up to 20 characters with the NDC, the sNDC should be sufficiently robust to support billions of units of marketed products without duplication of an SNI. This approach will allow manufacturers and repackagers to assign serial numbers to combine with the NDC for unique identification of individual product packages. The SNI can also be linked to databases containing such product attributes as lot or batch number, expiration date, distribution/transaction history information, and other identifiers related to a product. As already noted, defining the SNI is expected to be a first step to facilitate the development of other standards and systems for securing the drug supply chain. Many aspects of the implementation of package-level identification will take shape in the future, as the standards that make use of SNI are developed.

E. Should the SNI be in human- and machine-readable forms?

FDA believes that an SNI generally should be applied to each package in both human-readable and machine-readable forms. However, at this time, FDA is not specifying the means of incorporating the SNI onto the package. The SNIs described in this guidance are compatible with, and flexible for, encoding into a variety of machine-readable forms of data carriers, such as

[7] As described above, ISBT-128 and Codabar serve the same function for certain biologics that lack NDCs.

2-dimensional bar codes and radio-frequency identification (RFID),[8] leaving options open as technologies for securing the supply chain continue to be identified, and standards making use of SNI are developed. A redundant human-readable SNI on the package would provide the ability to identify the package when electronic means are unavailable (e.g., in the event of hardware/software failure). Due to the wide-variety of packaging required to accommodate different products and product integrity needs, FDA also is not specifying a location on the package where an SNI should be placed. If the NDC is already printed on the package in human-readable form, then the serial number could be printed in human-readable form in a non-contiguous manner elsewhere on the product package. Any SNI placed on the package must not obstruct FDA-required labeling information[9] and should be placed in a manner that allows it to be readily scanned/viewed without damaging the integrity of the packaging or product..

F. Is the SNI that FDA is recommending compatible with international standards?

In addition to facilitating other actions to secure the drug supply chain, adoption of the sNDC as the SNI for most prescription drugs, and of other recognized standards, such as ISBT 128, for certain biological products, satisfies the requirement in 505D(b)(2) that the SNI developed by FDA be harmonized, to the extent practicable, with internationally recognized standards for such an identifier. Specifically, use of an sNDC is compatible with, and may be presented within, a GTIN, which can be serialized using an Application Identifier (AI) (21) to create a serialized GTIN (sGTIN) for use with RFID or for certain barcodes.[10] GTIN is a global standard for item and object identification, established by GS1, a consensus-based, not-for-profit, international

[8] FDA's enforcement policy with respect to the application of current good manufacturing practices to RFID technology is provided in Compliance Policy Guide (CPG) Section 400.210. See http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074357.htm. This CPG would apply if an SNI were embedded into an RFID tag.

[9] See section 502(c) of the Act.

[10] See www.GS1.org -- Healthcare GTIN Allocation Rules (http://www.gs1.org/docs/gsmp/healthcare/GS1_Healthcare_GTIN_Allocation_Rules.pdf).

standards organization that works with manufacturers, distributors, retailers, and others in the drug supply chain. A GTIN may be used to uniquely identify items at the package level throughout the supply chain. FDA has been an active observer and participant in GS1 standards development related to healthcare and drug products. According to documentation from GS1, the GTIN is used worldwide by twenty-three industry sectors, including healthcare, and has been adopted by sixty-five countries to uniquely identify pharmaceutical products.