



October 18, 2010

Cynthia Tudor, Ph.D.
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Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Dear Dr. Tudor:

This is in response to your letter requesting that the FDA provide an updated version of the October 2009 "Non-Matched NDC List." More specifically, you requested that staff in the Office of Compliance of FDA's Center for Drug Evaluation and Research (CDER/OC) develop and provide an updated version of a "Non-Matched NDC List" that resulted from CDER/OC staff's comparison of NDCs in the FDA's NDC Directory with NDCs included in a National Library of Medicine database. We understand that CMS intends to compare the updated data that FDA has provided to the database that CMS uses to evaluate reimbursement claims before CMS posts a final Non-Matched NDC List on CMS's website. CMS intends to use the resulting updated list to enable CMS's processing systems, beginning on or around January 1, 2011, to reject prescription drug event (PDE) submissions from Part D sponsors for NDCs identified on the final Non-Matched NDC list once CMS posts it; therefore, those PDEs will not be processed or paid automatically.

Basic FDA Drug Listing Requirements

Under section 510 of the Federal Food, Drug, and Cosmetic Act, as amended (the Act), and Part 207 of FDA's regulations (with some limited exceptions) firms that manufacture, prepare, propagate, compound, or process drugs in the United States or that are offered for import into the United States must be registered with the FDA. 21 U.S.C. §§ 360(b), (c), (d), and (i). Every person who registers must, at the time of initial registration, list all drugs manufactured, prepared, propagated, compounded, or processed for commercial distribution. 21 U.S.C. § 360(j)(1), 21 CFR 207.20. Drug listing information must be updated in June and December each year. These updates must include drugs not previously listed (if any), and certain changes to information for previously listed drugs. 21 U.S.C. § 360(j)(2); 21 CFR 207.21(b), 207.30.

Prescription drug products that are properly listed appear in the FDA's NDC Directory. FDA does not consider a drug properly listed unless all data provided to the FDA for the product is correct and complete. However, neither the assignment of an NDC number nor inclusion in the NDC Directory denotes FDA approval of the product.

We understand that CMS is considering a drug product's inclusion in the NDC Directory in reviewing whether such drug products may be eligible or covered under one or more programs

administered by CMS. Our staff relies on drug listing data in responding to CMS inquiries about whether particular drugs have been approved by FDA for safety and effectiveness; commercially used or sold in the U.S. prior to 1962, or are identical, related or similar to such a drug (21 CFR 310.6); or have been subject to a final “new drug” determination under the Act. Therefore, FDA can only provide CMS with regulatory status determinations through our regular processes if a drug product is properly listed.

FDA Development of the Updated Non-Matched NDC List (CY 2011)

CDER/OC staff compared NDCs in the FDA’s NDC Directory as of September 1, 2010 with NDC data from a National Library of Medicine database as of August 2, 2010. CDER/OC staff reviewed the resulting non-matching NDC data, which contained a list of NDCs, trade names, ingredients, and other general product parameters.

As with the Non-Matched NDC List (CY 2010), CDER/OC staff identified certain types of products that would not ordinarily appear on the FDA NDC Directory so they could be excluded from the Updated Non-Matched NDC List. For example, the current edition of the NDC Directory is limited to prescription drugs and insulin products that have been manufactured, prepared, propagated, compounded, or processed by registered establishments for commercial distribution. We excluded from the Updated Non-Matched NDC List products that we identified as not insulin products or prescription drug products in final dosage form. We also excluded products that were clearly identifiable as bulk chemicals, devices, or device kits. Products that could not be clearly identified as belonging to one of the above categories may remain on the list.

For the updated version, CDER/OC staff also removed from the resulting, Updated Non-Matched NDC data the following products: NDCs associated with products identified by FDA and establishments as discontinued; NDCs with inactive Labeler Codes; NDCs identified by industry as incorrectly excluded from the NDC Directory (and thus identified on the Non-Matched NDC List (CY 2010)) that FDA has verified the registrant properly listed by submitting accurate and complete listing information for that product; NDCs associated with products identified by FDA as inactive because the firms are no longer in business; and NDCs deleted from the previous Non-Matched NDC List (CY 2010).

Based on our staff’s review of the Updated Non-Matched NDC data and FDA NDC Directory data, as well as our experience with FDA’s drug registration and listing system (subject to the qualifications and limitations described below) CDER/OC affirms that NDCs appearing on the Updated Non-Matched NDC data FDA has provided could not be matched with NDCs in FDA’s NDC Directory as of September 1, 2010. This includes NDCs not submitted to FDA and NDCs included in listing submissions that were not properly completed. Again, we understand CMS may further revise or refine that data before posting a final Updated Non-Matched NDC List.

Limitations of the NDC Directory and the Non-Matched NDC List

There are differences and limitations in the data maintained by the data sets used to create the Non-Matched NDC List. All of these data sources are vulnerable to some degree of inaccuracy; they also do not code or configure all product-related data in the same manner. As a result, the

Non-Matched NDC List also has limitations that affect what does, or does not, appear on the list. We describe these issues below, as well as steps that may be taken to address perceived inaccuracies that relate to drug listing. We are also attaching a set of “Questions and Answers” to help explain these issues and related matters. You may make this list available to those who may review or use the Non-Matched NDC List. We believe, however, that despite imperfections, the data remain useful.

- ❖ The Updated Non-Matched NDC List resulted from a comparison of NDC data included in a National Library of Medicine database as of the dates specified above, but data in those sources are periodically updated and may have changed. The fact that a product was not included in the NDC Directory as of September 1, 2010, does not preclude the possibility that it is listed with FDA now.
- ❖ The Non-Matched NDC List is not an all-inclusive list of NDCs that are not listed with FDA; there may be other marketed products with NDC numbers that are not listed with FDA, but if they are also not contained in the National Library of Medicine database, they would not appear on the Non-Matched NDC List.
- ❖ The fact that an NDC is included on the Non-Matched NDC List is not a finding that the drug product is not properly listed or is illegally marketed. For example, the Non-Matched NDC List might include NDCs for products that we would not expect to find included in the NDC Directory. Reasons for this may include:
 - a firm is exempt from registration and not subject to the drug listing requirements even though it has listed a drug NDC number in other commercial databases;
 - the drug was first in commercial distribution after the firm’s last drug listing update, and the firm was not yet required to update its listing information;
 - the drug has been identified to FDA as discontinued and is no longer marketed, but it still resides on wholesaler and pharmacy shelves and thus is reflected in commercial databases;
 - the product is not identified in our listing data as a prescription drug product; it is identified as a dietary supplement, a device, or an over-the-counter drug product, but has been coded as a prescription drug product in one or more data sets used to prepare the Non-Matched NDC List. Again, we flagged for exclusion only certain products that were clearly and consistently identifiable as products that we would not expect to be included in the NDC Directory. We would need additional information about these products individually to assist in determining the reasons for such differences or what classification is most accurate.

Compounded Drug Products

An NDC identified in a PDE for a compounded drug could appear on the Non-Matched NDC List if the NDC was included in the National Library of Medicine and in the database that CMS

uses for evaluating claims, but it is not listed with FDA. Under certain circumstances, a person that compounds prescription drug products is exempt from the registration and listing requirements of the Act, including:

- Pharmacies that operate under applicable local laws to regulate the dispensing of prescription drugs and only manufacture, prepare, propagate, compound, or process drugs for sale in the regular course of the practice of pharmacy, including dispensing and selling drugs at retail.
- Hospitals, clinics, and public health agencies that maintain establishments in conformance with applicable local laws regulating the practice of pharmacy or medicine, and regularly dispense drugs to patients under their care upon prescription of a licensed practitioner.
- Practitioners licensed to prescribe or administer drugs who manufacture, prepare, propagate, compound, or process drugs solely for use in their professional practice.

It is our understanding that for purposes of PDE submissions, CMS requires that compounded drugs be associated with an NDC. Thus, CMS may encounter claims/PDEs for compounded drug products that are associated with an NDC number that appears on the Non-Matched NDC List, even if it is not subject to FDA's listing requirements. We cannot determine based solely on NDC data whether a product was compounded or exempt from our rules. Pharmacies or other firms who compound drug products in the regular course of business may contact fda.cpdingteam@fda.hhs.gov with questions about whether they are subject to FDA drug registration and listing requirements.

How to Address Drug Listing Questions

Registered establishments, Part D sponsors, PBMs, pharmacies or other interested parties should contact the FDA at eDRLS@fda.hhs.gov or (301)-210-2890 if they believe a prescription drug product NDC is incorrectly excluded from the FDA NDC Directory and, therefore, identified on the Non-Matched NDC List or if they believe the Non-Matched NDC list is otherwise inaccurate at nonlisted@fda.hhs.gov or 301-210-2897.

- Before contacting the FDA, it would be helpful and most efficient if the firm can readily provide the following information: labeler code, product code, firm name, FEI and/or DUNS, product name, and printed copies of the electronically submitted Structured Product Label (SPL) for Listing.

Firms that wish to list a drug product, including one that appears on the Non-Matched NDC List, may find general information about registration and listing procedures at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/DrugRegistrationandListing/default.htm>. Firms must submit drug listing information electronically. As of June 1, 2009, the FDA only accepts electronic drug establishment registration and drug listing information (unless a waiver is granted). Firms may refer to the FDA guidance for industry on *Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Listing, May 2009* at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072339.pdf> for information about what listing information to submit and how to do so electronically.

As explained above, the registration and listing requirements are set forth in section 510 of the Act, 21 U.S.C. § 360, and Part 207 of FDA's regulations, 21 CFR 207. Although the next semi-annual period for listing updates required under our rules is December 2010, we want to emphasize that an establishment may update its listing(s) at any time prior to December.

We hope that this is helpful. Please contact us if you have any further questions.

Sincerely,

/s/

Michael M. Levy, Jr., Esq., Director
Division of New Drugs and Labeling Compliance
Center for Drugs Evaluation and Research
Office of Compliance

Attachment

NON-MATCHED NATIONAL DRUG CODE (NDC) LIST

(CY 2011)

SUMMARY AND QUESTIONS & ANSWERS

Overview

- ❖ The Centers for Medicare and Medicaid Services (CMS) and the Office of Compliance in the FDA's Center for Drug Evaluation and Research (FDA/CDER/OC) are working on a project to:
 - improve the accuracy of FDA's drug listing data; and
 - assist CMS in reducing the extent of reimbursement of claims under Medicare Part D for drugs that may not meet the statutory definition of a covered drug product, including unapproved drugs.
- On March 31, 2009, CMS published a final "Call Letter" guidance for organizations preparing to offer a Part D prescription drug benefit plan in 2010, and proposed that Part D sponsors consider the proper listing of a drug product with FDA a prerequisite for making a Part D drug coverage determination (<http://www.cms.hhs.gov/prescriptiondrugcovcontra>).
 - FDA is assisting CMS in its development of a "Non-Matched NDC List" that will support CMS's efforts to implement that guidance.
- In May 2009, CMS posted an initial version of the Non-Matched NDC List on its website. The list can be accessed from the CMS website. FDA/CDER/OC sent to CMS a letter explaining the FDA's role in providing NDC Directory data, and reviewing the Non-Matched NDC List, as well as qualifications and limitations of data reflected on the Non-Matched NDC List at least insofar as it reflects NDC Directory data maintained by FDA and to explain how firms can correct any inaccuracies. The initial list was preliminary, had no immediate impact on coverage under Medicare Part D, and may have contained inaccuracies.
- In October 2009, CMS posted an updated version of the Non-Matched NDC List (CY 2010) on its website. As explained in the CMS Call Letter, beginning in January 2010, CMS used this updated version of the Non-Matched NDC List to reject PDE submissions for prescription drug products that are not posted on the FDA NDC Directory, so that those PDEs are not processed or paid automatically. CMS posted regular monthly updates to the Non-Matched NDC List to reflect new FDA NDC Directory listings.
- In October 2010, CMS will post an updated version of the Non-Matched NDC List (CY 2011) on its website. Beginning January 2011, CMS plans to use this updated version of the Non-Matched NDC List to reject PDE submissions for prescription drug products that are not posted on the FDA NDC Directory, so that those PDEs are not processed or paid automatically. CMS plans to post regular updates to the Non-Matched NDC List to reflect new FDA NDC Directory listings.

Non-Matched NDC List Questions & Answers

➤ What is the Updated Non-Matched NDC List (CY 2011)?

- A comparison of drug product NDCs included in a National Library of Medicine database as of August 2, 2010, and in the database that CMS uses to evaluate claims, against NDCs included in the FDA NDC Directory.
- The Updated Non-Matched NDC List reflects NDCs that did not appear in the NDC Directory when the comparison was conducted, based on the NDC Directory as of September 1, 2010.
- *Terminology Note:* CMS refers to the submission of NDCs and other information to its systems that enables CMS to make payment to plans and administer the Part D benefit as a “prescription drug event,” or “PDE,” and its means of declining certain NDC submissions as “PDE edits.”

➤ Why was the Updated Non-Matched NDC List (CY 2011) prepared?

- The list was prepared to help highlight NDCs for which it has not been affirmatively established that the product meets the statutory definition of covered Part D drug as specified in Section 1860D-2(e)(1)(A) of the Social Security Act.
- CMS’s Call Letter explained that it is best practice for a Part D sponsor’s drug coverage determination to begin with confirming that a prescription drug product NDC is properly listed with FDA, because FDA can only provide CMS certain regulatory status information through its regular process for drugs that are properly listed.
- Beginning in January 2011, CMS will use this updated version of the Non-Matched NDC List to reject PDE submissions for prescription drug products that are not posted on the FDA NDC Directory, so that those PDEs are not processed or paid automatically.

➤ Are NDCs on the Updated Non-Matched NDC List (CY 2011) ineligible for coverage or reimbursement under Medicare Part D?

- The fact that an NDC appears on the Non-Matched NDC List does not necessarily mean that it fails to satisfy the definition of a Part D drug.
- The *initial* Non-Matched NDC List posted in May 2009 helped CMS refine the process of identifying drugs that do not appear in FDA’s NDC Directory and assist Part D sponsors and others in their efforts to address drug listing or other issues before an updated version of the list was prepared.
- CMS will use this updated list to establish PDE edits for 2011, so PDEs for those NDCs are not processed automatically.

➤ What are some of the limits of the data on the Non-Matched NDC List? Is it possible it includes NDCs that really are listed with FDA or that do not have to be listed?

- The updated list resulted from a comparison of NDC data included in a National Library of Medicine database as of certain dates (noted above) and in the database CMS uses to evaluate claims, but data in that database is periodically updated and may have changed.
 - The fact that a product is on the Non-Matched NDC List does not preclude the possibility that the product is listed with FDA now.
- The list may include NDCs for products that the FDA would not *expect* to find included in the NDC Directory. Examples include:
 - Newly introduced drugs that a firm was not yet required to identify in an update to its listing information
 - Drugs identified to the FDA as discontinued, but still reflected in drug databases
 - Products not identified in FDA listing data as a prescription drug product – such as a dietary supplement, a device, or an over-the-counter drug product - but coded as a prescription drug product in one or more of the commercial data sets used to prepare the Non-Matched NDC List

Additional information about what NDCs may and may not be included in the Non-Matched NDC list are described in FDA/CDER/OC's letter to CMS.

➤ **Do compounded drugs appear on the Non-Matched NDC List?**

- An NDC identified in a PDE for a compounded drug could appear on the Non-Matched NDC List if the NDC was included in a National Library of Medicine database and the database that CMS uses for evaluating claims, but it is not listed with FDA.
- Under certain circumstances, a person that compounds a prescription drug product is exempt from FDA's registration and drug listing requirements, including:
 - Pharmacies that operate under applicable local laws to regulate the dispensing of prescription drugs and only manufacture, prepare, propagate, compound, or process drugs for sale in the ordinary course of the practice of pharmacy.
 - Hospitals, clinics, and public health agencies that maintain establishments in conformance with applicable local laws regulating the practice of pharmacy or medicine, and regularly dispense drugs to patients under their care upon prescription of a licensed practitioner.
 - Practitioners licensed to prescribe or administer drugs who manufacture, prepare, propagate, compound, or process drugs solely for use in their professional practice.

➤ **I am a pharmacy that compounds drug products for dispensing and selling at retail to the public. Do I need to register and list with the FDA? How will I get reimbursed by CMS Medicare Part D?**

- Under 21 CFR § 207.10(a), pharmacies that do not manufacture or process drugs for sale other than in the regular course of practice of pharmacy, are exempt from registration and drug listing. Pharmacy practice includes dispensing and selling drugs at retail.

- A person that compounds drugs and has questions about whether they are subject to FDA drug registration and listing requirements may contact fda.cpdteam@fda.hhs.gov.
- FDA does not decide what products or services are eligible for coverage or what claims are reimbursed.
- Pharmacies or other firms seeking reimbursement for extemporaneously compounded drug products should follow the process defined by CMS.

➤ **I think an NDC number for a product I manufacture appears on the list in error. What do I do?**

- For questions or concerns about possible inaccuracies in the Non-Matched NDC List, please contact FDA at (301) 210-2897 or e-mail nonlisted@fda.hhs.gov.
- If a firm thinks an NDC appears on the Non-Matched NDC List in error because the NDC is listed with FDA, before contacting FDA, it would be helpful and most efficient if the firm is able to readily provide the following information: labeler code, product code, firm name, FEI and/or DUNS, product name, and printed copies of the electronically submitted Structured Product Label (SPL) for Listing.
- If a firm thinks an NDC appears on the Non-Matched NDC List in error because the NDC is discontinued and no longer being marketed, the firm should contact FDA and update its listing information.

➤ **Who prepared the Updated Non-Matched NDC List (CY 2011)?**

- FDA/CDER/OC staff's compared NDCs in the FDA's NDC Directory as of September 1, 2010 with NDC data from a National Library of Medicine database as of August 2, 2010.
- FDA/CDER/OC staff reviewed the resulting non-matching NDC data, which contained a list of NDCs, trade names, ingredients, and other general product parameters.
- As with the Initial Non-Matched NDC List, CDER/OC staff identified certain types of products that would not ordinarily appear on the FDA NDC Directory so they could be excluded from the Updated Non-Matched NDC List.
- For example, FDA/CDER/OC staff identified and removed the following products from the Updated Non-Matched NDC List: products that were clearly not prescription drug products in final dosage form or insulin products; products that were clearly identified as bulk chemicals, devices, or device kits; NDCs associated with products identified by FDA and establishments as discontinued; NDCs with inactive Labeler Codes; and NDCs identified by industry as incorrectly excluded from the NDC Directory (and thus identified on the Initial Non-Matched NDC List), that FDA has verified the registrant properly listed by submitting accurate and complete listing information for that product; NDCs associated with products identified by FDA as inactive because the firms are no

longer in business; and NDCs deleted from the previous Non-Matched NDC List (CY 2010) . Products that could not be clearly identified as belonging to one of the above categories may remain on the list.

- CMS compared the Updated Non-Matched NDC data that the FDA provided to the database that CMS uses to evaluate claims. The resulting list is the Updated Non-Matched NDC List (CY 2011) that CMS will post on its website.

➤ **Who decides whether a drug is covered under Medicare Part D? What is the FDA's role in this?**

- CMS administers the Medicare Part D program.
- FDA does not decide what products or services are eligible for coverage or what claims are reimbursed.
 - Part D sponsor coverage determinations may take into account information that FDA may be able to provide, such as whether a particular drug has, for example, been approved by FDA for safety and effectiveness. FDA can only provide Part D sponsors with this regulatory status information through its regular processes if a drug product is properly listed.

➤ **If an NDC is not on the Non-Matched NDC list, does that mean it is an FDA-approved drug? Is this basically a list of unapproved drugs?**

- No. Prescription drug products that are properly listed appear in the FDA's NDC Directory, but neither the assignment of an NDC number nor inclusion in the NDC Directory denotes FDA approval of the product.
- The Non-Matched NDC List simply reflects NDCs that were not in the NDC Directory, but were listed with the database that CMS uses in connection with its evaluation of claims for eligibility for reimbursement under the Part D Prescription Drug Program; it does not indicate approval status, although some products on the list might lack FDA approval.

➤ **How can I tell if a prescription drug with a particular NDC number is FDA-approved?**

- While the FDA works to ensure that all marketed unapproved drug products obtain approval or are removed from the market, healthcare practitioners and consumers can use Drugs@FDA (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>), the National Drug Code (NDC) Directory (<http://www.fda.gov/cder/ndc/database/>) or the Orange Book (<http://www.fda.gov/cder/ob/default.htm>) to determine whether a drug is FDA-approved. Drugs@FDA contains most FDA-approved drug products. The NDC Directory is limited to prescription drugs and insulin products. Search results from the NDC directory include a column marked "Application Number." FDA-approved products will have an associated NDA or ANDA number in this column. Identification of a drug product as "other" indicates that the product has not been FDA-approved (unless there is a data error

or the firm did not provide the product's application number). In the Orange Book, if the product is FDA approved, then the search results will list approved products (note the application number in the "Appl No" column) by dosage form, route, and name of applicant. If the product is not in the FDA approved list, then the results will state, "No matching records found." A manufacturer can clarify whether its drug has FDA approval by, among other things, providing the application number for the approved product when listing it with FDA.

- Questions about a firm's registration status or a product's listing status can be directed to the Drug Registration and Listing Team at eDRLS@fda.hhs.gov or (301) 210-2890.

➤ **Are NDCs on the Non-Matched List illegal?**

- The fact that an NDC is included on the Non-Matched NDC List is not a finding that the drug product is not properly listed or is illegally marketed.

➤ **Does this change the FDA requirements for drug registration and listing?**

- FDA requirements for drug registration and listing remain unchanged.
- Under section 510 of the Federal Food, Drug and Cosmetic Act, as amended ("the Act"), and Part 207 of FDA's regulations, with some limited exceptions, firms that manufacture, prepare, propagate, compound, or process drugs in the United States or that are offered for import into the United States must be registered with FDA. 21 U.S.C. §§ 360(b), (c), (d), and (i).
- Every person who registers must, at the time of initial registration, list all drugs manufactured, prepared, propagated, compounded, or processed for commercial distribution. 21 U.S.C. § 360(j)(1). *See also* 21 CFR 207.20.
- Drug listing information must be updated in June and December each year. These updates must include drugs not previously listed (if any), and certain changes to information for previously listed drugs.
- FDA is only accepting electronic drug establishment registration and drug listing information as of June 1, 2009 (unless a waiver is granted).
- Firms may refer to the FDA guidance for industry on *Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Listing, May 2009* at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072339.pdf> for information about what listing information to submit and how to do so electronically.

➤ **Where can one get more information?**

- For questions or concerns about FDA's NDC Directory, FDA's drug listing procedures please contact: FDA's Drug Registration and Listing Team at eDRSL@fda.hhs.gov or (301) 210-2890. For questions or concerns regarding possible errors in the Non-Matched NDC List, e-mail nonlisted@fda.hhs.gov.

- Questions about whether any drug – regardless of its FDA-approval status – is covered by CMS’ Part D program must be directed to CMS, at partD_NDC@cms.hhs.gov
- For questions or concerns about electronic drug listing submissions, please contact: FDA’s Drug Registration and Listing Team at (301) 210-2890 or e-mail spl@fda.hhs.gov.
- General information about the NDC Directory is available online at www.fda.gov/cder/ndc/ and FDA drug registration and listing is available online at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/DrugRegistrationandListing/default.htm>; FDA’s Guidance on Electronic Registration and Listing is available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072339.pdf>.
- Media inquiries can be directed to Shelly Burgess, FDA Public Affairs Specialist, at (301) 796-4651 or shelly.burgess@fda.hhs.gov.