4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 201 and 207

[Docket No. FDA-2021-N-1351]

RIN 0910-AI52

Revising the National Drug Code Format and Drug Label Barcode Requirements

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is issuing a final rule to standardize the format of the National Drug Code (NDC). Under this final rule, all FDA-assigned NDCs will be required to be 12 digits in length with 3 distinct segments and 1 uniform format. The first segment is a 6-digit labeler code, the second segment is a 4-digit product code, and the third segment is a 2-digit package code. Additionally, we are revising the drug product barcode label requirements to permit the use of other data carriers that meet the standards of this final rule.

DATES: This rule is effective March 7, 2033.

ADDRESSES: For access to the docket to read background documents or comments received, go to https://www.regulations.gov and insert the docket number found in brackets in the heading of this final rule into the "Search" box and follow the prompts, and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852-0001, 240-402-7500.

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SUPPLEMENTARY INFORMATION:

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I. Executive Summary

A. Purpose of the Final Rule

FDA is modifying our regulations to establish a uniform, 12-digit format for the NDC (21 CFR 207.33). FDA's transition to a uniform format for FDA-assigned NDCs is intended to facilitate the adoption of a single NDC format across the entire healthcare industry, eliminating the need to convert NDCs from one of FDA's prescribed formats to a different standardized format used by other sectors of the healthcare industry (e.g., healthcare providers and payors). FDA is also revising the drug product barcode label requirements (21 CFR 201.25) to allow the use of either linear or nonlinear barcodes, so long as the barcode format conforms to certain standards and is recognized by FDA.

B. Summary of the Major Provisions of the Final Rule

Under this final rule, FDA is amending its regulations to adopt a uniform, 12-digit format for the NDC. Under the revised format, NDCs will continue to consist of three segments: the

labeler code, the product code, and the package code. However, the labeler code will be 6 digits, the product code will be 4 digits, and the package code will be 2 digits. To provide maximum flexibility on the type of barcode used on the label of a drug product, this final rule allows the use of either linear or nonlinear barcodes, so long as the barcode format conforms to certain standards and is recognized by FDA.

On the effective date of this final rule, FDA will begin assigning new NDCs in the uniform, 12-digit format, and existing 10-digit NDCs assigned by FDA prior to the effective date will be required to convert to the uniform 12-digit NDC format.[1] As a result, all parties that use FDA-assigned NDCs will need to have systems capable of handling the new, uniform, 12-digit NDC format on the effective date of the final rule. Therefore, FDA is delaying the effective date of the final rule for a period of 7 years following its publication to allow interested parties time to develop and implement such systems.

Additionally, this final rule allows for a 3-year transition period following the effective date of the final rule. During this 3-year transition period, firms that use 10-digit NDCs assigned prior to the effective date on drug product labeling should begin updating their labeling to replace the 10-digit NDC format with the new 12-digit NDC format by adding leading zeros to the labeler code, product code, and/or package code segments as needed, as soon as possible. However, to aid with the transition, FDA does not intend to object to continued use of such 10-digit NDCs on the labeling of products remaining in interstate commerce after the effective date during the 3-year transition period. The purpose of the transition period is to mitigate the potential costs associated with reprinting labels for these products. Therefore, during this

[1] FDA considers the conversion of a 10-digit NDC assigned by FDA prior to the effective date to the new, uniform 12-digit NDC format to be a ministerial, administrative change and not the assignment of a "new" NDC. Furthermore, FDA considers such an NDC in its original 10-digit format and in its converted 12-digit format to be the same NDC with different formats. A drug product that was originally assigned a 10-digit NDC prior to the effective date would be considered to have a new NDC only if it were assigned a new NDC by FDA after the effective date (e.g., pursuant to a request for a new NDC because there was change to any of the information identified in 21 CFR 207.35(b) or (c)).

transition period, interested parties should ensure that their systems are capable of handling both the 10-digit and 12-digit NDC formats.

C. Legal Authority

FDA is amending our regulations on foreign and domestic establishment registration and listing for drugs, including biological products and animal drugs. FDA's authority for this rule derives from the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 321, *et seq.*) applicable to drugs, including biological products, and the biological product provisions of the Public Health Service Act (PHS Act) (42 U.S.C. 262, *et seq.*). In particular, the rule will standardize the format of NDCs assigned under section 510(e) of the FD&C Act (21 U.S.C. 360(e)) and will aid in efficient enforcement of the FD&C Act pursuant to section 701(a) of the FD&C Act (21 U.S.C. 371(a)) and section 351(j) of the PHS Act (42 U.S.C. 262(j)).

D. *Costs and Benefits*

This final rule requires that all NDCs, including any 10-digit NDCs issued by FDA prior to the effective date, be 12 digits in length with a uniform format: a 6-digit labeler code, a 4-digit product code, and a 2-digit package code. As a result, drug product labeling that includes a 10-digit NDC will need to be updated to convert to the standard 12-digit format.

FDA's transition to a uniform format for native NDCs is intended to facilitate the adoption of a single NDC format across the entire healthcare industry. Such an adoption will eliminate the need to convert NDCs from one of the FDA-assigned formats to a different standardized format used by other sectors of the healthcare industry (e.g., healthcare providers and payors). Eliminating the need to convert NDCs should reduce potential errors caused by converting the FDA-assigned NDC to a different NDC format used by other sectors of the healthcare industry. Standardization and adoption of a single format will also eliminate the need for additional quality control and validation by certain stakeholders, such as payors and prescribers, to ensure a drug product and its respective NDC are accurate; this is particularly important for insurance coverage and reimbursement claims. Another benefit of the rule will be

to avoid any potential risks to the public health from medication errors and the risk of confusion. We do not have enough information to quantify these potential benefits.

The costs to industry of converting current NDCs to the standardized format will include one-time costs of updating software systems, other transition costs, coordinating labeling updates, and reading and understanding the rule. We estimate annualized costs will be about $14.64 million ranging from $7.64 million to $22.79 million using a 7-percent discount rate over a ten-year horizon. Similarly, we estimate annualized costs will be about $14.90 million ranging from $7.79 million to $23.18 million using a 3-percent discount rate over a 10-year horizon.

II. Table of Abbreviations/Commonly Used Acronyms in This Document

Abbreviation/Acronym	What It Means
2D	Two-dimensional
AI	Application Identifier
ANDA	Abbreviated New Drug Application
BLA	Biologics License Application
DSCSA	Drug Supply Chain Security Act
EAN/UCC	European Article Number/Uniform Code
EHR	Electronic Health Record
FDA	Food and Drug Administration
FD&C Act	Federal Food, Drug, and Cosmetic Act
FRIA	Final Regulatory Impact Analysis
GTIN	Global Trade Item Number
HCT/P	Human Cells, Tissues, and Cellular and Tissue-Based Product
HIBCC	Health Industry Business Communications Council
HHS	Department of Health and Human Services
HIPAA	Health Insurance Portability and
ICD	International Classification of Diseases
IT	Information Technology
NDA	New Drug Application
NDC	National Drug Code
OMB	Office of Management and Budget
PHS Act	Public Health Service Act
PRA	Paperwork Reduction Act of 1995
PRIA	Preliminary Regulatory Impact Analysis
UPC	Universal Product Code

III. Background

A. Need for the Rulemaking

The NDC is an FDA standard for uniquely identifying drugs marketed in the United States. Section 510(j) of the FD&C Act requires each person who registers an establishment under section 510(b), (c), (d), or (i) to provide FDA with a current list of all drugs manufactured, prepared, propagated, compounded, or processed by the establishment for commercial distribution. Drug products are identified and listed using the NDC (21 CFR 207.49).

Currently, the NDC assigned by FDA (a "native" NDC) for each listed drug marketed in the United States is a unique 10-digit,[2] 3-segment number (§ 207.33(b)). The three segments of the NDC include the labeler code, product code, and package code (§ 207.33(b)). The first segment, the labeler code, is a unique 4-, 5-, or (in the future) 6-digit number assigned by FDA that identifies the manufacturer, repacker, relabeler, or private label distributor of the drug (§ 207.33(b)(1)). The second segment, the product code, is a 3- or 4-digit number that identifies a specific active ingredient, strength, dosage form, and other distinguishing characteristics of a drug manufactured, repackaged, relabeled, or distributed by the labeler (id.; § 207.35(b)). The third segment, the package code, is a 1- or 2-digit number that identifies package sizes and types (§ 207.33(b)(1)). Different package codes differentiate between different quantitative and qualitative attributes of the product packaging (§ 207.33(b)(iii)). The NDC for a given drug is currently in one of the following configurations (with each numeral representing the number of digits in that segment): 4-4-2, 5-3-2, or 5-4-1.

Currently, only 5-digit labeler codes are being assigned by FDA. A 5-digit labeler code format provides FDA with 90,000 labeler codes that could be assigned to drug manufacturers and private label distributors ranging from 10,000 to 99,999. Based on current assignment rates, FDA anticipates that it will run out of 5-digit labeler codes in approximately 10 to 15 years. At that point in the future, FDA will begin assigning 6-digit labeler codes due to exhaustion of 5-digit labeler codes. Under the current regulations, moving to 6-digit labeler codes will expand

[2] Under 21 CFR 207.33(b), an NDC must consist of 10 or 11 digits, divided into three segments. This FDA 11-digit NDC refers to the NDC length once the Agency starts assigning 6-digit labeler codes.

the entire NDC to 11 digits and, per regulation, allow for two additional NDC configurations: 6-3-2 and 6-4-1, for a total of 5 possible NDC configurations (including the three 10-digit NDC configurations) (see § 207.33(b)(2)).

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) (Pub. L. 104-191) contains administrative simplification provisions that require the Department of Health and Human Services (HHS) to adopt "national standards for electronic health care transactions and code sets, unique health identifiers, and security."[3] In its implementation of these rules, on August 17, 2000, HHS published the final rule, "Health Insurance Reform: Standards for Electronic Transactions" which addressed standards for electronic transactions that established NDCs as the standard medical data code set for reporting drugs and biological products in all standard transactions under HIPAA (65 FR 50312 at 50313). If a HIPAA-covered transaction includes a drug, the NDC is required to be part of the medical code data set (see 45 CFR 162.1002(c)(1)). However, in the preamble to the HIPAA regulations, HHS stated that it was adopting a uniform 11-digit format to conform with customary practice used in computer systems (65 FR 50312 at 50329). The HIPAA standard 11-digit NDC format is standardized such that the labeler code is always 5 digits, the product code is always 4 digits, and the package code always 2 digits (i.e., 5-4-2 configuration). To convert a 10-digit NDC to an 11-digit HIPAA standard NDC, a leading zero is added to the appropriate segment to create the 11-digit configuration as defined above.

If, in the absence of this final rule, FDA were to begin issuing 6-digit labeler codes under § 207.33(b), the resulting 11-digit native NDC configurations would have the same number of digits as required by the HIPAA standards, but they will not be in the same format. Specifically, an 11-digit native NDC would have an extra labeler code digit but will be short a digit in either the product code or package code. Additionally, some of the systems that utilize HIPAA

[3] See https://www.hhs.gov/hipaa/for-professionals/index.html (accessed November 7, 2025).

standard 11-digit NDCs[4] do not use hyphens to separate the segments which, as illustrated in Table 1, would result in some 11-digit native NDCs being indistinguishable from HIPAA standard 11-digit NDCs. Therefore, to ensure that native and HIPAA standard unhyphenated 11-digit NDCs would be distinguishable, FDA anticipated that the HIPAA standards, and other code sets that currently require 10-digit native NDCs to be converted to 11-digit NDCs, would likely need to be updated in some manner. We note that such updates are outside the scope of FDA authority.

Table 1.--NDC Conversion Example

Native NDC Format	Converted NDC Format		
	10-Digit Hyphenated	11-Digit Converted (Hyphenated)	11-Digit Converted (Unhyphenated)
Native 10-digit (5-3-2)	10010-001-01	10010-0001-01	10010000101
Native 11-digit (6-3-2)		100100-001-01	10010000101

B. History of the Rulemaking

1. 2016 Final Rule

In 2016, FDA published the final rule "Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs That Are Regulated Under a Biologics License Application, and Animal Drugs" (the Registration and Listing Final Rule). Recognizing that FDA would run out of 5-digit labeler codes in the near future, the Registration and Listing Final Rule established two additional NDC configurations: 6-3-2 and 6-4-1, for a total of five possible NDC configurations (including the three 10-digit NDC configurations) (§ 207.33(b)(2)). At the same time, FDA acknowledged in the preamble to the Registration and Listing Final Rule that some interested parties recommended that FDA adopt a single, standard format for NDCs and announced that it planned to initiate a public discussion of future formatting options (81 FR 60170 at 60187).

2. 2018 Public Hearing

[4] NDCs that contain additional digits necessary to comply with HIPAA standards are referred to as "converted" NDCs.

On November 5, 2018, FDA began these public discussions by holding a public hearing.[5] At the public hearing, FDA outlined several proposed formatting options that FDA could adopt once it begins issuing 6-digit labeler codes. Specifically, FDA outlined the following four formatting options:

Option A: Do not revise the regulations and continue with the status quo. Under this option, FDA would continue assigning the remainder of the 5-digit labeler codes and whenever the Agency runs out of 5-digit labeler codes, start assigning 6-digit labeler codes. This would expand FDA's NDC inventory to 10 and 11 digits, resulting in 5 different configurations. FDA would use 10- and 11-digit NDCs.

Option B: Same as Option A, except that FDA would stop issuing 5-digit labeler codes and start issuing 6-digit labeler codes on a specified date in the future, before FDA anticipated running out of 5-digit labeler codes. This option was intended to provide more certainty to interested parties by establishing a designated future date on which they would need to have systems in place to handle 11-digit NDCs in either 6-4-1 or 6-3-2 format.

Option C: Adopt the hyphenated NDC 11-digit format (5-4-2 format) currently used by the payor industry and convert all current 10-digit NDCs to the hyphenated 11-digit format by adding a leading zero to the short segment of the NDC. When the supply of 5-digit labeler codes is exhausted, FDA would begin assigning 6-digit labeler codes for use in 6-3-2 and 6-4-1 formats. Although this would establish a uniform total length for all NDCs, there would still be multiple formats. Additionally, there is the potential for an 11-digit format with a 6-digit labeler code and an 11-digit format with a 5-digit labeler code to be identical when the hyphens separating the various segments are removed.

Option D: Allow for the harmonization of NDCs between FDA and other interested parties by adopting 12-digit NDCs in a single, uniform 6-4-2 format. Once FDA starts assigning 6-digit labeler codes, all NDCs (new and existing) would be required to be presented in a 6-4-2

[5] See https://www.regulations.gov/document/FDA-2018-N-2610-0001 (accessed November 7, 2025).

format. Existing NDCs would be converted from their existing format by adding leading zeros to the short segments. This would create one standard configuration for all NDCs that can be used by all interested parties without conversion. As an added benefit, it would provide the industry with more product or package codes.

An appropriate number of years would be necessary to adapt existing databases and structures to be able to handle the new, uniform, 12-digit NDC format and for industry to adopt this as the single NDC format. Therefore, under Option D, FDA would implement this change on a prespecified date that would occur before the current pool of 5-digit labeler codes is exhausted, to provide certainty and predictability to industry parties, government payors, and other interested parties.

FDA received oral comments during the hearing, and written comments were submitted afterwards. Most of the comments were in favor of FDA's adoption of a single standardized format that could be used by all interested parties. The majority of the commenters were also in favor of FDA establishing a certain date when interested parties would be required to have systems capable of handling the new format, with many advocating for a 10-year delay. For the most part, the commenters were not in favor of Options A, B, or C. Instead, in general, the commenters either favored Option D or advocated for FDA to no longer be responsible for assigning NDCs and, instead, allow for a third party to take over that role. FDA considered these comments in developing this rulemaking.

3. The Proposed Rule

We proposed to adopt a single, uniform, 12-digit NDC format to avoid confusion and reduce medication errors that could result if, as described above, FDA were to begin issuing 11-digit NDCs when the HIPAA standards and other code sets that require 10-digit native NDCs to be converted to 11-digit NDCs are not updated. We noted that standardizing the FDA-assigned NDC to one format should eliminate the need for interested parties to constantly convert a drug's FDA-assigned NDC to a different standardized format if the HIPAA and other code sets are

modified to adopt FDA's new, uniform, 12-digit format. This should reduce errors caused by converting from FDA's current nonstandardized NDC format to a standardized NDC format. Additionally, standardization should eliminate the need for interested parties to use multiple versions of an NDC (e.g., the FDA-assigned 10-digit NDC and the converted HIPAA standard 11-digit NDC). Finally, we noted that using 12-digits would allow FDA to adopt a uniform NDC format without requiring extensive changes to existing 10-digit NDCs. Instead, interested parties would only need to add leading zeros to certain segments of the existing 10-digit NDC to convert it to the new 12-digit NDC format.

C. Summary of Comments to the Proposed Rule

We received approximately 50 comments on the proposed rule. The comments were submitted by a variety of interested parties, including healthcare professionals, consumers, drug manufacturers, wholesale distributors, trade associations, health information technology (IT) developers and vendors, and other organizations. The comments addressed a variety of topics, including (i) general support for or opposition to a uniform 12-digit NDC format; (ii) the proposal's intersection with Drug Supply Chain Security Act (DSCSA) requirements; (iii) implementation timeframe; (iv) FDA coordination with external parties; and (v) implementation costs.

IV. Legal Authority

FDA is amending our regulations on foreign and domestic establishment registration and listing for drugs, including biological products and animal drugs. FDA's authority for this rule derives from the FD&C Act (21 U.S.C. 321, *et seq.*) applicable to drugs, including biological products, and the biological product provisions of the PHS Act (42 U.S.C. 262, *et seq.*). In particular, the rule will standardize the format of NDCs assigned under section 510(e) of the FD&C Act (21 U.S.C. 360(e)) and will aid in efficient enforcement of the FD&C Act pursuant to section 701(a) of the FD&C Act (21 U.S.C. 371(a)) and section 351(j) of the PHS Act (42 U.S.C. 262(j)).

V. Comments on the Proposed Rule and FDA Response

A. Introduction

We describe and respond to the comments on the proposed changes in sections V.B. through V.E. of this document. Comments on the economic analysis are addressed in section VII.C. of this document and in the Final Regulatory Impact Analysis (FRIA). We have numbered each comment to help distinguish between different comments. We have grouped similar comments together under the same number, and in some cases, we have separated different issues discussed in the same comment and designated them as distinct comments for purposes of our responses. The number assigned to each comment or comment topic is purely for organizational purposes and does not signify the comment's value or importance or the order in which comments were received.

B. Description of General Comments and FDA Response

Some comments made general remarks regarding the proposed rule without focusing on a particular proposed provision. In the following paragraphs, we discuss and respond to such general comments.

(Comment 1) Many commenters agree that the NDC format must change and want assurance that this final rule would fully satisfy future needs without requiring another expansion or modification to the NDC format. One commenter requests that we disclose the number of NDCs that have been assigned and how many are currently in use.

(Response 1) We recognize that any revision to the NDC format is a complex and costly effort and that this final rule should be as future-proof as possible. FDA typically assigns an average of 1,000 new labeler codes each year. By expanding the labeler code from 5 to 6 digits, this final rule will add approximately 900,000 labeler codes. At our current labeler code assignment rate, this final rule should provide a 900-year supply of labeler codes and constitutes

a sufficiently future-proof solution. The number of NDCs assigned and currently in use can be determined by reviewing the FDA NDC Directory.[6]

(Comment 2) Some commenters are concerned that the conversion of a 10-digit NDC to the uniform 12-digit NDC format would result in a "new" NDC, which could trigger renegotiation of pricing and rebates for the drug at issue. The commenters request that FDA differentiate between a "new" NDC and a "reformatted" NDC in the regulation text and clarify the circumstances that would trigger the need for a "new" NDC instead of a "converted" NDC. One commenter asks whether the proposal, if finalized, would increase the number of products for which a sponsor would be required to pay user fees under the FD&C Act.

(Response 2) FDA considers the conversion of a 10-digit NDC to a 12-digit NDC format to be a ministerial, administrative change and not the assignment of a "new" NDC for purposes of drug registration and listing or FD&C Act user fees. Furthermore, FDA considers such an NDC in its original 10-digit format and in its converted 12-digit format to be the same NDC with different formats. We do not believe it is necessary to modify the codified regulation text to clarify this point. Our regulations address both the initial assignment of a new NDC (§ 207.33(c) and (d)) and the circumstances under which a new NDC must be obtained for a drug that has already been assigned an NDC (§ 207.35). None of those provisions requires that NDC formatting changes such as those required by this final rule would result in a "new" NDC.

(Comment 3) One commenter notes that the proposed rule refers to NDCs being "assigned by FDA." The commenter asserts that because the product and package codes are selected by the manufacturer, this final rule should clarify that an NDC "assigned by FDA" refers to the Agency's assignment of the labeler code in accordance with our existing regulation at § 207.33(b)(1)(i).

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[6] For human drug NDCs, see https://www.fda.gov/drugs/drug-approvals-and-databases/national-drug-code-directory and https://www.accessdata.fda.gov/scripts/cder/ndc/index.cfm; for animal drug NDCs, see https://www.fda.gov/industry/structured-product-labeling-resources/electronic-animal-drug-product-listing-directory.

(Response 3) Under § 207.33(d)(1), a manufacturer, repacker, or relabeler merely "propose[s] an NDC for assignment by FDA" when it submits the product's listing information for the first time. Specifically, the registrant proposes the product and package codes together with the applicable labeler code already assigned by FDA. FDA will assign the proposed NDC to the drug identified by the registrant only if the proposed NDC is in the correct format, is not reserved for a different drug, and has not previously been assigned to a different listed drug (§ 207.33(d)(2)). Thus, FDA ultimately assigns each NDC, including each component of an NDC. Accordingly, we decline to adopt the commenter's recommendation.

(Comment 4) One commenter advocates that FDA relinquish responsibility for assigning NDCs and permit a third party to assume that role.

(Response 4) In the proposed rule, we considered and rejected similar comments that were submitted to the 2018 public hearing docket (see 87 FR 44038 at 44042–44043). Specifically, the proposed rule noted that FDA is deeply involved in the assignment of NDCs and that changing the existing system would have the potential to cause significant disruption, particularly in transitioning the assignment of NDCs from FDA to a third party. We also recognized that although there would be disruption in transitioning to a 12-digit NDC, FDA would be in the best position to minimize and mitigate the disruption because it would continue to be involved in the process for assigning the reformatted 12-digit NDCs. In the proposed rule, we stated that if the responsibility for assigning the reformatted 12-digit NDCs were handed over to a third party, FDA would have less ability to minimize and mitigate the disruption. Accordingly, we did not propose to revise § 207.33 and other regulations to remove references to the assignment of NDCs by FDA. The commenter does not offer any reason why FDA should change course on this policy in this final rule, and we decline to make such a significant and potentially disruptive revision to our regulations in this final rule.

(Comment 5) Numerous commenters advocate that FDA should implement an extensive communication and outreach strategy to engage, coordinate, and inform all interested parties,

including Federal and State agencies; manufacturers, repackagers, and distributors; drug compendial services; insurers and pharmacy benefit managers; healthcare providers; software vendors; retailers; and other entities. The commenters believe that a comprehensive communication plan will increase awareness of the new NDC format and promote timely implementation among all interested parties, thereby minimizing or preventing disruption in drug purchasing, reimbursement, and delivery of patient care.

(Response 5) To help ensure industry readiness for the transition to a 12-digit NDC, FDA intends to broadly engage with relevant government and private parties during the 7-year period preceding the effective date of this rule.

(Comment 6) One commenter urges FDA and other Federal agencies to pursue a national synchronization effort to link 12-digit NDCs to 10-digit NDCs in every historical table and document.

(Response 6) This rule operates on a prospective basis only and does not mandate changes to historical government records. However, we intend to publish a database that will map each 10-digit NDC appearing in the NDC Directory to the corresponding 12-digit NDC at least until the end of the transition period.

(Comment 7) We received numerous miscellaneous comments. Most of these commenters seek clarification or changes to DSCSA requirements or labeling or registration and listing provisions that the proposed rule did not propose to modify. Two commenters advocate for the availability of investment credits or other types of government funding for the costs of implementing the transition to a 12-digit NDC.

(Response 7) These comments are outside the scope of the rule. In addition, the comments advocating for government funding of efforts to transition to a 12-digit NDC are outside the scope of FDA authority.

C. NDC Format

Currently, under § 207.33(b)(1), an NDC consists of either 10 or 11 digits, divided into the following three segments: (1) a labeler code of 4, 5, or 6 digits; (2) a product code of 3 or 4 digits; and (3) a package code consisting of 1 or 2 digits. Section 207.33(b)(2) specifies five different permitted NDC formats that differ based on the number of digits in each of the three segments: 4-4-2; 5-3-2; 5-4-1; 6-3-2; and 6-4-1. Section 207.33(b)(3) requires a registrant or private label distributor with a given labeler code to use a single product and package code configuration in all NDCs that include the given labeler code and are reserved or listed in accordance with applicable regulations. Finally, existing § 207.33(b)(4) permits FDA to approve an alternatively formatted NDC for certain human cells, tissues, and cellular and tissue-based products (HCT/Ps).

We proposed to amend § 207.33(b) to establish a uniform, 12-digit format for the NDC for all drug products that are required to be listed under section 510 of the FD&C Act and 21 CFR part 207. Specifically, we proposed to modify § 207.33(b)(1) to state that the NDC must consist of 12 digits, divided into three segments as follows: (i) a 6-digit labeler code; (ii) a 4-digit product code; and (iii) a 2-digit package code. We proposed to remove existing § 207.33(b)(2) and (3) as inapplicable to a uniform, 12-digit NDC format. We proposed to retain at new § 207.33(b)(2) the existing language of § 207.33(b)(4) regarding the permissibility of an alternatively formatted NDC for HCT/Ps. The proposed rule related only to FDA's assignment of NDCs; it did not propose any revisions to the HIPAA standard code set, which is outside the scope of FDA authority.

In the following paragraphs, we discuss comments on our proposed revisions of § 207.33(b). We are finalizing the proposal without change.

(Comment 8) A number of commenters support our proposal to require a single, uniform NDC format for FDA-assigned NDCs. In general, these commenters support a uniform FDA-assigned NDC format for reasons related to patient safety, efficiency, and/or reduced burden. One commenter asserts that it is very burdensome to transmit and accept NDCs in multiple

formats. Some commenters note that the coexistence of multiple NDC lengths and formats, with and without hyphens, can lead to incorrect drug inventory data, data loss, and transaction errors. Some commenters claim that a single, uniform NDC format could be used for all purposes and would eliminate the need to convert NDCs to a different format depending on the nature of the transaction, thereby reducing the potential for patient harm caused by errors in transmitting drug information. One commenter indicates that a uniform NDC format would eliminate the need for multiple layers of quality control. Another commenter notes that a single, uniform format is needed because the NDC is used for so many purposes other than drug identification, such as payment, controlled substance monitoring and reporting, and more. A trade association representing wholesale distributors of drugs strongly supports a uniform format for the NDC, arguing that, once the relevant parties are educated and acclimated to the new format, it will provide enormous efficiencies. This commenter notes that a uniform NDC format will eventually eliminate the need to cross-reference indexes and conversion tables, remove existing uncertainties regarding the lengths of the three NDC segments, and reduce errors.

(Response 8) We appreciate the support of the commenters. We agree that the various NDC formats (whether FDA-assigned or converted to another format) have created data quality and integrity issues. For example, as illustrated in Table 2, if hyphens are removed from an FDA-assigned NDC in an electronic system, there is no reliable way to know where the hyphens were in the original NDC. We believe that moving to a single, uniform format for the FDA-assigned NDC is an important and necessary improvement that will improve efficiency and reduce errors. Although we recognize that FDA's adoption of a single, uniform, 12-digit NDC format may require the NDC format currently used under HIPAA or other code sets to change, this final rule does not change the NDC format currently used under HIPAA and other code sets because that is outside the scope of FDA's authority. However, the Agency's adoption of a uniform NDC format may facilitate adoption of a uniform format industry-wide.

Table 2.--Illustration of Ambiguity With Unhyphenated NDC

FDA-assigned NDC (Unhyphenated)	FDA-assigned NDC Possibilities
9999912345	9999-9123-45 99999-123-45 99999-1234-5

(Comment 9) A number of commenters support our proposal to require a 12-digit NDC in 6-4-2 format. These commenters prefer a 12-digit NDC over an 11-digit NDC because it would not lead to overlapping NDCs (as illustrated in Table 1 of the proposed rule). In addition, these commenters believe that a uniform NDC length and format would minimize risk of error in a variety of processes (e.g., prescription processing, medication history analysis, drug utilization reviews, and more). One commenter notes that the proposed NDC format is the most concise and consistent data structure for the NDC, with the most uniform methodology for updating the NDC on current products and assigning new NDCs to new products. This commenter also believes that our proposal is the most efficient option because it would minimize mapping and programming costs. Another commenter notes that the proposed 12-digit format (6-4-2) would allow continued use of legacy labeler codes by adding leading zeros and would solve the scarcity of labeler codes for a longer period of time than an 11-digit NDC. Several commenters are concerned that errors in converting existing NDCs to a 12-digit NDC would cause ordering and medication administration errors.

(Response 9) We agree with the commenters that support FDA's adoption of a uniform, 12-digit NDC in the 6-4-2 format. Although we agree that there is potential for error in converting NDCs from the 10-digit format to the 12-digit format, a uniform format for FDA-assigned NDCs will result in greater efficiency over time and be less susceptible to error. Moreover, to minimize any potential for error, FDA intends to publish a database that will map each 10-digit NDC appearing in the NDC Directory to the corresponding 12-digit NDC at least until the end of the transition period.

(Comment 10) Several commenters advocate for an expanded labeler code of 7 or 8 digits, because they are concerned that a 6-digit labeler code would not be sufficient to satisfy

future demand. One commenter suggests that we increase the product code from 4 digits to 5 digits because it would increase the lifespan of labeler codes. This commenter reasons that an expanded product code could increase the lifespan of labeler codes since manufacturers cannot reuse codes. According to the commenter, NDCs get consumed faster than expected due to the requirement to assign NDCs to bulk active pharmaceutical ingredient, bulk intermediate, and finished products that are imported into the U.S. market. One commenter suggests that we eliminate the package code in an effort to reduce the number of NDCs assigned to each manufacturer.

(Response 10) We decline the suggestions to expand the labeler codes to more than 6 digits because, as explained in Response 1, a 6-digit labeler code will satisfy demand for hundreds of years. We also decline the suggestion to expand the product code to 5 digits. A 4-digit product code accommodates up to 10,000 different product codes (0000 to 9999). Because only a very small number of manufacturers and private label distributors need more than 10,000 product codes, it would be more efficient and less burdensome to assign those manufacturers an additional labeler code when they use up all of the product codes under an existing labeler code rather than expand the product code. We disagree with the suggestion to eliminate the package code. The package code is a useful segment of the NDC because it identifies a drug's package size and type and distinguishes different quantitative and qualitative attributes of the product packaging (21 CFR 207.33(b)(1)(iii)). For example, the package code is used to distinguish bottles of 30, 100, and 500 tablets of the same drug and whether the tablets are packaged in a bottle or blisterpack. Thus, the package code allows FDA, manufacturers, and other interested parties to more precisely identify and trace a drug throughout the supply chain. Eliminating the package code would hinder FDA efforts to ensure a secure drug supply chain and cause disruption in reimbursement, order fulfillment, inventory and supply chain management, and other matters. We are finalizing without change our proposal to standardize the package code as a 2-digit, final segment of the NDC.

(Comment 11) A large number of commenters advocate that we continue to allow 10-digit NDCs in the currently permitted formats (4-4-2, 5-3-2, 5-4-1) and that we address the need for additional labeler codes by issuing 5-character alphanumeric labeler codes only for new labelers after exhausting the supply of 5-digit numerical labeler codes. To eliminate the potential for medication errors that could occur when certain letters are misread as numerals, these commenters suggest that the alphanumeric labeler code should be limited to only 21 letters (all letters except B, D, I, O, and Q) or 20 letters (all letters except B, D, I, O, Q, and S).

According to the commenters, this approach has numerous advantages. First, the commenters assert that a limited 5-character alphanumeric labeler code would provide an abundant supply of labeler codes, thereby resolving the problem that prompted this rulemaking. A few commenters assert that such a limited 5-character alphanumeric labeler code would expand the supply of labeler codes to over 26 million codes.

Second, the commenters advocate for an alphanumeric labeler code on the grounds that it would be far less costly and disruptive and much easier and faster to implement because it would preserve much of the status quo. Under this approach, there would be no change for existing labelers. Only new labelers would be issued an alphanumeric labeler code after the supply of numeric labeler codes has been exhausted. The commenters note that the transition to an alphanumeric labeler code would be less costly because many entities, including pharmacy system vendors, already store NDCs in alphanumeric fields that would not require any software adjustments. In addition, commenters note that this approach would preserve the HIPAA-mandated 11-character format (5-4-2) already in use for many transactions, eliminating the need to modify the NDC format used under HIPAA. These commenters also believe that an alphanumeric labeler code would allow historical records to be preserved without change, thereby reducing change management costs.

Third, numerous commenters favor an alphanumeric labeler code because it would cause less confusion and minimize risks to patient safety. Many of these commenters disagree with our

statement in the proposed rule that a uniform, 12-digit NDC format would reduce medication errors by eliminating the need to convert the various nonstandardized 10-digit NDCs to the HIPAA 11-digit NDC format. These commenters note that there is already little risk of error in such conversions because conversions are executed by drug data vendors (compendia) that publish the standardized National Council for Prescription Drug Programs (NCPDP) 11-digit product identifier NDC, and most affected parties use the compendium-published NDC. These commenters believe that the risk of medication errors and patient harm would be greater if every existing 10-digit NDC is converted to a 12-digit NDC and both NDCs appear on the product during the transition period. A number of commenters assert that an alphanumeric labeler code would be less disruptive to industry and patient care because it avoids impact to other identifiers, such as the Universal Product Code (UPC), that are currently reformatted into an NCPDP 11-digit product identifier NDC for use in the pharmacy industry. In addition, one commenter notes that a numeric labeler code that begins with a zero may be misread by those systems that treat the Product Service ID as a numeric field (that is, leading zeros would be dropped, resulting in errors). Some commenters argue that there is precedent for use of an alphabetic code to reduce confusion; they cite FDA's implementation of a four-character alphabetic code for biological products to reduce confusion in identifying biosimilar products.

Finally, a small number of commenters assert that an alphanumeric labeler code would make it easier for State Medicaid programs and their vendors to invoice and dispute claims. Specifically, these commenters argue that it would be very burdensome to pursue historical claims from as far back as 1991 for drugs bearing a 10-digit NDC.

In contrast, our decision not to propose an alphanumeric labeler code is supported by a trade association representing wholesale distributors and a healthcare services company with operations throughout the drug delivery and supply chain. In addition, comments from an organization responsible for implementation of global standards in the U.S. healthcare industry (GS1 US) identify some important disadvantages of an alphanumeric labeler code after engaging

a workgroup comprised of nearly 40 organizations from throughout the supply chain, including manufacturers, wholesale distributors, providers, technology solutions companies, and industry associations. These commenters recognize that the transition to an alphanumeric labeler code would never achieve the goal of a uniform NDC sought by many in the industry. They assert that a single, standardized, and uniform NDC format will reduce errors and inefficiencies, particularly if it does not include letters. Two of the commenters note that it may be even more difficult to transition to an alphanumeric NDC compared to a 12-digit NDC and could require additional time to make the transition.

According to the three commenters, many IT systems currently in use cannot accommodate alphabetic characters ("alpha characters"), and an alphanumeric NDC would not relieve many interested parties from the requirement to update their systems. One of these commenters states that the addition of an alpha character to the NDC would increase the difficulty and expense of developing, mapping, and testing the new NDC format, possibly requiring additional transition time. Another of these commenters, the global standards organization, expresses its concern that an alphanumeric NDC would not be compatible with the global supply system because alphanumeric codes are not used in all countries and organizations. Moreover, the organization states that an NDC of uniform length and structure would help eliminate some of the variability that undermines the integrity of the standardized numerical identifier, which uses the NDC combined with a serial number to uniquely identify each package or homogenous case in the supply chain, as required by the DSCSA. All three of these commenters also share concern that, unlike numeric barcodes, barcodes that include letters cannot be compressed to conserve space on drug packages and labels, which is particularly critical for small drug packages. In addition, the commenters note that the transition to an alphanumeric NDC would require all barcode formats and scanners to be updated, which could potentially require additional transition time and create potential patient safety risks.

(Response 11) We appreciate the thoughtful and comprehensive comments advocating for a 5-digit alphanumeric labeler code, and we seriously considered adopting an alphanumeric labeler code. Ultimately, we believe that the safer, more efficient approach is to finalize without change our proposal to institute a uniform, 12-digit NDC.

According to the Institute for Safe Medication Practices (ISMP), information that contains both numerals and letters is particularly prone to errors, and even typed, computer-generated, or electronic prescription orders and transcriptions may not prevent confusion among certain alphanumeric symbols (Ref. 1). Moreover, the alpha characters that the commenters suggested should be excluded from the NDC to minimize confusion is likely underinclusive. In addition to the uppercase letters suggested by the commenters, ISMP has identified the following uppercase and lowercase letters as commonly confused for another letter or a numeral (Table 3).

Table 3.--Commonly Confused Letters and Numerals

Uppercase Letter for Another Uppercase Letter	Uppercase Letter for a Numeral	Lowercase Letter for Another Lowercase Letter	Lowercase Letter for a Numeral
T and I	G and 6	g and q	l and 1
C and G	F and 7	p and n	b and 6
L and I	Z and 2	m and n	o and 0
M and N	Q and 2	y and z	g and 9
P and B	Y and 5	u and v	q and 9
F and R	Z and 7	c and e	
U and O	T and 7		
U and V	U and 4		
E and F	U and 0		
V and W			
X and Y			

We believe that a numeric-only NDC has less potential to generate medication errors compared to an alphanumeric NDC. Simply put, there is less opportunity for confusion when a human user must input only numerals instead of numerals and letters. In retail and hospital pharmacy practice, the printed patient prescription label placed on the dispensed bottle identifies the NDC of the source bottle from which the drug was dispensed. When visually comparing the NDC on the printed patient prescription label to the NDC on the source bottle, a person may mistake a letter for a numeral and vice versa. It is less taxing and less error prone for the human brain to consider only 10 possible digits as potential options for each character in a 6-digit

labeler code. In contrast, under the approach desired by the commenters, there would be a total of 50 possible characters (10 numerals, 20 uppercase letters, and 20 lowercase letters) for each character in an alphanumeric 6-digit labeler code. Moreover, this plethora of possibilities would not be limited only to newly issued alphanumeric labeler codes. The knowledge that some NDCs are alphanumeric may cause a human to misread a numeral as a letter even when trying to process an entirely numeric labeler code. This is likely to generate medication errors when the NDC must be manually typed into an electronic health record (EHR) or pharmacy information system. We note that phonetic factors can also contribute to medication errors with the use of alphanumeric NDCs. For example, if an NDC is confirmed by reading it aloud, the letter "A" may be mistaken for the numeral "8." Alphanumeric NDCs may also contribute to confusion with other required label information, such as alphanumeric lot numbers, suffixes used for biosimilar and biological nonproprietary names, salt abbreviations (e.g., HCl (hydrogen chloride) or NaCl (sodium chloride)), and product identifiers used for investigational drug products.

Limiting the alpha characters as suggested by some commenters would not eliminate the potential for medication and inventory errors. Although we suspect that some of the additional letters identified in Table 3 above may be more susceptible to confusion only when handwritten (e.g., the letter "U" being confused with the numeral "4"), it appears that an alphanumeric NDC should be limited to fewer alpha characters than suggested by the commenters. Regardless of whether FDA were to further limit the scope of alpha characters beyond that advocated by the commenters, the mere existence of an alphanumeric code is likely to increase the possibility that a letter is confused for a different letter or for a numeral (e.g., an "F" could be misread as an "R" or as the numeral "7") or that a numeral is misread as a letter (e.g., the numeral "6" may be confused for the letter "G"). This is particularly true because not all people who will be interacting with the NDC will know that the letters assigned by FDA do not include all letters in the English alphabet. Thus, the commenters' approach does not eliminate the possibility that a letter or a numeral will be misread as a letter that FDA would never assign to a labeler code (e.g.,

an “L” could still be misread as the capital letter “I” and a zero could still be misread as the letter “O”). In addition, a numeric-only NDC is more efficient to work with because the use of alphanumeric characters slows down human verification. Specifically, it may be natural to read strings of letters and numbers together as a word (Refs. 2, 3, 4). Therefore, it may take cognitive effort to reject that interpretation and re-read the string as separate alphanumeric characters.

We disagree with the suggestion made by some commenters that an alphanumeric labeler code is similar to the alphabetic suffixes used by FDA in assigning a nonproprietary name for certain biological products licensed under section 351(a) or 351(k) of the PHS Act. Under FDA’s current naming convention for such biological products, the Agency designates a nonproprietary name that is a combination of the core name and a distinguishing suffix that is composed of four lowercase letters. In contrast to the use of an alphabetical suffix as part of a product name, the commenters propose to add alphabetic characters to the numeric NDC, which for the reasons discussed above risks confusion.

Finally, we disagree that the concerns raised about claiming and disputing historical Medicaid drug rebates should outweigh the advantages of promulgating a uniform, 12-digit NDC format that contains a numeric labeler code. As noted above, FDA does not view conversion of a 10-digit NDC to a 12-digit NDC as resulting in a “new” NDC. Moreover, nothing in this final rule requires a change to the NDC format used for purposes of claiming or disputing historical claims for Medicaid drug rebates.

In summary, although a limited 5-digit alphanumeric labeler code would result in additional labeler codes that would extend the use of 10-digit NDCs, FDA must consider not just sheer numbers, but also safety and useability. As noted above, adding an alpha character to the numeric NDC entails a greater potential for confusion and medication errors. Moreover, it would not result in an NDC of uniform length because, under the commenters’ approach, some FDA-assigned NDCs will remain 10-digits in length, while other FDA-assigned NDCs will have 11 characters. In addition, the commenters’ approach would not achieve a uniform NDC

configuration because each segment of the NDC would vary in length. Even if an alphanumeric labeler code might be an easier solution to implement in the short term, we believe a standardized, numeric 12-digit NDC eliminates the potential for medication errors that could occur with an alphanumeric labeler code and will be more efficient to work with in the long term. We note that because the linear barcode cannot accommodate alpha characters, adopting an alphanumeric NDC would require barcode formats and scanners to be updated.

(Comment 12) Some commenters advocate for a uniform, 11-character NDC in the HIPAA-mandated 5-4-2 format, except that it would eventually incorporate an alphanumeric labeler code for new labelers. These commenters note that this approach would provide an adequate supply of labeler codes, achieve the goal of an NDC of uniform length and configuration, and be less costly and safer to implement for the reasons summarized in Comment 11. Under this approach, there would be very little change for the existing labelers because their native 10-digit NDCs would simply be converted to an 11-digit NDC format in the same manner that such NDCs are currently converted to the 11-digit HIPAA NDC format.

(Response 12) We decline to adopt an 11-character NDC with an alphanumeric labeler code for the reasons discussed in Response 11. We note that for firms that currently have FDA-assigned 10-digit NDCs, the adoption of an 11-character NDC would not reduce the costs of updating labeling to include the new 11-digit NDC.

(Comment 13) A number of commenters request that FDA permit the elimination of dashes in the NDC format when the NDC is communicated and stored electronically. The commenters reason that dashes increase the amount of data that must be exchanged and stored and can be misread, which interferes with interoperable data exchange and may result in errors. They note that electronic messaging and electronic data interchange standards do not include dashes and that dashes will not be necessary with a uniform NDC format. In contrast, one commenter asserts that dashes should not be eliminated because it is difficult to know where to place leading zeros when NDCs are transmitted without dashes. This commenter states that

FDA should ensure interoperable data communication by providing clear guidance regarding the use of dash separators.

(Response 13) We appreciate the concerns of the commenters, but the electronic storage and exchange of NDCs is outside the scope of this rulemaking. Nothing in this final rule governs the use of dashes in the NDC when the NDC is communicated and stored electronically. We note that the new uniform format (6-4-2) should eliminate any existing uncertainty regarding placement of dashes for human-readable formats of the NDC.

(Comment 14) A comment from a pharmacy benefit manager (PBM) asserts that the proposed rule does not address the format for the product and package codes in a 12-digit NDC. The PBM advocates that leading zeros be added to existing 3-digit product codes and existing 1-digit package codes, noting that it would be consistent with the current NCPDP product identifier standard.

(Response 14) We addressed the format for product and package codes in the proposed rule. Specifically, we proposed that all existing 10-digit NDCs would be converted to the uniform, 12-digit format by the addition of leading zeros to the labeler code, the product code, and/or the package code segments as needed to produce the 6-4-2 format (87 FR 44038 at 44042–, 44043). We are finalizing this proposal without change.

(Comment 15) One commenter notes concern that leading zeros are often truncated and requests clarification that truncation of leading zeros would not be permitted. Another commenter notes that the addition of leading zeros to existing NDCs could lead to medication errors if software systems are not programmed to read NDCs correctly.

(Response 15) Leading zeros are part of the NDC, whether they exist under the current regulations or will be added in accordance with this final rule. FDA believes that leading zeros should not be truncated, and both existing and future electronic systems will need to be designed accordingly.

(Comment 16) One commenter requests confirmation that FDA would not assign a labeler code consisting entirely of a single repeating numeral (e.g., 000000, 111111). The commenter asserts that such a policy would preserve existing industry use of these values.

(Response 16) We decline to accept the commenter's request. The commenter does not provide any context for how industry may use such values and the likelihood that industry's use of these values would be confused with an NDC. We note that there are no 4- or 5-digit labeler codes that consist entirely of zeros, but FDA has assigned labeler codes consisting entirely of other repeating numerals. We are not persuaded to change the current practice.

(Comment 17) One commenter seeks confirmation that 6-digit labeler codes for new labelers would be assigned starting at 100000.

(Response 17) The commenter is correct. Because leading zeros will be added to existing labeler codes of less than 6 digits, new 6-digit labeler codes that begin with a zero will not be issued.

(Comment 18) Several commenters ask how historical patient records containing NDCs should be handled. These commenters query whether it will be necessary to convert to the new format any NDCs that appear in patient records regarding medication history and drug allergy information. The commenters note that there could be drug-drug interactions or a drug allergy that must be considered in the patient's ongoing treatment. They also believe that it will be very burdensome to convert NDCs in patient records, especially if the conversions cannot be safely automated and would require clinician review.

(Response 18) These comments are beyond the scope of this rulemaking. This final rule does not set forth any requirements with respect to historical paper or electronic patient records that include an NDC.

(Comment 19) Comments from a health IT vendor and an association representing EHR software developers appreciate our statement in the proposed rule indicating that FDA will continue to maintain and publish 10-digit NDCs for listed drugs simultaneously with their

converted 12-digit NDC equivalents during the transition period (87 FR 44038 at 44044). Both commenters request that FDA make this information available in perpetuity to avoid potential confusion after the effective date of the final rule.

(Response 19) We intend to publish a database that will map each 10-digit NDC appearing in the NDC Directory to the corresponding 12-digit NDC at least until the end of the transition period. We may consider the matter further as the end of the transition period approaches. We note that if FDA discontinues publication of this database, a similar database could be made available by a third party.

(Comment 20) Two commenters representing health IT vendors advocate that the final rule should require health IT vendors to include only the converted 12-digit NDC in interoperable outbound messages that occur on or after the effective date of the final rule. The commenters suggest that such a policy would support interoperability in the exchange of patient data.

(Response 20) Although FDA agrees that the interoperable exchange of patient health data is important and necessary, the commenters' suggestion is outside the scope of this rulemaking. This final rule does not set forth any requirements with respect to the electronic exchange of patient data containing NDCs. As we indicated in the proposed rule (87 FR 44038 at 44044), one of the purposes of the delayed effective date is to allow sufficient time for the HIPAA standards to be updated to accommodate the uniform, 12-digit format for NDCs and for all interested parties to update their systems and make other changes necessary for handling the uniform, 12-digit NDC upon the effective date of this final rule. To the extent that any messages transmitted after the end of the transition period are required by the FD&C Act to include the NDC, the NDC set forth in such message must be in the uniform 12-digit format.

(Comment 21) A comment from an association representing pharmacists requests additional guidance regarding how FDA intends to handle the practice of converting 10-digit NDCs to 11-digit NDCs during the transition to 12-digit NDCs. The commenter states that once

the 12-digit NDC is introduced, the use of all three formats at the same time may introduce confusion and increase the likelihood of errors.

(Response 21) The commenter is mistaken; NDCs of 10, 11, and 12 digits will not all be used at the same time. As explained in section I.B. of this document, FDA will continue to assign new 10-digit NDCs until the effective date of this final rule. Upon the effective date of this final rule, all existing FDA-assigned 10-digit NDCs will be converted to 12-digit NDCs, and FDA will begin assigning new NDCs in the uniform, 12-digit format. As explained in section V.E. of this document, this final rule has a 7-year delayed effective date. Because the current HIPAA standards cannot accommodate a 12-digit NDC, we expect that the current HIPAA 11-digit standard will be discontinued, and a new HIPAA standard that can accommodate a 12-digit NDC will be implemented on or before the effective date of this rule. To minimize any potential for confusion during the 3-year transition period that begins on the effective date, FDA will publish both the 10-digit and 12-digit NDCs for all listed drugs that had been assigned a 10-digit NDC.

D. Barcode Format Requirement

The FDA regulation at 21 CFR § 201.25 specifies when, where, and in what format a barcode must appear on the label of a human prescription drug product, a biological product, and an over-the-counter drug product. Currently, § 201.25(c) provides that each drug product subject to the barcode label requirements must have a barcode that contains, at a minimum, the appropriate NDC in a linear barcode that meets European Article Number/Uniform Code Council (EAN/UCC) or Health Industry Business Communications Council (HIBCC) standards or another standard or format that has been approved by the relevant FDA Center Director. Section 201.25(c)(1) further states that the barcode must be surrounded by sufficient blank space so that it can be scanned correctly, and it must remain intact under normal conditions of use.

We proposed to revise § 201.25(c) to allow use of barcodes in a linear or nonlinear format that is approved by the relevant FDA Center Director. We also proposed that approved

standards would include those that meet EAN/UCC or HIBCC standards. In the proposed rule, we recognized that the current barcode standards that utilize GS1's Global Trade Item Number (GTIN)-14 cannot accommodate the embedding of a 12-digit NDC (87 FR 44038 at 44042, 44044). Therefore, we stated that the delayed effective date of the rule would allow time for the development of new data standards, data carriers, and systems and processes to accommodate a 12-digit NDC.

In the following paragraphs, we discuss comments on proposed § 201.25(c)(1). We are finalizing the proposal with modification. Specifically, we are amending § 201.25(c)(1) to allow the use of a barcode in a linear or nonlinear format if it "conforms to the standards developed by a widely recognized international standards development organization and that format and standard is recognized by the relevant Food and Drug Administration Center Director." We have removed references to specific standard-setting organizations, two of which became outdated (according to comments submitted by GS1 US, EAN and UCC merged in 2005 and are now known as GS1 and GS1 US, respectively). The more general term "widely recognized international standards development organization" is understood throughout industry, unlikely to become obsolete, and does not constitute a change in the status quo because GS1, GS1 US (a member of GS1), and HIBCC are "widely recognized international standards development organizations." In addition, this change has the benefit of characterizing the nature of the organizations whose barcode formats and standards FDA may recognize in the future.

Although the proposed rule and the existing regulation text refer to barcode formats and standards "approved" by FDA, this final rule requires that barcode standards and formats be "recognized" by FDA. The purpose of this change is to clarify FDA's role with regard to industry's adoption of barcode formats and standards that can comply with all requirements of § 201.25(c). Specifically, FDA is not a standards development organization; it does not develop, prescribe, or officially "approve" highly technical barcode standards and formats. Rather, FDA relies on the expertise and activities of widely recognized international standards development

organizations to develop barcode formats and standards for drug labels that will satisfy the requirements of § 201.25(c) while accommodating industry needs and leveraging technological innovations. The Agency will ensure that industry is notified if an FDA Center Director recognizes a new barcode format and standard or revokes the recognition of a barcode format and standard. In the meantime, FDA recognizes those barcode formats and standards developed by GS1, GS1 US, and HIBCC that comply with the requirements of § 201.25(c).

(Comment 22) A number of commenters support our proposal to permit the use of nonlinear barcodes. Some drug products must include on their labels both the linear barcode currently required under existing § 201.25(c) as well as a two-dimensional (2D) data matrix barcode that is required for certain prescription drug packages under the DSCSA (Title II of Pub. L. 113-54).[7] One commenter advocates eliminating linear barcodes for any drug label that bears a 2D data matrix barcode encoding a product identifier. The commenter reasons that space constraints make it difficult to fit both types of barcodes on a single product package, and barcodes can be difficult to scan when placed too close together. Two commenters assert that the GS1 UPC-A linear barcode, which is commonly used to implement the current barcode labeling requirement, is already of limited future utility because it cannot accommodate the 11-digit NDC authorized under existing § 207.33(b)(1). A different commenter encourages FDA to continue supporting the use of linear barcodes.

(Response 22) We appreciate the commenters' support and believe that allowing the use of nonlinear barcodes will accommodate advancements in technology and industry needs by providing more options for labeling compliance. After the effective date of this final rule, if a

[7] The DSCSA was enacted to help secure the integrity of the drug supply chain by, among other things, requiring serialization and tracing of prescription drugs. For certain prescription drugs, under sections 582(b)(2) and (e)(2) of the FD&C Act (21 U.S.C. 360eee-1(b)(2) and (e)(2)), manufacturers and repackagers are required to affix or imprint a "product identifier" on each package and homogenous case of product intended to be introduced in a transaction into commerce (see section 581(24)(B) of the FD&C Act (21 U.S.C. 360eee(24)(B)) for exemptions to the definition of "transaction"). A "product identifier" is a standardized graphic that includes the product's NDC and serial number (collectively, the "standardized numerical identifier"), lot number, and expiration date (sections 581(14) and (20) of the FD&C Act). The product identifier must be in human-readable form and on a machine-readable data carrier that conforms to standards developed by a widely recognized international standards development organization (section 581(14) of the FD&C Act). For packages of product, the data carrier is a 2D data matrix barcode (section 582(a)(9) of the FD&C Act).

product is required under § 201.25 to include on its label a barcode that encodes the drug's NDC, the manufacturer or repackager will be able to encode the NDC into either a linear or nonlinear barcode that complies with the requirements of § 201.25. If the same drug label is also required under the DSCSA to include a product identifier, the 2D data matrix barcode could satisfy both sets of barcode requirements (§ 201.25 and DSCSA) because the 2D data matrix barcode includes encoding of the NDC. Accordingly, this final rule should reduce scanning failures due to close placement of multiple barcodes and avoid potential errors from manual entry of drug information, thereby improving patient care and increasing efficiency across the supply chain. This final rule does not prohibit the use of both linear and nonlinear barcodes on the same label, as long as applicable requirements under § 201.25 and the DSCSA are met.

(Comment 23) Many commenters are concerned that the proposed changes to the NDC format would require modifications to how the NDC is encoded within a barcode. Commenters seek additional guidance regarding the impact of a 12-digit NDC on barcode standards, such as a UPC barcode or a 2D data matrix barcode used for the product identifier required under the DSCSA.

(Response 23) We understand from comments submitted by GS1 US that a 12-digit NDC would be incompatible with the current barcode standards that utilize GS1's GTIN-12 or GTIN-14 (e.g., GS1's UPC-A and 2D data matrix barcode) because a 12-digit NDC is too long to be embedded into the current GTIN structure. GS1 US indicated that industry will no longer be able to use the UPC-A barcode. To continue to support industry in its NDC-based requirements, GS1 US states that it has created an application identifier (AI) for the NDC, referred to as "AI (715)." GS1's AI (715) is an additional data element that enables the NDC to be encoded in barcodes that can manage multiple AIs and an increased number of characters. According to GS1 US, the following barcodes can encode AI (715) for the 12-digit NDC: (i) the GS1 2D DataMatrix barcode (nonlinear); (ii) the GS1-128 barcode (linear); and (iii) the GS1 DataBar barcode (linear). Therefore, for purposes of § 201.25(c) requirements, linear barcodes (e.g.,

GS1-128 or GS1 DataBar barcode) or nonlinear barcodes (e.g., GS1 2D DataMatrix barcode) can transition to encoding the 12-digit NDC through the use of GS1's AI (715). In addition, for DSCSA product identifier requirements, the 2D data matrix barcode can encode the 12-digit NDC through the use of GS1's AI (715), along with other required data elements (e.g., serial number, lot number, expiration date). According to GS1 US, barcodes that encode the NDC using the AI (715) can be read only with camera-based scanners. Affected parties should consider this to ensure they have equipment and systems capable of handling the new, uniform, 12-digit NDC format on the effective date of the final rule.

(Comment 24) One commenter requests that FDA provide examples of barcodes that would comply with this final rule. Several commenters note the need for consistency between the FDA barcode rule and DSCSA requirements.

(Response 24) The barcode labeling requirements of this final rule would be satisfied by any barcode that encodes the appropriate NDC and conforms to a standard developed by GS1, GS1 US, HIBCC, or another organization whose linear or nonlinear barcode format is recognized by FDA. We cannot provide examples of barcodes that will satisfy the requirements of this final rule because GS1, GS1 US, and HIBCC may change barcode formats and standards over time. We note, as summarized in Comment 23, that GS1 has made it possible for linear and nonlinear barcodes to encode the new 12-digit NDC on the effective date of this final rule. Although the UPC-A linear barcode may not be used to encode a 12-digit NDC, it would not have been able to encode the 11-digit NDC that would have been issued under existing § 207.33(b)(1) had this rule not been finalized.

We presume that the commenters advocate for consistency between the barcode labeling requirements of this final rule and the DSCSA product identifier requirements to ensure that, when appropriate, a single barcode could be used to satisfy both sets of requirements. We agree that regulatory consistency on requirements related to barcodes is desirable whenever possible, and based on comments received from GS1, the addition of AI (715) will allow the 12-digit

NDC to be incorporated into one or more types of barcodes that could satisfy the requirements of this final rule as well as DSCSA requirements. We anticipate that standards organizations will continue to support industry's efforts to integrate NDCs into barcodes for supply chain security purposes in a manner that ensures consistency with the barcode labeling requirements in this final rule.

(Comment 25) Some commenters seek guidance regarding how the new NDC format would affect the use of GTINs, particularly for purposes of DSCSA compliance. One commenter asks FDA to confirm that manufacturers may continue to use the GTIN in barcodes where feasible (for example, when package size is sufficient to accommodate the relevant barcode). Another commenter asks FDA to recognize the GTIN-14 as an optional data element of the unique product identifier required under section 582(b)(2) of the FD&C Act so that GTIN-14 can continue to be used for global supply chain harmonization efforts; it could then be voluntarily included within a 2D data matrix barcode and provided in human-readable format on the package.

(Response 25) The direct relationship between GS1's GTIN-12 or -14 and NDC will no longer exist once the new 12-digit NDC format is fully adopted because the use of 10- and 11-digit NDCs will be phased out and the GTIN-12 and GTIN-14 cannot accommodate the embedding of a 12-digit NDC. Regarding prescription drugs subject to DSCSA requirements, manufacturers and repackagers may continue to voluntarily include their associated GTIN as part of the product identifier, as long as the product package remains compliant with applicable DSCSA product identifier requirements and inclusion of the GTIN-12 or -14 does not violate the barcode requirements under § 201.25.

(Comment 26) One commenter asks whether the current GS1 GTIN without leading zeros would be accepted.

(Response 26) This final rule sets forth how 10- and 11-digit NDCs will be converted to 12-digit NDCs. While this conversion will include the addition of leading zeros in some

segments of the NDC, FDA cannot speak to how this would affect GS1 GTINs and general GS1 requirements beyond the information that the Agency has received from GS1 through this notice and comment process. FDA has addressed GTIN-related comments in Responses 23 and 25.

(Comment 27) One commenter states that this final rule should define a common barcode symbol and specify how it should be encoded. The commenter suggests a specific encoding format and believes that allowing GS1 to establish the barcode and encoding standards would involve too much delay and would not result in uniform standards across industry.

(Response 27) We decline to accept the commenter's suggestion. We are concerned that promulgating a single barcode symbol and encoding format could impede innovation in barcode technology for drug products subject to the barcode label requirements. We note that given the delayed effective date and GS1's development of AI (715) as an option for encoding the 12-digit NDC in certain linear and nonlinear barcodes, the commenter's concerns regarding delay have been addressed.

(Comment 28) In response to our solicitation of comment in section V.C.3 of the proposed rule, an association of biopharmaceutical research and manufacturing companies urges FDA not to further revise § 201.25(c) to accommodate potential advances in technologies by allowing the use of unspecified automatic identification and data capture formats other than linear or nonlinear barcodes. The association notes that such a generic standard should not be implemented without providing an opportunity for public notice and comment. In addition, the association notes that any additional changes to the regulation should be specific in nature to ensure alignment and interoperability among all supply chain partners.

(Response 28) We understand the commenter's concern and will not permit the use of unspecified automatic identification and data capture formats at this time. We may consider the matter in future rulemaking.

E. Delayed Effective Date and Transition Period

In the following paragraphs, we discuss comments on our proposal to delay the effective date of the final rule for 5 years after its publication and to provide a 3-year transition period during which FDA would exercise enforcement discretion with respect to drugs labeled with a 10-digit NDC. In light of the public comments and the current rate at which labeler codes are assigned, we are delaying the effective date of this final rule for a period of 7 years after the date of its publication. We are finalizing without change our proposal for a 3-year transition period.

(Comment 29) Some commenters support the proposal to set a specific effective date for the use of 12-digit NDCs, rather than implement the new NDC format only after the supply of 5-digit labeler codes is exhausted. These commenters note that a specific effective date would mitigate disruption, patient risk, and the cost of the transition. In particular, the commenters support a definitive effective date because it allows for adequate planning and budgeting and is less likely to result in a chaotic and inconsistent implementation.

(Response 29) We agree with the commenters and appreciate their support.

(Comment 30) Several commenters believe that the proposed 5-year delayed effective date and 3-year transition period are sufficient to accomplish an orderly transition to the uniform, 12-digit NDC format while minimizing the potential for drug shortages and patient harm. Many other commenters, however, urge FDA to further delay the effective date of the final rule or to adopt a longer transition period, or both. Although most commenters do not suggest a specific alternative implementation timeframe, several commenters suggest that full implementation of the final rule (delayed effective date and transition period) should occur over at least a 10-year period. One commenter advocates for a 7-year delayed effective date, and another commenter urges FDA to adopt a 10-year delayed effective date. A third commenter asserts that the transition period should end at least 10 years from the close of the comment period on the proposed rule (i.e., November 2032). Drug manufacturers and associations representing manufacturers advocate for a 5-year transition period.

Commenters supporting a longer implementation timeframe assert that the complexity and burden of migrating to a new NDC format warrants a longer period of time for full implementation. Those supporting a longer delayed effective date argue that pharmacies, payors, and other parties throughout the healthcare supply chain and delivery system would need more time to develop, test, and upgrade software systems to handle both 10- and 12-digit NDCs; invest in new hardware for barcode scanning; implement new internal processes; and train personnel. These commenters assert that without more time, there would be significant data exchange errors that would affect product delivery and impede patient access.

Commenters representing the drug manufacturing sector assert that the proposed 3-year transition period is too short to accommodate the required labeling, barcode, and packaging changes, especially for generic drug manufacturers with large numbers of labeler codes, drug products, and packaging that must be updated. These commenters note their belief that FDA's proposed 3-year transition period is based on a flawed premise that most drug products have a 2-year expiration date and most drug product labeling is updated at least once every 3 years. The commenters note that many older generic drugs with stable safety profiles expire after 3 or more years, and a few expire after 10 years. One large generic drug manufacturer notes that it markets over 500 products with expiration dates longer than 2 years. In addition, commenters argue that generic drug companies may have dozens or hundreds of products for which labeling changes are not needed as frequently as every 3 years, and carton and container labeling is changed far less frequently. Moreover, commenters assert that, because 12-digit NDCs will not be assigned before the effective date of the final rule, manufacturers cannot use the 7-year period before the effective date to begin transitioning all labeling and packaging to the new NDC format. According to the commenters, it will not be possible for some manufacturers with large product portfolios to update all drug product labeling and packaging within 3 years, and there will be a substantial amount of product labeled with 10-digit NDCs on the market at the end of the transition period. The commenters further note that, as a practical matter, even drugs with a 2-

year expiration date would need to have their labeling updated by the end of the first year of the transition period to avoid having unexpired inventory on the market after 3 years. According to the commenters, a transition period of at least 5 years is necessary to ensure that there is sufficient time to make labeling changes for all products (including barcode changes), minimize the amount of inventory that will need to be taken off the market at the end of the transition period, and avoid drug shortages. The commenters also believe that a longer transition period would minimize the need to expedite a large volume of labeling changes, thereby imposing a lower economic burden.

Two commenters, including a trade association of EHR developers, advocate for a transition period shorter than 3 years, arguing that the coexistence of 10- and 12-digit NDCs during the transition period would pose a risk to public health that would not be outweighed by the challenges manufacturers will face in updating their labeling to conform to the final rule. The commenters suggest that the potential for public health and safety risks would be reduced if the final rule minimizes the amount of time during which health information systems must accommodate multiple NDC formats. Another commenter is concerned about the potential for confusion and medication errors during the transition period.

(Response 30) In response to the comments we received asking for a longer time period between the publication of the final rule and the effective date, we are revising the proposed 5-year delayed effective date to a 7-year delayed effective date. We reevaluated the supply of 5-digit labeler codes. Based on that reevaluation, we determined that we could delay the effective date for 2 additional years without significantly increasing the risk of running out of 5-digit labeler codes prior to the effective date. Accordingly, we are delaying the effective date of this final rule for 7 years. We have chosen a 7-year delayed effective date because it responds to the needs of the commenters, will help ensure an orderly and safe transition to the new NDC format, and is not likely to occur before the supply of 5-digit labeler codes is exhausted. Further delaying the effective date could jeopardize the supply of 5-digit labeler codes.

We decline to extend the transition period beyond 3 years. We continue to believe that the coexistence of drug labeling with either the 10- or 12-digit NDC poses risks to public health. Simultaneously accommodating 10- and 12-digit NDCs raises the risk of confusion, which in turn could increase medication errors and the potential for illegitimate product to be introduced into the market. We disagree with the commenters' assertion that manufacturers cannot use the 7-year period before the effective date of this final rule to begin the work of transitioning all labeling and packaging to the new NDC format. Although the new labeling cannot be used before the effective date, manufacturers will know how each existing 10-digit NDC will be converted to the new format. Thus, they can begin preparing new labels and packaging before the start of the transition period. Accordingly, we do not believe the need for a transition period longer than 3 years outweighs the risks of extending the time period during which both 10-digit and 12-digit NDCs will be used. Nevertheless, given the challenges cited by these commenters, we are concerned that a transition period shorter than 3 years would not be feasible. We are finalizing a 3-year transition period to support a smooth transition that minimizes the potential for confusion and medication errors.

(Comment 31) In lieu of a longer transition period, some commenters advocate for a more flexible approach that would alleviate some of the challenges they perceive with a 3-year transition period. These commenters suggest that FDA implement a waiver process pursuant to which manufacturers could apply for an extension of the transition period upon a demonstration of need. Under this approach, manufacturers would still use the new NDC format, but would have more time to transition products with 10-digit NDC labeling from the market. Alternatively, commenters suggest a staggered or phased implementation approach that would permit companies with large numbers of NDCs to have a longer transition period. Finally, commenters suggest that FDA treat products that bear a 10-digit NDC as exempt from the requirements of this final rule as long as the products entered interstate commerce (i.e, were packaged) or were actually distributed (i.e., changed ownership) prior to the end of the transition

period. According to one commenter, this approach would give manufacturers more time to deplete stock of remaining product with the 10-digit NDC while introducing little additional risk into the market.

(Response 31) No enforcement action would be taken against any unexpired product for being labeled with a 10-digit NDC (rather than a 12-digit NDC) if it remains in interstate commerce after the transition period ends, so long as it was introduced or delivered for introduction into interstate commerce prior to the effective date of this final rule. We decline, however, to extend the transition period in the manner suggested by the commenters for the reasons noted in Response 30. Accordingly, any products that are introduced into interstate commerce with a 10-digit NDC after the effective date and before the end of the transition period are subject to enforcement action if they remain in interstate commerce after the end of the transition period. We believe this approach will encourage prompt transitioning of labeling while decreasing compliance costs and the potential for drug shortages.

(Comment 32) One commenter representing allergen manufacturers requests that its members be exempt from the requirement to identify their drug products with a 12-digit NDC. The commenter reasons that converting allergen extract products to a 12-digit NDC format after they have been identified by 10-digit NDCs for over 50 years may cause confusion and is too burdensome.

(Response 32) We see no reason to treat allergen manufacturers any differently than manufacturers of other drugs. For the reasons explained in Responses 8 and 9, we believe that using the uniform, 12-digit format NDC for all drugs is ultimately safer, less confusing, and less expensive. Moreover, FDA considers an NDC in its original 10-digit format and in its converted 12-digit format to be the same NDC with different formats.

(Comment 33) Some commenters advocate for FDA to exercise flexibility regarding the implementation of the final rule if unanticipated events arise that interfere with industry's ability to implement the necessary system changes by the effective date.

(Response 33) We are extending the effective date of this final rule to 7 years after publication, which provides additional flexibility. Although FDA has provided some flexibility with respect to other effective dates, affected parties should not expect or anticipate any extensions in the effective date of this final rule given the limited supply of labeler codes. Affected parties should be prepared to accommodate the 12-digit NDC no later than 7 years after the publication of this final rule. Once the Agency begins issuing 12-digit NDCs, affected parties must be ready to handle that NDC; the inability to do so could jeopardize patient care and access to medication.

(Comment 34) A commenter representing wholesale distributors seeks clarity on the legal status of drug products that bear only a 10-digit NDC and enter the supply chain before the effective date of this final rule. The commenter urges FDA to clarify that such products may remain in the supply chain indefinitely after the effective date. Similarly, another comment from an association of wholesale distributors advocates that products packaged prior to the effective date should be permitted to remain on the market until the expiration date of those products. The comment reasons that this approach would allow patient access to products already in the market.

(Response 34) Products that are introduced into interstate commerce or delivered for introduction into interstate commerce before the effective date can remain on the market and accessible to patients after the 3-year transition period, as long as they have not expired. We note that most products introduced or delivered for introduction into interstate commerce before the effective date of this final rule will expire before the end of the transition period. Products that are packaged before the effective date but are introduced into interstate commerce or delivered for introduction into interstate commerce with a 10-digit NDC (rather than a 12-digit NDC) after the effective date are subject to enforcement action if they remain in interstate commerce after the end of the transition period.

(Comment 35) One commenter suggests that FDA conduct a study to determine if the proposed delayed effective date and transition period allow sufficient time for all interested parties to implement the final rule.

(Response 35) We decline to conduct a study as suggested by the commenter. Such a study is unnecessary because the public comments have provided sufficient feedback on our proposed implementation timeframe. Moreover, a study would further delay the final rule and jeopardize FDA's ability to transition to 6-digit labeler codes before exhausting the supply of 5-digit labeler codes.

(Comment 36) Several commenters urge FDA to provide periodic updates identifying the remaining number of 5-digit labeler codes or estimating how much longer FDA can continue to issue 5-digit labeler codes. The commenters note that this information would be useful in determining when to begin or accelerate efforts to comply with the final rule.

(Response 36) We decline to provide the requested updates because the volume of remaining 5-digit labeler codes will not impact the effective date of the final rule, and FDA does not intend to extend the effective date even if the number of 5-digit labeler codes may allow for such an extension. Therefore, interested parties should work with all diligence to ensure that, as of the effective date of this final rule, they have systems in place to handle the new 12-digit NDC format. FDA has carefully established the effective date of this final rule to occur before the supply of 5-digit labeler codes is exhausted.

(Comment 37) One commenter requests clarification on when FDA will begin issuing 6-digit labeler codes and converting 10-digit NDCs to 12-digit NDCs. The commenter also seeks clarification on when repackagers must begin labeling products using the 12-digit NDC format.

(Response 37) Starting on the effective date of this final rule, FDA will issue only 6-digit labeler codes and all new NDCs will be assigned in the uniform, 12-digit format (except in the case of certain HCT/Ps for which an alternatively formatted NDC is approved by FDA pursuant to § 207.33(b)(2) of this final rule). In addition, on the effective date, FDA will convert all

existing 10-digit NDCs in all product listing structured product labeling (SPL) and NDC labeler code request SPLs (hereinafter "drug listing files") to the 12-digit format by adding leading zeros to the labeler code, product code, and/or package code segment of the NDC, as needed to produce the uniform 6-4-2 format. All drug listing files submitted after the effective date must identify the NDC using the 12-digit NDC format. Manufacturers and repackagers should start labeling drugs that were assigned a 10-digit NDC with the 12-digit NDC as soon as possible after the effective date of this final rule.

(Comment 38) A comment from an association representing a variety of parties in the pharmaceutical distribution system urges FDA to retain the proposed policy under which FDA would automatically convert NDCs to the 12-digit format on the effective date of the final rule. This comment notes that requiring registrants to resubmit existing drug listing files to reflect a reformatted NDC would be unmanageable and impose an enormous burden. Several commenters representing the manufacturing sector oppose the proposed automatic conversion policy on the grounds that it will result in confusion and could render product immediately unsellable. One commenter notes that distributors could put a 10-digit NDC product into a non-sellable status and eventually return the product to the manufacturer for destruction, which would be wasteful. This commenter also notes that current purchasing systems would require significant changes to allow for the same drug product to be sold with different NDCs. Commenters opposed to the automatic conversion policy advocate that FDA should not activate new 12-digit NDCs until the manufacturer has introduced product with that NDC into the market after submitting an SPL file with updated labeling reflecting the 12-digit NDC. According to the commenters, their proposed approach would ensure that the NDC that appears on a drug label will match the NDC that appears for that product in the NDC Directory and the DailyMed searchable database. The commenters also note that their approach would reduce confusion and the potential for medication errors and would avoid the need to discard labeling stock and usable product.

(Response 38) We agree that it would be unduly burdensome for manufacturers to resubmit all existing drug listing files merely to reflect a reformatted NDC that is not a "new" NDC. The commenters opposed to the automatic conversion policy appear to have misunderstood the nature of the proposed NDC conversion. As explained in Response 2, FDA considers the conversion of a 10-digit NDC assigned by FDA to the new, uniform 12-digit NDC format to be a ministerial, administrative change and not the assignment of a "new" NDC. Furthermore, FDA considers such an NDC in its original 10-digit format and in its converted 12-digit format to be the same NDC with different formats. Because the converted NDC is not a "new" NDC, the commenters' concerns that the labeling update renders product immediately unsaleable are unfounded. Moreover, by publishing both the 10-digit and 12-digit NDCs for all listed drugs that had been assigned a 10-digit NDC, FDA would minimize the potential for confusion that may occur during the transition period before a drug's labeling is updated. We recognize that electronic systems will require significant changes to process transactions involving NDCs under both formats after the effective date and for this reason have delayed the effective date for 7 years. We note that the alternative approach suggested by the opposing comments would not ensure that the NDC that appears on a drug label will match the NDC that appears for that product in the NDC Directory and DailyMed, except in the unlikely event that all stock of the product labeled with a 10-digit NDC has been removed from the market at the time the manufacturer has submitted a new SPL file and introduced into interstate commerce product labeled with the 12-digit NDC.

Accordingly, upon the effective date, FDA will update existing SPL files to reflect the 12-digit NDC by linking or otherwise associating both NDC formats. For those products that are required to include an NDC on their labeling, a manufacturer must report that it has updated a product label to reflect the 12-digit NDC by using the annual reporting process under 21 CFR 314.81(b)(2)(iii) for drugs subject to a new drug application (NDA) or abbreviated new drug application (ANDA) or 21 CFR 601.12(f)(3) for biological products subject to a biologics license

application (BLA). Manufacturers that voluntarily include the NDC on the label of an animal drug must make a similar report in accordance with 21 CFR 514.80(b)(4)(ii). In addition, in accordance with § 207.49(a)(15), the manufacturer must update the relevant SPL file with the new labels and packaging that includes the 12-digit NDC format.

(Comment 39) A comment from a generic drug manufacturer asserts that, in the case of a labeling update required under section 505(o)(4) of the FD&C Act (21 U.S.C. 355(o)(4)), FDA should not require the revised labeling to update the NDC to the new 12-digit format. The commenter notes that, under section 505(o)(4)(B)(i) of the FD&C Act, a manufacturer has only 30 days to propose labeling changes to reflect new safety, effectiveness, or other information regarding a reference listed drug (RLD). The commenter conveys concern that RLD sponsors could "force" generic drug manufacturers to update labeling with respect to the NDC before the manufacturer has prepared new packaging and other materials featuring the reformatted NDC, thereby disrupting complex internal systems and processes.

(Response 39) As stated in the proposed rule, if a firm includes an NDC in its labeling, it should start labeling drugs that were assigned a 10-digit NDC with the 12-digit NDC as soon as possible after the effective date, but no later than when it runs out of its existing labeling for the drug and orders or begins printing new labeling (87 FR 44038 at 44044). We recognize that the speed with which labeling changes must be made pursuant to section 505(o)(4)(B)(i) of the FD&C Act may be challenging, particularly if they are unexpected. However, firms can take advantage of the 7-year delayed effective date to plan and prepare for timely implementation of labeling updates after the effective date of this final rule. Such preparation will minimize the challenges posed by labeling changes that must be made to reflect new safety, effectiveness, or other information under section 505(o)(4) of the FD&C Act. We note that FDA cannot approve new labeling that is not in compliance with applicable requirements. Therefore, in the case of a drug whose labeling must include the NDC, the 12-digit NDC format must be used in any new

labeling that includes the NDC that is submitted for FDA approval after the effective date of this rule.[8]

(Comment 40) Several commenters seek more detailed information regarding the revision and submission of drug listing files. Specifically, the commenters seek clarification on when manufacturers should begin incorporating the 12-digit NDC format into drug listing files, whether such updates would be accomplished by amending existing drug listing files or if manufacturers would need to submit new drug listing files, and whether FDA would accept an updated drug listing if the data elements in the drug listing file reflect the 12-digit NDC, but the drug's labeling has not yet been updated to reflect the 12-digit NDC format.

(Response 40) Upon the effective date of this final rule, FDA will update all drug listing files to reflect the 12-digit NDC format. Accordingly, manufacturers will not need to submit new or updated drug listing files solely to effectuate the NDC format change. If a drug listing file must be updated for other reasons after the effective date, the manufacturer should follow the usual procedures for such updates. During the transition period, FDA will accept an updated drug listing file that includes the NDC in a 12-digit format, even if the drug's labeling still reflects a 10-digit NDC.

(Comment 41) A commenter seeks clarity on whether it could begin to initiate conversion of 10-digit NDCs to the 12-digit NDC format on product labeling after the effective date of the final rule. Another commenter notes concern that some manufacturers would wait until after the transition period to begin labeling updates to reflect the 12-digit NDC.

(Response 41) Firms should not delay their labeling compliance efforts until the end of the transition period. Rather, they should use the 7-year period before the effective date to plan and prepare for updating their labeling during the transition period. For products whose labels must include the NDC, firms should start labeling products with the 12-digit NDC format as

[8] We note that FDA only assigns an NDC in accordance with 21 CFR 207.33(d). Approval of a drug's labeling that includes an NDC that has yet to be assigned by FDA in accordance with § 207.33(d) should not be interpreted as FDA's assignment of such NDC.

soon as possible after the effective date and no later than when existing labeling stock is depleted.

(Comment 42) A few commenters inquire whether the NDC Directory and DailyMed would be updated and searchable on both the 10-digit and 12-digit NDCs.

(Response 42) For products previously assigned a 10-digit NDC, the NDC Directory will be updated on the effective date to reflect NDCs in the 12-digit format, and we anticipate that it will be searchable using either the 10-digit or 12-digit format. Although the DailyMed database is maintained by the National Institutes for Health (NIH), not FDA, the Agency will coordinate with NIH to help ensure that DailyMed is similarly updated and searchable on both NDC formats as of the effective date.

(Comment 43) One commenter seeks confirmation that the NDC format appearing on certain prescription drug packages is expected to match the NDC included in the transaction information required to be exchanged to satisfy DSCSA requirements. The commenter notes that the product identifier for DSCSA purposes should match what appears on the physical label and packaging.

(Response 43) This comment is outside the scope of this final rule and will be addressed through DSCSA implementation efforts. Detailed information on DSCSA implementation can be found at https://www.fda.gov/drugs/drug-supply-chain-integrity/drug-supply-chain-security-act-dscsa.

(Comment 44) A commenter seeks clarification regarding compliance obligations at the end of the transition period. Specifically, the commenter questions whether all drug products in the supply chain at the end of the transition period must be labeled with a 12-digit NDC or if only those drug products manufactured after expiration of the transition period must bear a 12-digit NDC.

(Response 44) Most drug products in the supply chain at the end of the transition period must be labeled with a 12-digit NDC. Drug products labeled with a 10-digit NDC that are

introduced into interstate commerce or delivered for introduction into interstate commerce after the effective date and that remain on the market after the end of the transition period are subject to enforcement action. In contrast, drug products labeled with a 10-digit NDC that are introduced into interstate commerce or delivered for introduction into interstate commerce before the effective date of this rule can remain on the market after expiration of the 3-year transition period, as long as they have not expired. Because many drug products expire within 3 years, we do not expect a large supply of drug products labeled with 10-digit NDCs to remain on the market after expiration of the transition period.

As stated above, drug products manufactured after the effective date should be labeled with the new NDC format no later than when new labels need to be printed. We recognize that drug products labeled with a 10-digit NDC will likely be introduced into the market during the first year after the effective date, as firms attempt to deplete their labeling inventory. By the second year after the effective date, we expect most firms to be using new labeling that conforms to the 12-digit NDC format. Firms still using old labeling during the third year after the effective date will be at risk for enforcement action if drug products with such labeling remain on the market after the transition period ends.

F. Technical Amendments

After the proposed rule was published, FDA modified the authority citation for 21 CFR part 201 to include the following additional statutory provisions: 21 U.S.C. 343, 360ccc, 360ccc-1, and 360ee. The authority citation set forth in this final rule repeats the current authority citation without change.

VI. Effective Date

This rule will become effective 7 years after the date of its publication in the *Federal Register*. In addition, as discussed in section V.E. of this document, this rule provides for a 3-year transition period following the effective date. We expect the transition period to minimize possible disruption to the distribution of products subject to this rule and to minimize the burden

on manufacturers and labelers. During the transition period, firms with products that were assigned 10-digit NDCs prior to the effective date of the final rule must use a 12-digit NDC for all drug listings submitted to FDA and should transition to using a 12-digit NDC on labeling.

VII. Final Economic Analysis of Impacts

A. Introduction

We have examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, Executive Order 14192, the Regulatory Flexibility Act (5 U.S.C. 601-612), the Congressional Review Act/Small Business Regulatory Enforcement Fairness Act (5 U.S.C. 801, Pub. L. 104-121), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4).

Executive Orders 12866 and 13563 direct us to assess all benefits and costs of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits. Rules are economically significant under Executive Order 12866 if they have an annual effect on the economy of $100 million or more; or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities. The Office of Information and Regulatory Affairs (OIRA) has determined that this final rule is not a significant regulatory action under Executive Order 12866.

Executive Order 14192 requires that any new incremental costs associated with certain significant new regulations "shall, to the extent permitted by law, be offset by the elimination of existing costs associated with at least 10 prior regulations." This final rule is not considered an Executive Order 14192 regulatory action because this rule is not significant under Executive Order 12866.

Because this rule is not likely to result in an annual effect on the economy of $100 million or more or to meet other criteria specified in the Congressional Review Act/Small Business Regulatory Enforcement Fairness Act, OIRA has determined that this rule does not fall within the scope of 5 U.S.C. 804(2).

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the one-time costs could be as much as 0.59 percent of average annual revenue for some very small entities in the pharmaceutical industry, 0.33 percent of average annual revenue for some very small entities in the insurance industry, and 0.40 percent of average annual revenue for some very small entities in the healthcare industry, we certify that the final rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes estimates of anticipated impacts, before issuing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year." The current threshold after adjustment for inflation is $187 million, using the most current (2024) Implicit Price Deflator for the Gross Domestic Product. This final rule will not result in an expenditure in any year that meets or exceeds this amount.

B. Overview of Benefits, Costs, and Transfers

The final rule amends regulations governing the format of the NDC by standardizing it to 12 digits in length. Currently, the NDC assigned by FDA is 10-digits and can be in multiple formats. The NDC for each listed drug in the United States is a unique 3-segment number, where the three segments are the labeler code, product code, and package code. Under this final rule, the standardized NDC will consist of three segments: a 6-digit labeler code, a 4-digit product code, and a 2-digit package code. When the rule becomes effective, FDA-assigned 10-digit NDCs will be converted to the uniform 12-digit format by adding leading zeros to the labeler code, product code, or package code segment of the NDC, as needed to produce the uniform 6-4-2 format.

FDA's transition to a uniform format for FDA-assigned NDCs is intended to facilitate the adoption of a single NDC format across the entire healthcare industry. Such an adoption will eliminate the need to convert NDCs from one of the FDA-assigned formats to a different standardized format used by other sectors of the healthcare industry (e.g., healthcare providers and payors). Eliminating the need to convert NDCs should reduce potential errors caused by converting the FDA-assigned NDC format to a different NDC format used by other sectors of the healthcare industry. Standardization and adoption of a single format will also eliminate the need for additional quality control and validation by certain interested parties, such as payors and prescribers, to ensure a drug product and its respective NDC are accurate; this is particularly important for insurance coverage and reimbursement claims. Another benefit of the rule will be to avoid any potential risks to the public health from medication errors and the risk of confusion. We do not have enough information to quantify these potential benefits, so we only qualify them in this analysis.

The costs to industry of converting current NDCs to the standardized format will include one-time costs of updating software systems, other transition costs, coordinating labeling updates, and reading and understanding the rule. Table 4 shows a summary of the quantified costs of the rule. We estimate annualized costs will be about $14.64 million ranging from $7.64 million to $22.79 million using a 7-percent discount rate over a 10-year horizon. Similarly, we estimate annualized costs will be about $14.90 million ranging from $7.79 million to $23.18 million using a 3-percent discount rate over a 10-year horizon.

Table 4.--Summary of Benefits, Costs, and Distributional Effects of the Final Rule ($millions, 2024)

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Benefits	Annualized Monetized ($millions/year)					7%		
						3%		
	Annualized Quantified					7%		
						3%		
	Qualitative	Potential cost savings by eliminating different formats of the NDCs. Reductions in annual audits, billing issues, cost of software, and potential medication errors.						
Costs	Annualized	$14.64	$7.64	$22.79	2024	7%	10 years	

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
	Monetized ($millions/year)	$14.90	$7.79	$23.18	2024	3%	10 years	Costs to labelers increase with the quantity of NDCs they handle.
	Annualized Quantified					7%		
						3%		
	Qualitative	The net monetized costs are likely overestimated because they do not account for cost-savings.						
Transfers	Federal Annualized Monetized ($millions/year)					7%		
						3%		
	From/To	From:			To:			
	Other Annualized Monetized ($millions/year)					7%		
						3%		
	From/To	From:			To:			
Effects	State, Local, or Tribal Government: No estimated effect. Small Business: One-time costs will be no more than 1 percent of average revenue for some very small stakeholders in the pharmaceutical, insurance, and healthcare industries. We certify that the final rule will not have a significant economic impact on a substantial number of small entities. Wages: No estimated effect. Growth: No estimated effect.							

The total present value, in 2024 millions of dollars, across all three industries ranges from $53.65 million to $160.08 million with a primary estimate of $102.85 million using a 7-percent discount rate. By contrast, using a 3-percent discount rate, the total present value of estimated costs ranges from $66.42 million to $197.76 million with a primary estimate of $127.08 million. These costs are likely to be spread out over the 7-year period between publication of the rule and its effective date. Thus, we assume that one-seventh of these costs occur each year of this period and that the first year of the rule is 2026. We assume the reading and understanding costs, however, will occur the first year after the rule is published.

In line with Executive Order 14192, in Table 5 we estimate present and annualized values of costs, cost savings, and net costs over a perpetual time horizon. We estimate that this rule will generate $7.90 million in annualized costs at a 7-percent discount rate, discounted relative to year 2024, over a perpetual time horizon.

Table 5.--EO 14192 Summary Table of Costs and Cost Savings ($millions, 2024)

	Primary Estimate 7%	Low Estimate 7%	High Estimate 7%
Present Value of Costs	$112.90	$53.65	$160.08
Present Value of Cost Savings			
Present Value of Net Costs	$112.90	$53.65	$160.08
Annualized Costs	$7.90	$3.76	$11.21
Annualized Cost Savings			
Annualized Net Costs	$7.90	$3.76	$11.21

Note: Values discounted over an infinite time horizon and year one is assumed to be 2026.

C. Comments on the Preliminary Economic Analysis of Impacts and Our Responses

On July 25, 2022, we published the proposed rule "Revising the National Drug Code Format and Drug Label Barcode Requirements" (87 FR 44038). We received several comments on the Preliminary Regulatory Impact Analysis (PRIA) of the proposed rule (Ref. 5). Below, we group the comments by topic and offer a brief description of each and our responses. The order of comments and responses is not a reflection of importance.

1. Cost Estimates

(Comment 45) Some commenters express that the cost estimates of transitioning 10-digit NDCs to a 12-digit format are underestimated and that they should be three to ten times the International Classification of Diseases (ICD) conversion reference cited in the PRIA.

(Response 45) We disagree. We clarify that the ICD-9 to ICD-10 conversion is only a reference to assess the burden of updating information systems. We agree that the NDC and the ICD conversion do not involve the same amount of effort. The mapping of ICD-9 to ICD-10 codes involved the mapping of 57 ICD-10 codes per each ICD-9 code on average (according to the RAND Corporation (RAND) 2004 report we use, Ref. 6). In the PRIA, we use an effort relative to the ICD conversion of 10 percent because the mapping of NDCs is 1-to-1 instead. This is a conservative approach because estimates are likely higher than what the costs will be. However, in section II.F.2 of the FRIA, we are updating estimates in the cost category entitled "Other Transition Costs," previously named "Learning and Training." In addition, in the sensitivity analysis in section II.I.1 of the FRIA, we include a range of 1 percent to 50 percent relative to the ICD-conversion estimates.

(Comment 46) Some commenters express that the cost estimates do not represent the cost burden some large companies will experience.

(Response 46) Feedback from industry helps us with estimates. We note that larger companies may refer to the upper bound costs rather than the average estimates for reference. This feedback, however, may only represent a few companies.

(Comment 47) Commenters express that estimating costs based on the ICD-9 to ICD-10 transition is not appropriate because ICD codes are not used by as many interested parties as NDCs.

(Response 47) We disagree. We do not use the ICD estimates to calculate that the NDC transition will cost the same amount. We emphasize that the estimates that use the ICD conversion only apply to some elements in the calculation of software updates and to other transition costs. Other categories of costs, such as coordination of label updates, are estimated using other additional inputs. We also clarify that we use the ICD estimates to assess certain cost inputs rather than to claim that an entire industry group will have a fixed amount of costs; that is, we use the breakdown of cost items and not the aggregate ICD cost per interested party.

(Comment 48) Some commenters express that the cost estimates do not account for the need to update the physical packaging in addition to the labeling.

(Response 48) The labeling cost model that we use from RTI International accounts for the coordinated and uncoordinated relabeling costs, which include packaging updates (Ref. 7). In the PRIA, however, we opted not to include the cost element of disposing old inventory or updating it with new labels over the old ones because we stated that during the 3-year transition period, we do not intend to object to products being introduced into interstate commerce with the 10-digit NDC that they were previously assigned. That is, in general, we will allow old labels to be exhausted and thus minimize the need to discard old inventory.

In addition, we note that we are increasing the delay in effective date of the rule to 7 years instead of 5 years to allow interested parties sufficient time to update their systems and

make other changes necessary to ensure a safe and orderly transition to the new NDC format occurs on the effective date. This way, labelers can better assess the inventory of labels with 10-digit NDCs that will be needed. Furthermore, the 3-year transition period provides time to perform updates to the affected packaging.

(Comment 49) Commenters express that the costs are underestimated because the rule will have a greater impact on products subject to DSCSA requirements. For example, under DSCSA, firms must include the NDC in transaction information.

(Response 49) We acknowledge that the NDC is to be included in the transaction information under the DSCSA. We do not, however, ignore this cost or other transaction costs that may arise with the new NDC format. This FRIA provides higher estimates in the cost category entitled "Other Transition Costs," previously named "Learning and Training," and makes it more explicit that the costs of transitioning to the uniform, 12-digit NDC format, including the transaction information required under the DSCSA, are included in this category, as well as meetings for pre-planning, execution, additional quality controls, adjustments to the reformatted NDCs, and correction of any discrepancies that arise.

(Comment 50) Commenters convey that the costs are underestimated for pharmacies as there are more changes needed beyond software updates, such as updates to purchase orders and controlled substances reporting requirements.

(Response 50) We agree that these costs are not included in the cost category entitled "Software and Updates of NDC Records" in the PRIA. We cover these potential costs, and some others, in section II.F.2 of the FRIA, entitled "Other Transition Costs," previously named "Learning and Training." We update the costs in this category to nearly double the previous estimates to account for potential underestimates in the PRIA.

(Comment 51) Commenters express that the PRIA fails to recognize that many systems cannot handle two codes for the same product and there will be costs to update those systems.

(Response 51) We include estimated costs for such system updates, and some other costs, in a general category we call "Software and Updates of NDC Records" in the FRIA (see section II.F.1 of the FRIA).

(Comment 52) Some commenters express that the estimated costs were based on an accurate but incomplete list of interested parties. The commenters identify additional interested parties, including state prescription drug monitoring programs; State Medicaid agencies; drug compendia; drug distributors; pharmacy benefit managers; pharmacy claims processors; other payors beyond insurers, such as employers' health plans and claim sponsors; rebate processors; software vendors; auditors; intermediate and clearing houses; data aggregators; other government agencies; health information exchanges; and regulatory agencies.

(Response 52) We disagree with this interpretation of the PRIA. We classify interested parties into aggregate categories. Listing all the different disaggregated interested parties is not feasible as exemplified in the comment submitted. For example, the commenters express that the interested parties affected "include, but are not limited to," the entities listed. By acknowledging that the interested parties are "not limited to" the list submitted, commenters show how difficult it is to list all of them. More importantly, many parties identified by the commenters can be grouped into more general and useful categories. For example, other government agencies and Medicaid agencies can be grouped together with other payors that perform that function. Pharmacy benefit managers, pharmacy claims processors, and any other intermediary in processing claims, rebates, audits, or any activity related to a drug product transaction can be grouped into the larger insurance component, as we do by referring to them as other involved intermediaries. Note that software vendors are included in the pharmaceutical industry category we use because the former will bill the latter when they perform system updates; separating these two groups and adding costs for each would double count the costs. Our analysis also acknowledges interested parties that process information but do not perform distribution or

transactions. In sum, further dividing interested parties into subgroups beyond what we describe in the economic analysis does not add any accuracy or completeness to the analysis.

(Comment 53) Some commenters offered different cost estimates than what we presented in the PRIA. For example, some commenters express an amount of $100 million per wholesale distributor due to the many databases to update and systems to modify. Others express costs of $5 million for manufacturers and costs of up to $50 million for the largest generic companies.

(Response 53) We appreciate this kind of feedback. The more information we have, the better our estimates become. We have adjusted some of our estimates. However, we also note that these comments offer cost figures as an opinion and do not offer details about how these costs are estimated. We used the RAND 2004 report (Ref. 6) for these types of costs and the report dissects the different parts, which make our estimates trackable as compared to the ones offered by the commenters. We also note that the NDC updates, unlike the ICD updates, can be programmed as the update only needs a leading digit added to the respective sequence of digits. We agree that the communication for multiple systems may add a layer of quality control. We do account for this layer, and we have updated our "Other Transition Costs," previously named "Learning and Training," estimates to represent a higher burden.

(Comment 54) Some commenters express support for the Agency's proposal to convert 10-digit NDCs to the uniform, 12-digit format by adding a leading zero to the appropriate NDC segment. According to the commenters, this is the most efficient conversion option because it minimizes mapping and programming costs, and the standardization eliminates the use of multiple NDC formats.

(Response 54) We agree. This comment highlights that the effort to update systems can be automated to greatly reduce the burden.

2. Long-Term Cost Savings

(Comment 55) Some commenters highlight that current processing of NDCs between providers of drug products and payors is substantial and costly due to the lack of a standard

format. These commenters highlight the potential for cost savings in the long term despite some transition costs in the short term.

(Response 55) We agree with these comments.

(Comment 56) Some commenters highlight that the standardization will mitigate the potential for disruption, patient risk, and high costs by ensuring there will be a single NDC format and predetermined date for implementation. The comments also highlight that having multiple NDC formats can lead to incorrect drug inventory and errors in sending and receiving drugs.

(Response 56) We agree with these comments. Although we are not able to quantify the cost savings, we agree that in the medium-to-long term, cost savings will be realized as the multiple formats for FDA-assigned NDCs are eliminated and multiple related quality control steps become unnecessary. In the short term, industry will experience a transition process and eliminate inefficiencies caused by multiple formats for the FDA-assigned NDC.

3. Misunderstanding Incremental Cost

(Comment 57) Some commenters express that maintaining the 10-digit NDC and adopting a limited alphanumeric labeler code for new labelers would be less costly than adopting a 12-digit NDC format. Commenters argue that fewer entities would have major conversions to perform and that any needed conversions would be less expensive than under this rule because they would be performed faster. These commenters also express that preserving the 10-digit NDC format and using an alphanumeric format would avoid any changes to the HIPAA 11-digit NDC format.

(Response 57) We disagree. As explained in Response 11, the alphanumeric option may lead to some confusion. In addition, the alphanumeric option may be costlier than commenters expect because systems that currently can process only numeric NDCs would need to be updated to handle both alphanumeric NDCs as well as the existing numeric NDCs that would be retained

under the alphanumeric option. Thus, the alphanumeric option would also add to the use of multiple formats and the perpetual additional quality control costs associated with this.

As for permitting continued use of existing 10-digit NDCs, we agree that in the short term, this would be less costly to labelers who use them than to reformat them because it would not require them to update their drug labels to reflect a reformatted NDC. However, this option would not result in a uniform NDC format for all FDA-assigned NDCs. Even without this final rule, the 6-digit labeler code would roll out after the supply of 5-digit labeler codes is exhausted, thereby creating 11-digit NDCs that affected parties would have to process along with all the other different formats in perpetuity. Any quality assurance costs involved in handling multiple formats would likely negate any cost savings from continued use of existing 10-digit NDCs.

(Comment 58) Several commenters express that the rule will be overly burdensome and that it would cost billions of dollars to update IT systems across multiple interested parties beyond labelers such as pharmacies as well as government and private payors.

(Response 58) We disagree that the rule will cost billions of dollars. We note that under current § 207.33, industry will eventually need to accommodate 11-digit NDCs, which will entail some implementation costs. The cost estimates for this final rule need only consider the incremental costs that this final rule will generate over and above the costs associated with transitioning to 11-digit NDCs. We also disagree that the cost estimates do not incorporate other interested parties beyond labelers. The economic analysis considers the overall healthcare sector (hospitals, physician establishments, nursing care facilities, pharmacies, dentists, residential health, home healthcare, outpatient care centers, medical and diagnostic centers, medical equipment suppliers, other health practitioners, etc.) and the insurance sector (administrators of claims for commercial and public-sponsored insurance plans, and other involved intermediaries).

(Comment 59) Some commenters express that it would be very burdensome to convert historical medication information in patient records.

(Response 59) These comments are outside the scope of the final rule. This final rule does not mandate that historical patient records be updated to reflect a 12-digit NDC.

(Comment 60) A commenter expresses that any changes to the NDC will require changing the automatic process by which GTINs are generated. The commenter believes that coordinating NDC and GTIN formatting and implementing the requisite system changes would increase costs and create opportunities for error.

(Response 60) We understand that a 12-digit NDC would be incompatible with the current barcode standards that utilize GS1's UPC-A and 2D data matrix barcodes because the GTIN cannot embed an NDC longer than 10 digits. We acknowledge that there are transition costs associated with reformatting 10-digit NDCs to 12-digit NDCs, and our final economic analysis includes such costs. We note that even without the rule, under existing § 207.33(b)(1), industry would incur costs to transition away from the GTIN, which cannot accommodate the 11-digit NDCs that would have been assigned absent this rule.

We have developed a comprehensive Economic Analysis of Impacts that assesses the impacts of the final rule. The full analysis of economic impacts is available in the docket for this final rule (Ref. 8) and at https://www.fda.gov/about-fda/economics-staff/regulatory-impact-analyses-ria.

VIII. Analysis of Environmental Impact

We have determined under 21 CFR 25.30(k) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IX. Paperwork Reduction Act of 1995

This final rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521). The title, description, and respondent description of the information collection provisions are shown in the following paragraphs with an estimate of the annual

recordkeeping burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

Title: Format of National Drug Code

Description: This rulemaking requires the respondents identified below to revise the format of their NDCs and to update any of their product labeling that includes the NDC to incorporate the new NDC format.

For drugs subject to an NDA or ANDA, the respondents must report these labeling changes through an annual report in accordance with § 314.81(b)(2)(iii). For biological products subject to a BLA, the respondents must report these labeling changes through an annual report in accordance with § 601.12(f)(3). Including the NDC on the label of an animal drug is voluntary. Manufacturers that voluntarily include the NDC on the label of an animal drug must report the labeling change in accordance with § 514.80(b)(4)(ii).

Section 314.81(b)(2)(iii) requires the submission of an annual report containing a representative sample of the package labels, currently used professional labeling, patient brochures, package inserts, and a summary of labeling changes (or if no changes have been made, a statement to that effect) since the previous report. The change in the NDC format required by this rule will result in a labeling change.

One-time costs and annual operating and maintenance costs associated with this rule are discussed in section VII.B. of this document and in the FRIA. However, many of these costs are not associated with the information collections subject to OMB review under the PRA but, instead, are associated with changes in their usual and customary business operations as a result of the new NDC format. Additionally, many of the costs discussed in the FRIA are incurred by firms other than the respondents described below.

To minimize recordkeeping burden resulting from changes to the NDC format, this final rule has a 7-year delay in the effective date followed by a 3-year transition period. The purpose

of the transition period is to mitigate potential labeling costs by allowing respondents to deplete labeling inventory and update labels with the new NDC format at the time of a periodic labeling update that may be made during the 3-year transition period. Based on the frequency at which drug labeling is typically updated, we anticipate that nearly all firms will be able to incorporate the labeling change required by the final rule as part of a periodic labeling change that they intend to make unrelated to this rule. Therefore, we believe that the incremental information collection burden associated with this rule is likely to be de minimis. As a result of the extension in the delayed effective date, which allows for more precise timing of labeling changes, and for consistency with the FRIA, we have modified our estimate of the one-time burden associated with the final rule, assuming that all finished prescription drug products and all finished over-the-counter drug products include the NDC on the label and that 95 percentof the label updates with the new NDC format will be made in coordination with a periodic labeling change that they intend to make unrelated to this rule.

In the proposed rule, we sought comments on our burden analysis. We did not receive any comments that were specific to our numeric hour burden estimates. However, on our own initiative, we modified our estimates to include burden hours related to animal drug label changes, which were inadvertently not included in the analysis of the proposed rule. We received numerous comments on the provisions of the proposed rule having to do with the proposed NDC format, the barcode format requirement, and the effective date. This final rule contains comment summaries and responses for these comments in sections V.C. through E. Additionally, we received comments about our cost estimates in the PRIA. This final rule contains comment summaries and responses for these comments in section VII.C.

Description of Respondents: Manufacturers, repackers, relabelers, drug product salvagers, and private label distributors are subject to the regulatory requirements in 21 CFR parts 201 and 207; application holders are subject to the regulatory requirements of §§ 314.81 and 514.80; and license holders are subject to the regulatory requirements of § 601.12.

We estimate the burden of the information collection as follows:

Recordkeeping burden related to labeling updates:

Table 6.--Estimated One-Time Recordkeeping Burden[1]

21 CFR Section; Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
Section 201.25 (barcode labeling requirements); and part 207, subpart D (requirements for the NDC)	13,583	1	13,583	1	13,583
Section 314.81(b)(2)(iii) (other postmarketing reports)	1,324	9	11,916	10 minutes (0.167 hours)	1,990
Section 601.12(f)(3) (changes to an approved BLA)	104	6	624	10 minutes (0.167 hours)	104
Section 514.80(b)(4)(ii) (periodic reports; labeling)	79	20	1,580	20 minutes (0.333 hours)	526
TOTAL			27,703		16,203

[1] Figures have been rounded.

We have characterized the information collection as a recordkeeping burden consistent with 44 U.S.C. 3502(13)(C), which defines the term "recordkeeping requirement" to include records disclosed to third parties, the Federal government, or the public. Our estimates are based on the following assumptions:

- We assumed that all listed drug packages include the NDC format on their label and that 95 percent of the label updates with the new NDC format will be made in coordination with a periodic labeling change that respondents intend to make unrelated to this rule during the transition period.
- We assumed that each label change would take a respondent 1 hour because only a slight change and not a substantial redesign would be needed to modify the existing NDC format and barcode already included on the label.
- Based on the drug listing database maintained by FDA, we understand that there are approximately 271,655 listed drug packages. We estimate that 5 percent of the 271,655 label updates (13,583 labels) will not be made in coordination with a periodic labeling change, resulting in an estimated one-time burden of 13,583 hours.

Section 314.81(b)(2)(iii)(*c*) requires firms to submit an annual report that includes a summary of any changes in labeling since the last annual report. For prescription drugs whose label changes would be reported in an annual report pursuant to § 314.81, there are approximately 1,324 respondents that would submit reports, and there are approximately 11,593 active approved applications. This means that, on average, each application holder subject to § 314.81 will need to submit 8.76 annual reports (rounded to 9). Information on listed drugs indicates there are approximately 117,367 separate, identifiable product packages that that are subject to an approved ANDA or NDA. This means that, on average, each separate and distinct approved application includes approximately 10 separate and distinct product packages (117,367 unique distinct product packages ÷ 11,593 unique approved applications). We expect that the updating of the NDC format on a label would necessitate a simple statement in the annual report declaring that the NDC format has been updated, so we have assigned an estimate of 1 minute for such statements per label. As each annual report under § 314.81(b)(2)(iii)(*c*) will include 10 such declarations (one for each unique product package), we estimate the burden to report these changes to be approximately 10 minutes (0.167 hours) per annual report. Thus, we estimate the total burden under § 314.81(b)(2)(iii)(*c*) to be 1,990 hours (1,324 respondents × 9 annual reports per respondent × 0.167 hours = 1,990 hours).

Similarly, § 601.12(f)(3)(i)(A) requires manufacturers of biologics to include in their annual reports editorial or similar minor labeling changes. For drug products whose label changes would be reported in an annual report pursuant to § 601.12(f)(3) for biological products, there are approximately 104 respondents that would submit reports and there are approximately 588 active approved applications. This means that, on average, each application holder will need to submit 5.65 annual reports (rounded to 6). There are approximately 5,940 separate, identifiable product packages that that are subject to an approved BLA. This means that, on average, each separate and distinct approved application includes approximately 10 separate and distinct product packages (5,940 unique distinct product packages ÷ 588 unique approved

applications). Thus, we estimate the total burden under § 601.12(f)(3)(i)(A) to be 104 hours (104 respondents × 6 annual reports per respondent × (0.167 hours) = 104 hours).

For animal drugs whose label changes would be reported in an annual report pursuant to § 514.80(b)(4)(ii), we estimate there are 79 respondents that would submit reports and there are approximately 1,582 active approved applications. On average, each respondent will submit 20 annual reports (1,582 active approved applications × 1 annual report per active approved application ÷ 79 unique application holders). We expect that the updating of the NDC format on a label would necessitate a simple statement in the annual report declaring that the NDC format has been updated. We estimate 1 minute for such statements per label. As each annual report will include 20 such declarations (1 for each unique product package), we estimate the burden to report these changes to be approximately 20 minutes per annual report (0.333 hours). Thus, we estimate the total burden to be 526 hours (79 respondents × 20 annual reports per respondent × 0.333 hours = 526 hours).

The information collection provisions in this final rule have been submitted to OMB for review as required by section 3507(d) of the Paperwork Reduction Act of 1995.

Before the effective date of this final rule, FDA will publish a notice in the *Federal Register* announcing OMB's decision to approve, modify, or disapprove the information collection provisions in this final rule. An Agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

X. Federalism

We have analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we conclude that the rule does not contain policies that have federalism

implications as defined in the Executive Order and, consequently, a federalism summary impact statement is not required.

XI. Consultation and Coordination with Indian Tribal Governments

We have analyzed this rule in accordance with the principles set forth in Executive Order 13175. We have determined that the rule does not contain policies that have substantial direct effects on one or more Indian Tribes, on the relationship between the Federal Government and Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes. Accordingly, we conclude that the rule does not contain policies that have tribal implications as defined in the Executive Order and, consequently, a tribal summary impact statement is not required.

XII. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff (see ADDRESSES) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at https://www.regulations.gov. References without asterisks are not on public display at https://www.regulations.gov because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. Although FDA verified the website addresses in this document, please note that websites are subject to change over time.

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List of Subjects

21 CFR Part 201

Drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 207

Drugs, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 201 and 207 are amended as follows:

PART 201—LABELING

1. The authority citation for part 201 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 343, 351, 352, 353, 355, 358, 360, 360b, 360ccc, 360ccc-1, 360ddd, 360ddd-1, 360ee, 360gg-360ss, 371, 374, 379e; 42 U.S.C. 216, 241, 262, 264.

2. In § 201.25:

a. Remove the word “bar code” wherever it appears and add the word “barcode” in its place; and

b. Revise the section heading and paragraph (c)(1) introductory text to read as follows:

§ 201.25 Barcode label requirements.

* * * * *

(c) * * *

(1) Each drug product described in paragraph (b) of this section must have a barcode that contains, at a minimum, the appropriate National Drug Code (NDC) number in a linear or nonlinear format that conforms to the standards developed by a widely recognized international standards development organization and that format and standard is recognized by the relevant Food and Drug Administration Center Director. Additionally, the barcode must:

* * * * *

PART 207—REQUIREMENTS FOR FOREIGN AND DOMESTIC ESTABLISHMENT REGISTRATION AND LISTING FOR HUMAN DRUGS, INCLUDING DRUGS THAT ARE REGULATED UNDER A BIOLOGICS LICENSE APPLICATION, AND ANIMAL DRUGS, AND THE NATIONAL DRUG CODE

3. The authority citation for part 207 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 355, 360, 360b, 371, 374, 381, 393; 42 U.S.C. 262, 264, 271.

4. In § 207.33, revise paragraph (b) to read as follows:

§ 207.33 What is the National Drug Code (NDC), how is it assigned, and what are its requirements?

* * * * *

(b) *What is the format of an NDC?* (1) Except as described in paragraph (b)(2) of this section, the NDC must consist of 12 digits, divided into three segments as follows:

(i) The first segment of the NDC is the labeler code and consists of 6 digits. The labeler code is assigned by FDA.

(ii) The second segment of the NDC is the product code and consists of 4 digits.

(iii) The third segment of the NDC is the package code and consists of 2 digits. The package code identifies the package size and type of the drug and differentiates between different quantitative and qualitative attributes of the product packaging.

(2) An alternatively formatted NDC that is approved for use by the relevant Center Director may be used for the following HCT/Ps if they are minimally manipulated: Hematopoietic stem/progenitor cells derived from peripheral and cord blood, and lymphocytes collected from peripheral blood.

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Robert F. Kennedy, Jr.

Secretary,

Department of Health and Human Services

[FR Doc. 2026-04368 Filed: 3/4/2026 8:45 am; Publication Date: 3/5/2026]