Department of Health and Human Services

OFFICE OF INSPECTOR GENERAL

FDA'S APPROVAL STATUS OF DRUGS PAID FOR BY MEDICAID

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EXECUTIVE SUMMARY

OBJECTIVE

To determine the Food and Drug Administration's (FDA) approval status of drugs paid for by Medicaid in 2008.

BACKGROUND

Before a new drug may be legally marketed in the United States, it must be approved by FDA for safety and effectiveness. According to FDA, drugs lacking this approval may pose a significant public health concern because they may not meet FDA standards for safety, effectiveness, quality, and labeling.

FDA's system for collecting and maintaining drug product and approval information is known as the Drug Registration and Listing System (DRLS). As part of the DRLS, FDA maintains a publicly accessible database of currently listed drugs called the National Drug Code (NDC) Directory. The NDC Directory contains the name; the NDC (i.e., a numeric drug identifier); and the approved application number for each listed drug. The DRLS also includes nonpublic files of pending and discontinued NDCs. FDA acknowledges that the databases in DRLS may be inaccurate and incomplete.

FDA has additional databases containing approval information. One of these databases contains biological products, such as vaccines and blood (among others), used in the prevention, treatment, or cure of a disease or condition. Another is Drugs@FDA, which is a publicly available FDA database that provides each drug's approval history, including approved labels (i.e., the official description of a drug product that includes indications for which the drug is approved, states who should take it, and provides safety information), and indicates whether it was approved under a new drug application or an abbreviated new drug application; it does not list any of this information by the NDC.

To qualify for Federal payment under Medicaid, drugs generally must be approved by FDA, with certain exceptions. Medicaid payments for prescription drugs totaled approximately $24 billion in 2008. In 2008, the Office of Inspector General (OIG) received a congressional request to examine the FDA approval status of drugs paid for by Medicaid.

We used 2008 Medicaid utilization data for prescription drugs, approval and listing data from FDA, and a targeted manual review to accomplish our objective.

FINDING

Sixty-two percent of drugs paid for by Medicaid in 2008 had an approved application number in the NDC Directory; the remaining 38 percent either did not have an approved application number listed or were not in the NDC Directory at all. In 2008, Medicaid paid for prescription drugs associated with 27,143 NDCs. The NDC Directory listed approved application numbers for 16,945 (62 percent) of these NDCs. Medicaid payment for these drugs totaled $17.8 billion in 2008. The remaining 38 percent of drugs paid for by Medicaid were either (1) listed in the NDC Directory but did not have an approved application number or (2) not listed in the NDC Directory at all.

Twelve percent (3,158) of NDCs paid for by Medicaid in 2008 were listed in the NDC Directory but did not include an approved application number (i.e., the approved application number was "other," was blank, or could not be determined). More than three-quarters of these NDCs (2,426) had an approved application number listed as "other" in the NDC Directory and were not included in the other FDA databases. Medicaid payments for drugs associated with these 2,426 NDCs totaled $803 million in 2008. Each of the remaining 732 NDCs had (1) an application number of "other" but was included in 1 of FDA's other databases, (2) an approval status that was blank, or (3) an approval status that could not be determined.

A manual review of 25 of the 2,426 NDCs for which the approved application number was "other" (and that were not included in the other FDA databases) indicates that many of the associated drugs may actually be approved products. Fourteen of these twenty-five NDCs appear to be approved products because they are actually included on the drugs' approved labels; 3 additional NDCs appear to be associated with products approved by FDA; and the remaining 8 of these 25 NDCs do not have approval information in Drugs@FDA.

Twenty-six percent (7,040) of the 27,143 NDCs associated with drugs paid for by Medicaid in 2008 were not listed in the NDC Directory. More than half (3,893) of these NDCs were listed in the pending, discontinued, or biological files. The remaining 3,147 NDCs were not listed in any of these files. Therefore, FDA would be unable to determine the approval status based on the NDCs alone. Medicaid payments for these 3,147 NDCs in 2008 totaled $1.1 billion.

A manual review of 25 of the 3,147 NDCs that were not listed in the NDC Directory or the pending, discontinued, or biological files indicates that

many of these drugs may actually be approved products. Fourteen of the twenty-five unlisted NDCs that underwent manual review were included on approved labels (i.e., the FDA-approved labels for the drugs contained the NDCs under review); the remaining 11 unlisted NDCs did not appear on any approved labels. Eight of these eleven NDCs were associated with drugs that appeared in Drugs@FDA; however, the specific NDC that underwent manual review was not on the approved label.

RECOMMENDATION

Generally, covered outpatient drugs must be approved by FDA to qualify for Federal payments under Medicaid. Sixty-two percent of drugs paid for by Medicaid in 2008 had an approved application number in the NDC Directory. However, data contained in the NDC Directory were inaccurate and incomplete, thereby preventing us from determining whether FDA approved the remaining 38 percent. As a result, Medicaid could potentially pay for drugs that are not approved. This report highlights the fact that the NDC Directory cannot reliably be used to verify the approval and listing status of drugs paid for under Medicaid.

Previous OIG reports also found problems with the accuracy and completeness of the NDC Directory and recommended changes to improve the database. Given the previous recommendations and the potential impact on beneficiary health and the integrity of Medicaid payments, we continue to recommend that FDA:

Improve the completeness and accuracy of the NDC Directory

FDA could take the following steps:

- Conduct frequent reviews of its NDC Directory to ensure its completeness and accuracy.
- Work with the Centers for Medicare & Medicaid Services (CMS) and Congress to seek a legislative or regulatory change that compels manufacturers to list all approved products with FDA before the products become eligible for Medicaid payment. By making payment under Medicaid contingent upon listing, manufacturers would have an increased incentive to ensure that FDA had the most complete and timely information on the products in the NDC Directory.

AGENCY COMMENTS AND OFFICE OF INSPECTOR GENERAL RESPONSE

In its comments on our draft report, FDA generally agreed with OIG's recommendation to improve the completeness and accuracy of the NDC Directory. FDA stated that it recognizes that data quality has suffered in the past, agrees that the accuracy and completeness of data in the NDC Directory are imperfect, and remains committed to robust quality improvements. FDA noted that it has already begun implementing several initiatives for evaluating and enhancing the quality of drug-listing data.

FDA has agreed that it should work with CMS to examine changes that could further strengthen CMS's ability to ensure that drugs are listed with FDA prior to reimbursement. FDA stated that it was pleased that OIG, by encouraging collaboration, recognized that both FDA and CMS have a role in identifying drug products potentially eligible for CMS payments.

FDA stated that it is important to note some data limitations to ensure that OIG's findings are not misunderstood. Specifically, FDA pointed out that OIG's manual review examined a small sample of NDCs, that most inaccuracies did not result in improper Medicaid payments, and that the NDC Directory is now more complete and accurate.

OIG acknowledges that our manual review examined only a small number of high-dollar NDCs and that the results from this portion of the analysis cannot be projected to the entire universe of NDCs under review. Although the analysis did not determine whether there were improper Medicaid payments, it did highlight the incomplete and inaccurate nature of the NDC Directory and the subsequent vulnerability for the Medicaid program. Finally, our results reflect the state of the NDC Directory at the time of the review and show that in 2008, the NDC Directory did not contain approval or listing information for nearly 40 percent of NDCs paid under Medicaid.

In its comments on our draft report, CMS deferred to FDA regarding the response to OIG's recommendation and stated that it will continue to work with FDA on issues related to drug approval and Medicaid reimbursement.

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INTRODUCTION

OBJECTIVE

To determine the Food and Drug Administration's (FDA) approval status of drugs paid for by Medicaid in 2008.

BACKGROUND

Before a new drug may be legally marketed in the United States, it must be approved by FDA for safety and effectiveness. According to FDA, drugs lacking this approval may pose a significant public health concern because they may not meet FDA standards for safety, effectiveness, quality, and labeling.[1] FDA tracks drug approvals using various databases, but acknowledges that certain of these databases may be inaccurate and incomplete.[2] Previous Office of Inspector General (OIG) reports found problems with the accuracy and completeness of FDA's drug listing directory, identified factors that contributed to missing or obsolete drug listings, and recommended changes to improve the database.[3]

To qualify for Federal payments under Medicaid, drugs generally must be approved by FDA, with certain exceptions.[4] In a 2008 letter to OIG, a member of Congress expressed concern that Medicaid pays for drugs that do not meet this criterion and requested that OIG examine the FDA approval status of drugs paid for by Medicaid.

FDA Approval and Listing Requirements

FDA approval. Section 505(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) prohibits new drugs without FDA approval from being introduced into interstate commerce.[5] As part of FDA's responsibility to protect public health, the agency evaluates new drugs based on

[1] FDA, *FDA's Concerns About Unapproved Drugs.* Accessed at http://www.fda.gov on November 9, 2009.

[2] FDA's Response to Representative Edward J. Markey. Accessed at http://www.ascp.com on February 18, 2010.

[3] OIG, *The Food and Drug Administration's National Drug Code Directory*, OEI-06-05-00060, August 2006; and *The FDA Prescription Drug File,* OEI-03-90-02300, November 1991.

[4] An example of an exception would be a drug for which the Secretary of Health & Human Services (Secretary) had determined that there was a compelling justification for its medical need and for which a proposed order to withdraw approval had not been issued.

[5] Pursuant to section 201(b) of the FD&C Act, the circumstances that generally place a product in interstate commerce are commerce between any State or territory and any place outside thereof or commerce within the District of Columbia.

scientific evidence obtained from clinical studies and other research conducted by a drug's sponsor, typically a pharmaceutical company. The sponsor of an innovator (i.e., not generic) drug submits this information to FDA in a new drug application (NDA) (or supplemental NDA, if the sponsor is seeking approval for a new use for the drug), which the agency reviews to assess the drug's safety and effectiveness for the proposed use. Similarly, the sponsor of a new generic drug submits an abbreviated new drug application (ANDA) to demonstrate that the drug is bioequivalent to an approved drug. Based on the application review, FDA determines whether the drug can be approved to be marketed in the United States. Upon approval, the sponsor receives a letter from FDA with the agency's approval as well as the approved NDA or ANDA number.[6]

FDA listing requirements. Section 510(b) of the FD&C Act requires firms (e.g., manufacturers) engaged in manufacturing, preparation, propagation, compounding, or processing drugs to register with the Secretary.[7] In addition, section 510(j) of the FD&C Act requires these firms to list with the Secretary (i.e., report) all of the drugs they produce for commercial distribution. These firms fulfill this requirement by providing drug-listing information to FDA.[8]

Firms report drug information using national drug codes (NDC). Each listed drug product is assigned a unique 11-digit, 3-segment NDC consisting of labeler, product, and package code segments.[9] The first segment (the labeler code) identifies the firm that labels the drug and is assigned by FDA. The second segment (the product code) identifies the drug formulation, and the third segment (the package code) identifies the package size. The product and package segments are assigned by

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[6] According to a section of FDA's Web site entitled *How Drugs are Developed and Approved*, new drugs, like other new products, are frequently under patent protection during development. The patent protects the sponsor's investment in the drug's development by giving it the sole right to sell the drug while the patent is in effect. Additionally, under certain circumstances, sponsors may receive a certain period of marketing exclusivity when their drugs are approved. When a patent and exclusivity on brand-name drugs expires or has been successfully challenged, other firms can obtain FDA approval of an ANDA to sell generic versions of the drug.

[7] Pursuant to 21 CFR § 207.21(a), firms first entering into the production of drugs must register within 5 days after beginning operations.

[8] Firms that distribute drugs produced by another firm under their own label may opt to submit listing information to FDA. See 21 CFR § 207.20(b).

[9] A complete NDC may be 10 or 11 digits. Databases that list NDCs typically convert 10-digit NDCs to 11-digit NDCs. See 21 CFR 207.35(b)(2).

the firms.[10] Each June and December, firms are required to report updated lists of their drugs, including certain information, such as newly introduced drugs, discontinued drugs, and material changes to other listing information previously submitted.[11] As a result of these reporting timeframes, there is up to a two-quarter lag between the time a drug enters the market and the time it is required to be listed with FDA. During this period, FDA may not have any record of the drug.

The system FDA uses to collect and maintain drug-listing information from labelers is known as the Drug Registration and Listing System (DRLS).[12] A drug product and its associated NDC may reside in one of the following databases within DRLS:

- The DRLS Listings Table—includes drug products (including prescription drugs as well as foreign and some domestic over-the-counter products), insulin, and certain biologics that are currently marketed and that have been successfully listed with FDA; this file is the source of the NDC Directory (described below) and includes approved NDA and ANDA numbers for each drug, where applicable.
- The DRLS Discontinued Drug File—includes discontinued drug products that were listed with FDA but are no longer on the market (as reported by labelers).
- The DRLS Pending Drug File—includes drug products for which the listing process has begun but is not complete.

None of these databases is publicly accessible. However, the NDC Directory, created from the DRLS Listed Drug File, is available for download from FDA's Web site.[13] 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. This database contains the

[10] 21 CFR § 207.35(b)(2)(ii).

[11] 21 CFR §§ 207.21(b) and 207.30 and section 510(j)(2) of the FD&C Act.

[12] According to FDA, the agency no longer accepts paper submissions for registration (unless a waiver is granted) and has transitioned to the electronic DRLS effective June 1, 2009. Further, FDA states that electronic submissions have enabled it to implement fully automated validations for select data elements as well as allowed firms to voluntarily update their drug listing more often.

[13] The NDC Directory is available online at http://www.fda.gov.

NDC, approved application number, and drug product information for each drug listed.[14]

FDA has additional databases containing approval information. One of these contains data on biological products (such as vaccines and blood, among others,[15] used in the prevention, treatment, or cure of a disease or condition).[16] In addition, the FDA Approved Drug Products directory (Drugs@FDA) is a publicly available FDA database that provides each drug's approval history, including the FDA-approved label, and states whether it was approved under an NDA or ANDA; however, it does not list any of this information by NDC.[17]

Medicaid Prescription Drug Coverage

Title XIX of the Social Security Act (the Act) established the Medicaid program to pay for medical and health-related assistance for certain vulnerable and needy individuals and families. This program is administered by States and financed with State and Federal funds. Individual States establish eligibility requirements, benefit packages, and payment rates for their Medicaid programs under broad Federal standards administered by the Centers for Medicare & Medicaid Services (CMS). Currently, all 50 States and the District of Columbia provide coverage for prescription drugs under the Medicaid program. In 2008, Medicaid expenditures for prescription drugs totaled approximately $24 billion.[18, 19]

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[14] According to FDA, NDC Directory updates are published online twice monthly.

[15] According to FDA, biological products are viruses, therapeutic sera, toxins, antitoxins, vaccines, blood, blood components or derivatives, allergenic products, proteins (except for any chemically synthesized polypeptides), or analogous products, or arsphenamine or derivatives of arsphenamine (or any other trivalent organic arsenic compound) applicable to the prevention, treatment, or cure of a disease or condition of human beings.

[16] Some biological products are also included in the NDC Directory.

[17] FDA, *Drugs@FDA: Frequently Asked Questions*. Accessed at http://www.fda.gov on November 9, 2009. Drugs@FDA is searchable by drug name. The Web site contains each drug's FDA-approved label, which is the official description of a drug product found inside drug packaging that includes indications for which the drug is approved, states who should take it, lists NDCs associated with the approval, lists adverse side effects, and provides other safety information. According to FDA, for some older drugs that have not had labeling supplements approved in recent years, the labeling may not in fact be on Drugs@FDA.

[18] For this report, our discussion of Medicaid payments and rebates refers only to fee-for-service Medicaid and does not include managed care.

[19] This amount was calculated using national summary data for 2008 and includes Federal and State payments. Rebates collected by States under the Medicaid drug rebate program (MDRP) were not subtracted from this figure.

Medicaid Drug Rebate Program

For Federal payment to be available for covered outpatient drugs provided under the MDRP, sections 1927(a)(1) and (b)(1) of the Act mandate that drug manufacturers enter into rebate agreements with the Secretary and pay quarterly rebates to State Medicaid agencies. Generally, covered outpatient drugs must be approved by FDA, with certain exceptions, to qualify for Federal payment. Covered outpatient drugs are defined by section 1927(k)(2) of the Act as those drugs which are treated as prescribed drugs under section 1905(a)(12) and which are:

- approved for safety and effectiveness as prescription drugs under sections 505 or 507 of the FD&C Act,
- commercially used or sold in the United States before the date of enactment of the Drug Amendments of 1962 and which have not been the subject of a final determination by the Secretary, or
- described in section 107(c)(3) of the Drug Amendments of 1962 and for which the Secretary has determined that there is a compelling justification for their medical need and for which a proposed order to withdraw approval has not been issued.[20]

When a drug manufacturer initially seeks to enter into a rebate agreement with the Secretary, the manufacturer must provide its FDA-assigned labeler code (i.e., the first segment of the NDC) and a complete list of NDCs for drugs marketed by the company. CMS compares this information to information that the manufacturer provides to FDA (e.g., data in the NDC Directory) to determine whether each drug meets the definition of a covered outpatient drug under the MDRP.[21] Therefore, inaccuracies in FDA's databases could make it difficult for CMS to determine whether drugs should be paid for under the MDRP.

Once a manufacturer gains entry into the MDRP, all of its drugs are subsequently covered under the rebate agreement. New drugs from manufacturers with existing rebate agreements are automatically paid for under the MDRP (i.e., the manufacturer does not need to go through an additional approval process). To verify the coverage status of these

[20] Covered outpatient drugs can also refer to certain biological and insulin products.

[21] CMS, *National Drug Rebate Agreement*. Accessed at http://www.cms.hhs.gov on November 9, 2009.

new drugs, CMS compiles a list of their associated NDCs twice yearly. CMS provides this list to FDA to determine the drugs' rebate eligibility and to determine whether they meet the definition of a covered outpatient drug (i.e., they are approved by FDA).

Drugs Without FDA Approval

According to FDA and CMS, there is no complete list of drugs that do not have FDA approval. FDA relies on DRLS databases (including the NDC Directory), which the agency acknowledges may be incomplete and inaccurate, to determine whether a drug is approved.[22, 23] According to FDA, one reason that the NDC Directory component of DRLS is neither fully accurate nor complete is that drug manufacturers do not always submit the required information.[24] In addition, the presence of an NDC in the NDC Directory does not denote approval.[25]

Congressional Interest in Drugs Without FDA Approval

In a letter sent to CMS and FDA,[26] a member of Congress expressed concern that Medicaid is being billed inappropriately for unapproved drugs. In response, CMS began conducting research on the approval status of certain drugs to determine whether they are eligible for payment under the MDRP. As a result of this effort, CMS has identified products[27] that do not meet the definition of a covered outpatient drug (e.g., drugs that are not approved by FDA) and removed them from the MDRP. In addition, FDA published a compliance policy guide in 2006 to explain how it intends to exercise its enforcement discretion with regard to drugs without approval.[28] According to FDA, this compliance policy

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[22] FDA's Response to Representative Edward J. Markey. Accessed at http://www.ascp.com on February 18, 2010. OIG, *The Food and Drug Administration's National Drug Code Directory,* OEI-06-05-00060, August 2006.

[23] According to FDA, the agency has implemented a pilot program and other data validations to examine the quality of data in the NDC Directory and compare these data to commercial databases.

[24] FDA's Response to Representative Edward J. Markey. Accessed at http://www.ascp.com on February 18, 2010.

[25] 21 CFR § 207.39.

[26] Senator Charles Grassley. *Grassley Questions Government Response to the Marketing and Use of Unapproved Drugs.* Accessed at http://www.grassley.senate.gov on November 10, 2009.

[27] For example, in 2009, CMS sent letters to State Medicaid agencies and the manufacturers of sodium hyaluronate and ergotamine informing them that the agency was removing specific NDCs from the MDRP because these drugs did not meet the definition of a covered outpatient drug, i.e., they did not have the appropriate FDA approval status.

[28] FDA, *Marketed Unapproved Drugs – Compliance Policy Guide,* § 440.100. Accessed at http://www.fda.gov on November 9, 2009.

guide emphasizes that illegally marketed drugs must receive FDA approval.[29] Finally, as previously mentioned, a member of Congress requested that OIG examine the FDA approval status of drugs paid for by Medicaid.

Related OIG Work

Previous OIG reports examined the completeness and accuracy of FDA's NDC Directory and identified factors that contribute to missing or obsolete product listings.[30, 31] The most recent report (August 2006) found that the NDC Directory was incomplete (primarily because of insufficient reporting by drug manufacturers) and inaccurate (because it included drugs that were no longer on the market or were listed in error). The report also found that FDA's lack of oversight contributed to inaccurate and incomplete information in its NDC Directory.

Another recent OIG report found that there was a potential problem with Medicaid payment for drugs that do not have FDA approval.[32] The report's objective focused on the accuracy of drug categorizations for Medicaid rebates. However, a manual review of 75 NDCs with questionable drug categorizations revealed that over 40 percent were associated with unapproved drugs. Based on the findings of that report, OIG recommended that CMS work closely with FDA to identify drugs not approved by FDA for safety and effectiveness. In its response, CMS stated that it has worked and will continue to work closely with FDA to identify payments for drugs not meeting the definition of a covered outpatient drug.

METHODOLOGY

Scope

This review determined the approval status of drugs paid for by Medicaid in 2008. We examined only fee-for-service Medicaid payments for prescription drugs in the MDRP, i.e., we excluded Medicaid managed care and over-the-counter drugs from this analysis. Further, we

[29] In general, FDA has used a risk-based enforcement approach to marketed unapproved drugs that includes efforts to identify illegally marketed drugs, prioritization of those drugs according to potential public health concerns, and regulatory followup.

[30] OIG, *The Food and Drug Administration's National Drug Code Directory,* OEI-06-05-00060, August 2006.

[31] OIG, *The FDA Prescription Drug File*, OEI-03-90-02300, November 1991.

[32] OIG, *Accuracy of Drug Categorizations for Medicaid Rebates*, OEI-03-08-00300, July 2009.

examined only approval status according to information available in the NDC Directory and Drugs@FDA.

Data Sources

We reviewed relevant laws, guidelines, regulations, and policies to obtain information about procedures related to the approval status of and payment for drugs in the MDRP.

CMS data. We obtained 2008 State utilization files for the MDRP from CMS's Web site in June 2009.[33] Using these files, we obtained Medicaid expenditures and utilization data for 27,143 prescription drug NDCs in 2008. Medicaid payment for these NDCs totaled $23.8 billion. See Appendix A for a more detailed description of the data collection and analysis.

FDA data. We downloaded FDA's NDC Directory (i.e., the publicly accessible file created from the DRLS Listed Drug File) in August 2009. The file was updated on July 31, 2009, and contains the name, NDC, and the approved application number (assigned by FDA) for each listed drug. A number in the approved application number field signifies that the product has been approved by FDA for marketing based upon a review of its safety and effectiveness. An "other" in this field signifies that listing information for the product did not include an approved application number; this product may not have been approved for safety and efficacy by FDA; or the data may have been omitted.[34]

We also obtained the pending and discontinued files from DRLS, as well as a file containing biological products from FDA, in June 2009.[35] These files contain the drug names, NDCs, and associated labelers/manufacturers. We also downloaded two lists of approved biological products from FDA's Web site. The lists contained the names and approved application numbers for certain biological products.[36] We also used FDA's online searchable database Drugs@FDA during our

[33] These files were downloaded from http://www.cms.hhs.gov in June 2009 and contain State-reported expenditure and utilization data by NDC. These data are not validated by CMS.

[34] During the period covered by this review, the application number for biologics was identified as "other" in the NDC Directory. However, these products are now identified as biological licensing agreement (BLA), according to FDA.

[35] The NDC Directory used for this review was updated in July 2009. The pending, discontinued, and biological files from FDA were updated in May 2009.

[36] FDA approves biologics with BLAs. Many approved biologics are considered covered outpatient drugs under Medicaid.

manual review. The database contains a drug's approval status and history, is organized by product name, and is not searchable by NDC.

Data Analysis

NDC approval and listing. We matched the 27,143 NDCs listed in the aggregated 2008 State Medicaid utilization file against FDA's NDC Directory to identify the number of NDCs reimbursed under the MDRP that (1) had an approved application number in the NDC Directory, (2) were listed in the NDC Directory but did not have an approved application number, and (3) were not listed in the NDC Directory at all. NDCs listed in the Directory without an approved application number generally had an application number of "other" indicating that the drug is not approved by FDA, may be subject to an efficacy and safety review, and/or may be one for which FDA lacks sufficient data.

We also determined how many NDCs for which the application number was "other" were listed in the DRLS pending or discontinued files or FDA's biological file or were associated with drugs on FDA's approved biological products lists.[37] For NDCs not listed in the NDC Directory, we determined how many were listed in the DRLS pending and discontinued files or FDA's biological file.

Manual reviews. We conducted two manual reviews: one for NDCs with an application code of "other" and one for NDCs that were not listed in the NDC Directory or other DRLS files. From the group of NDCs that had an application code of "other" and were not included in the other FDA files under review, we selected the 25 associated with the highest Medicaid expenditures for a manual review. We reviewed the approval status and history on these drugs using Drugs@FDA to identify possible reasons for their lack of approval or determine whether they were misclassified by FDA.

We conducted a similar manual review of the 25 NDCs with the highest Medicaid reimbursement that were not listed in the NDC Directory or other DRLS files. We reviewed available drug product information in Drugs@FDA to identify the characteristics of these drugs and determine whether they were included in this database.

[37] FDA's biological file lists products by NDC. In addition to identifying this database, we identified two lists of approved biological products. FDA's lists of approved biological products contain the biological product names and approved BLAs; they do not include NDCs. For this analysis, we identified all NDCs that had an approval code of "other" that were associated with drug names on one of these lists.

Limitations

We did not verify the accuracy of CMS's Medicaid utilization data or any of FDA's files (i.e., DRLS files, biological files, lists of approved biological products). The results of this review reflect the status of FDA's databases at the time they were updated (i.e., July 2009 for the NDC Directory and May 2009 for the pending, discontinued, and biological files). The results of the manual review (which examined only a small number of high-expenditure NDCs) cannot be projected to the entire universe of NDCs.

This review identifies the number of drugs that did not have an approved application number in the NDC Directory; it does not determine the appropriateness of Medicaid payment for these drugs. Additionally, we did not verify that the drugs with approved application numbers listed in the NDC Directory had actually been approved by FDA.

Standards

This study was conducted in accordance with the *Quality Standards for Inspections* approved by the Council of the Inspectors General on Integrity and Efficiency.

FINDING

Sixty-two percent of drugs paid for by Medicaid in 2008 had an approved application number in the NDC Directory; the remaining 38 percent either did not have an approved application number listed or were not in the NDC Directory at all

In 2008, Medicaid paid for prescription drugs associated with 27,143 NDCs (numeric drug identifiers) under the MDRP. The NDC Directory listed approved application numbers for 16,945 (62 percent) of these NDCs. Medicaid payment for these NDCs totaled $17.8 billion, or 75 percent of 2008 MDRP expenditures for prescription drugs. The remaining 38 percent were (1) listed in the NDC Directory but did not have an approved application number or (2) not listed in the NDC Directory at all. See Table 1 for additional information on drugs paid for by Medicaid.

Table 1. Approval and Listing Status of NDCs Paid for by Medicaid in 2008

Approval and Listing Status in NDC Directory		Number of NDCs	Medicaid Payment Amount
Listed in NDC Directory	Application number is an approved new drug application or abbreviated new drug application.	16,945	$17,808,828,801
	Application number is "other"—NDC is not found in DRLS pending file, discontinued file, FDA biological file, or list of approved biological products.	2,426	$803,201,005
	Application number is "other"—NDC is in DRLS pending file, discontinued file, FDA biological file or NDC is associated with drugs on FDA list of approved biological products.[38]	380	$1,542,121,481
	Application number is blank or approval status cannot be determined.	352	$924,301,493
Not Listed in NDC Directory	NDC is not listed in NDC Directory but is included in the DRLS pending file, discontinued file, or FDA biological file.	3,893	$1,564,048,798
	NDC is not listed in the NDC Directory, DRLS pending file, discontinued file, or FDA biological file.	3,147	$1,117,824,229
Total		**27,143**	**$23,760,325,807**

Source: OIG analysis of Medicaid utilization data, FDA DRLS databases, and biological files.
Note: Totals may not add up because of rounding.

[38] Twenty of these NDCs were in the pending file, 21 were in the discontinued file, and 339 were in the biological file or were associated with approved biological products.

Twelve percent of drugs paid for by Medicaid were listed in the NDC Directory but did not include an approved application number

In 2008, Medicaid paid for 3,158 NDCs (12 percent of NDCs under review) that were listed in the NDC Directory but did not have an approved application number (i.e., the approved application number was "other," was blank, or could not be determined). Medicaid payments for these drugs totaled $3.3 billion (14 percent of Medicaid expenditures for prescription drugs) in 2008.

More than three-quarters of these NDCs (2,426) had "other" listed in the approved application number field in the NDC Directory and were not included in the other FDA databases. These NDCs did not appear in the pending, discontinued, or biological files or were not associated with drugs that were on FDA's list of approved biological products. Medicaid payments for drugs associated with these 2,426 NDCs totaled $803 million in 2008.

Each of the remaining 732 NDCs had (1) an application number of "other" but was included in one of FDA's other databases, (2) an approval status that was blank, or (3) an approval status that could not be determined.

The majority of these NDCs that underwent a manual review appear to be associated with approved application numbers. A manual review of 25 of the 2,426 NDCs that were listed as "other" (and that were not included in the other FDA databases) indicates that 14 appear to be approved products. Searching Drugs@FDA revealed that although the application numbers for these 14 NDCs were "other" on the NDC Directory, they were included on the drugs' approved labels and appear to be approved products. The information in the NDC Directory was likely inaccurate as it did not contain the appropriate approval information found in another FDA database.

Three additional NDCs in this manual review appear to be associated with products approved by FDA. However, FDA's databases did not contain enough information to verify approval. Two of these NDCs are associated with approved products; however, the specific NDCs are not on the approved labels. For the other NDC, Drugs@FDA contains an approved application number; however, there is no labeling information to verify the approval for the particular NDC.

The remaining eight NDCs do not have any approval information available on Drugs@FDA, meaning the drugs potentially do not have FDA approval. Based on information obtained from manufacturer

Web sites, these drugs were enzyme replacement products, cough suppressants, antihistamines, and pain relievers.

Twenty-six percent of drugs paid for by Medicaid were not listed in the NDC Directory; however, more than half of these drugs were listed in other FDA databases

Over one quarter (7,040) of the 27,143 NDCs associated with drugs paid for by Medicaid in 2008 were not listed in the NDC Directory. Medicaid expenditures for these drugs totaled $2.7 billion (11 percent of Medicaid prescription drug expenditures) in 2008.

More than half (3,893) of these NDCs were listed in the pending, discontinued, or biological files. The remaining 3,147 NDCs were not listed in any of these databases. Therefore, FDA would be unable to determine their approval status based on the NDCs alone. Medicaid payments for these 3,147 NDCs in 2008 totaled $1.1 billion.

The majority of NDCs that underwent a manual review appear to be associated with approved application numbers. A manual review of 25 of the 3,147 NDCs that were not listed in the NDC Directory or the pending, discontinued, or biological files indicates that many of these drugs may actually be approved products, further illustrating the incomplete nature of the NDC Directory.

According to Drugs@FDA, 14 of the 25 unlisted NDCs that underwent manual review were included on approved labels (i.e., the FDA-approved labels for the drugs contained the NDCs under review). These 14 drugs were associated with approved drug applications, even though they are not listed in the NDC Directory. For 8 of the 11 remaining NDCs, the associated drug name appeared in Drugs@FDA but the specific NDC that underwent manual review was not included on the approved label (i.e., the drug itself is approved by FDA, but the specific NDC under review is not included on the approved label).

RECOMMENDATION

Generally, covered outpatient drugs must be approved by FDA to qualify for Federal payments under Medicaid. Sixty-two percent of drugs paid for by Medicaid in 2008 had an approved application number in the NDC Directory. However, data contained in the NDC Directory were inaccurate and incomplete, thereby preventing us from determining whether FDA approved the remaining 38 percent. Twelve percent of NDCs under review did not have an approved application number listed in the NDC Directory, and an additional 26 percent were not listed in the NDC Directory at all. As a result of this inaccurate and incomplete information, Medicaid could potentially pay for drugs that are not approved. Without accurate approval and listing information, it is impossible to determine whether these drugs were appropriately paid for under the MDRP.

This report highlights the fact that the NDC Directory cannot reliably be used to verify the approval and listing status of drugs paid for under the MDRP. Previous OIG reports also found problems with the accuracy and completeness of the NDC Directory and recommended changes to improve the database. Given the previous recommendations, the potential impact on beneficiary health and the integrity of Medicaid payments, we continue to recommend that FDA:

Improve the completeness and accuracy of the NDC Directory

FDA could take the following steps:

- **Conduct frequent reviews of its NDC Directory to ensure its completeness and accuracy**
  According to FDA, the agency does not verify manufacturer data and does not follow up with manufacturers that do not list their data. FDA could routinely review all listed NDCs that do not have an approved application number to identify drugs that may be approved but just missing approval data. FDA could use the NDC Directory in conjunction with its other databases (e.g., Drugs@FDA) to identify the approval and listing status of certain drugs. Further, FDA could use some of its other databases as well as national compendia to acquire readily accessible drug product data.

- **Work with CMS and Congress to seek a legislative or regulatory change that compels manufacturers to list all approved products with FDA before the products become eligible for Medicaid payment**
  A legislative or regulatory change requiring manufacturers to list all approved products with FDA prior to being accepted into the

MDRP would reduce Medicaid payment for drugs lacking FDA approval. By making payment under MDRP contingent upon listing, manufacturers would have an increased incentive to ensure that FDA has the most complete and timely information on the products in the NDC Directory.

AGENCY COMMENTS AND OFFICE OF INSPECTOR GENERAL RESPONSE

In its comments on our draft report, FDA generally agreed with OIG's recommendation to improve the completeness and accuracy of the NDC Directory. FDA stated that it recognizes that data quality has suffered in the past, agrees that the accuracy and completeness of data in the NDC Directory are imperfect, and remains committed to robust quality improvements. FDA noted that it has already begun implementing several initiatives for evaluating and enhancing the quality of drug-listing data.

FDA has agreed that it should work with CMS to examine changes that could further strengthen CMS's ability to ensure that drugs are listed with FDA prior to reimbursement. FDA stated that it was pleased that OIG, by encouraging collaboration, recognized that both FDA and CMS have a role in identifying drug products potentially eligible for CMS payments. FDA then cited its collaboration with CMS on several related measures, including developing a list of drugs that are not properly listed with FDA and identifying the regulatory status of listed drug products. In addition, FDA stated that it will identify new approaches it and CMS may use to reduce inappropriate reimbursement for drugs under Medicaid.

FDA also stated that it is crucial to recognize that its efforts to enhance data quality remain limited by certain regulatory constraints, e.g., product-listing changes are required to be reported to FDA only twice yearly, which means listed information can quickly become inaccurate unless manufacturers voluntarily provide more frequent updates. To that end, FDA noted that it has implemented an electronic reporting system for drug product information that may encourage manufacturers to update their listings more frequently. FDA stated that clarifying its authority to remove listings that are incorrect or out-of-date would give it an efficient, powerful tool for prompting compliance and correcting errors or omissions.

Additionally, FDA stated that it is important to note some data limitations to ensure that OIG's findings are not misunderstood. Specifically, FDA pointed out that OIG's manual review examined a small sample of NDCs, that most inaccuracies did not result in improper Medicaid payments, and that the NDC Directory is now more complete and accurate than at the time of OIG's review.

OIG acknowledges that our manual review examined only a small number of NDCs and that the results from this portion of the analysis cannot be projected to the entire universe of NDCs under review. Given the time-intensive nature of these manual reviews, we focused on a purposive sample of NDCs associated with the highest Medicaid expenditures. Additionally, although the analysis did not determine whether there were improper Medicaid payments, it did highlight the incomplete and inaccurate nature of the NDC Directory and the subsequent vulnerability for the Medicaid program. As outlined in the limitations on page 10, we acknowledge that the NDC Directory undergoes frequent updates and that it may thus become more complete and accurate over time. However, our results reflect the state of the NDC Directory at the time of the review and show that in 2008 the NDC Directory did not contain approval or listing information for nearly 40 percent of NDCs paid under Medicaid. FDA's comments are provided in Appendix B.

In its comments on our draft report, CMS deferred to FDA regarding the response to OIG's recommendation and stated that it will continue to work with FDA on issues related to drug approval and Medicaid reimbursement. CMS's comments are provided in Appendix C.

Detailed Methodology

Redbook. Redbook is a national drug compendium published by a private company (Thomson Healthcare) using data from such sources as drug manufacturers and the Food and Drug Administration (FDA).[39] National drug compendia provide access to drug-pricing and drug product data. We obtained drug product and classification data from the first-quarter 2009 edition of Redbook.

Centers for Medicare & Medicaid Services data. We downloaded 2008 State Medicaid utilization data from the Centers for Medicare & Medicaid Services' (CMS) Web site in June 2009. This file contains 36,767 national drug codes (NDC) representing total Medicaid expenditures and utilization by NDC for 47 States in 2008.[40] Based on CMS's recommendation, this review included only prescription drugs. We used drug product data from Redbook to exclude all nonprescription NDCs (i.e., over-the-counter drugs). NDCs for which there was no drug product data in Redbook were excluded from our analysis. As a result, there were 27,143 NDCs for prescription drugs associated with Medicaid payment in 2008. Medicaid payment for these NDCs totaled $23.8 billion in 2008. See Table A-1 for a detailed description of Medicaid utilization data.

Table A-1. 2008 Medicaid Utilization Data

Category	Number of NDCs	Medicaid Expenditures
NDCs in State Medicaid utilization files	36,767	$24,133,357,264
NDCs in State Medicaid utilization files and with Redbook drug product data	32,701	$24,070,132,410
NDCs in Medicaid utilization files identified by Redbook as prescription drugs	27,143	$23,760,325,807

Source: Office of Inspector General analysis of 2008 State Medicaid utilization data.

FDA data. We downloaded FDA's NDC Directory in August 2009. This version of the database was updated as of July 31, 2009. The NDC Directory contains over 159,000 unique NDCs. FDA staff also provided

[39] Publishers of compendia do not perform formal data reviews for every new release. Further, Redbook is not limited to products with FDA's approval.

[40] The remaining four States were not included in this analysis because they did not have any utilization data available on CMS's Web site at the time of download or did not participate in the Medicaid drug rebate program.

the pending file and discontinued file as well as a database containing biological products.

APPENDIX ~ B

Food and Drug Administration Comments

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

DATE: August 2, 2010

TO: Deputy Inspector General

FROM: Principal Deputy Commissioner of Food and Drugs

SUBJECT: FDA's General Comments to OIG's Draft Report entitled, *FDA's Approval Status of Drugs Paid for by Medicaid,* OEI-03-08-00500

FDA is providing the attached general and technical comments to the Office of Inspector General's draft report entitled: *FDA's Approval Status of Drugs Paid for by Medicaid,* OEI-03-08-00500.

FDA appreciates the opportunity to review and comment on this draft report before it is published.

/S/

Joshua M. Sharfstein, M.D.
Principal Deputy Commissioner of Food and Drugs

Attachment

FDA's General Comments to OIG's Draft Report entitled, *FDA's Approval Status of Drugs Paid for by Medicaid*, OEI-03-08-00500

In general, FDA agrees with the recommendations found in OIG's draft report entitled, *FDA's Approval Status of Drugs Paid for by Medicaid* (OEI-03-08-00500). The National Drug Code (NDC) Directory, and more broadly the Drug Registration and Listing System (DRLS), are key repositories for information central to important governmental oversight functions. FDA recognizes that data quality has suffered in the past, agrees that the accuracy and completeness of data in the NDC Directory is imperfect, and remains committed to robust quality improvements.

FDA has already implemented several initiatives to enhance data quality, including efforts since the periods represented in the Medicaid and NDC data sampled for this OIG report. For example:

- FDA has implemented an electronic system for firms to submit drug product listings to FDA using the structured product label (SPL) submission process. This system enables processing efficiencies that may encourage firms to voluntarily update their listing more frequently than the twice-yearly requirement under current law. When fully implemented, the system will also enable FDA to rely more on faster, automated processes for identifying and correcting listing errors or omissions.

- FDA publishes NDC Directory updates to the internet *twice* monthly. The increased publication rate decreases the gap for products in "pending" status, ultimately contributing to reducing uncertainty in CMS decision-making about listing status.

- FDA identified biologic products, for which application status was previously identified as "Other" in the NDC Directory, as "BLA," which better clarifies their approval status.

Maintaining data quality presents a continuing challenge, especially in a dynamic industry marked by rapid change. However, FDA has made significant progress in improving data quality and will continue to explore and implement additional strategies to enhance the completeness and accuracy of the NDC Directory.

FDA is pleased that OIG, by encouraging collaboration, recognizes that FDA and CMS both have a role in identifying drug products potentially eligible for CMS payments. FDA has provided longstanding support for CMS efforts, and continues to explore opportunities for cooperation. In 2009, for example, FDA and CMS collaborated on the development of a "Non-Matched National Drug Code List," to identify prescription drugs products that are not yet properly listed with FDA. In March 2009, CMS published a final "Call Letter" guidance for organizations preparing to offer prescription drug plans under Medicare Part D explaining that proper listing of a drug product with FDA should be considered as a pre-requisite to reimbursement eligibility; in January 2010, CMS began using the Non-Matched NDC List (NML) to program its payment systems to prevent claims for NDCs on the list from being processed or paid automatically. The NML not only supports CMS in identifying drugs that might not meet the statutory criteria for a covered drug product (including unapproved drugs), but also is a means to promote FDA's maintenance of accurate drug listing data, by helping FDA

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to identify drug products not properly listed as required under section 510 of the Federal Food, Drug, and Cosmetic Act (FDCA of the Act), section 351 of the Public Health Service Act (PHS Act), and 21 CFR Part 207. It also provides strong incentive for compliance with those requirements if manufacturers want their products covered. Additional details about the Non-Matched NDC List are also available at www.cms.gov/PrescriptionDrugCovContra/03_RxContracting_FormularyGuidance.asp.

FDA also works regularly – indeed, daily – to help identify for CMS the regulatory status of drug products that are listed with FDA and submitted to the MDRP, including the following:

- Drug Efficacy Study Implementation drug products and those "identical, related, or similar" to them;
- Dietary supplements, devices, and any other non-drug products;
- Over-The-Counter drug products;
- Approval status of drug products that have provided their application number to DRLS;
- Products that are candidates for pre-1938/1962 drug product classification; and
- Products subject to FDA regulatory action.

Finally, FDA will seek to identify new approaches it and CMS may use to reduce inappropriate reimbursement for drugs under the Medicaid program.

It is important to note some data limitations, to ensure the significance or implications of OIG's findings are not misunderstood.

- Although the samples sizes OIG used are useful for describing the types of errors possible in record-level entries, they may not allow for a robust prediction of the *overall* accuracy of the data in the NDC. OIG conducted a manual review of only 25 NDCs, or 0.8 %, out of 3,147 NDCs that were not listed in the NDC Directory or other selected FDA databases. OIG also conducted a manual review of only 25 NDCs, or 1%, out of 2,426 identified in the NDC Directory with "other" in the field for application. FDA recognizes OIG's interest in focusing its manual review for this report on NDCs associated with highest Medicaid expenditures. FDA also recognizes the time-intensive nature of reviewing listings may necessitate modest samples and faces the same challenges. Small samples, however, may not be a very accurate predictor of the overall accuracy of the NDC Directory.

- Most inaccuracies OIG identified did not result in improper Medicaid payment based on lack of FDA approval. That is, OIG concludes that a majority of the NDCs identified as not listed in the NDC Directory, and a majority of those identified as "Other," actually appear to be approved products. Although any error calls into question overall data quality, FDA believes errors of the type OIG identifies are less problematic in terms of preventing improper payment by CMS or wasting of resources, because corrected data would not have affected (reduced) payments that CMS actually made. Nonetheless, FDA requested, and appreciates OIG sharing its query results with the Agency, and intends to follow-up on individual inaccuracies as needed to improve data quality.

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- FDA believes the NDC Directory is currently more complete and accurate since the time OIG sampled Medicaid data from 2008. FDA also believes that the NDC Directory data are more complete and accurate than they were in August 2009, when OIG downloaded them for the purposes of this audit. These improvements are a direct result of initiatives described above. For instance, NDC Directory data from August 2009 might not yet have reflected listings submitted during the transition to electronic listing in June 2009. They also likely did not capture increases in listing generated by the Non-Matched NDC List.

OIG Recommendation

That FDA improve the completeness and accuracy of the NDC Directory by

1. Conducting frequent reviews of its NDC Directory to ensure its completeness and accuracy.

FDA Comment

FDA generally agrees with OIG's recommendation, and is working on several different strategies for evaluating and correcting drug listing data.

- Electronic submission of drug registration and listing data has enabled FDA to implement more automated validations of all submissions for select data elements, including the application number. This automated validation means submissions with missing or incorrect approval data can be more rapidly identified and excluded from the NDC Directory until corrected. Additional automated validations are in process, and as systems and processes are refined, FDA expects continued improvements in data quality.

- The FDA/CMS collaboration to produce the Non-Matched NDC List (NML) also helps FDA identify missing data. The collaborative project has already led to removal of payment status for about 400 product-level NDCs (or about 1100 package-level NDCs). In fact, the NML was based in part on "second-source" data validation using RxNORM (on the National Library of Medicine website), which compiles information about drug products from multiple commercial and governmental drug product databases. It has also enabled FDA to identify why some data may be missing or incomplete and work toward corrections. Since the NML was posted, for instance, firms have contacted FDA to address previously incorrect or incomplete listing data, including discontinued products that are no longer marketed. It has also helped FDA identify non-drug products that should not appear in the NDC Directory, and DRLS data entry errors that can subsequently be corrected.

- FDA has proposed to update its 21 CFR Part 207 regulations. According to the proposed rule, firms would be required to submit not only updates for changes affecting an existing listing (as is currently required), but also certify that no change has occurred when that is the case. The goals of this proposal are to prompt better compliance with listing obligations, as well as provide greater confidence in the integrity of listing data that remain unchanged for long periods.

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FDA will also continue to explore the utility of second-source comparisons or other mechanisms to periodically review the accuracy of data in the NDC Directory. These undertakings, however, tend to be very resource intensive. In FDA's experience, there is not currently another uniformly "better" data set against which the Agency can reliably compare the NDC Directory, and commercial databases are often built on different data requirements and for different purposes, which means direct, 1:1 comparison of different databases is not always possible.

OIG Recommendation

2. Working with CMS and Congress to seek a legislative or regulatory change that compels manufacturers to list all approved products with FDA before the products become eligible for Medicaid coverage.

FDA Comment

FDA believes both CMS and FDA should work together to examine changes that could further strengthen CMS's ability to ensure listing with FDA prior to reimbursement; as part of this goal, expressly mandating proper listing with FDA when required by the FDCA, as a predicate to reimbursement eligibility, could be helpful. Such an obligation, however, should not be limited to "approved" drug products, and instead extend to all drugs subject to listing under the FDCA and FDA's implementing regulations to best ensure FDA has complete data needed to provide regulatory status about all drugs for which CMS may be assessing eligibility.

Both Agencies could also work together to assess the potential for achieving similar goals in the context of rebate agreements or other mechanisms even without legislative change. For instance, FDA's collaboration with CMS to develop the Non-Matched NDC List to identify unlisted products supports implementation of CMS guidance explaining that Part D sponsors should consider proper listing with FDA as a prerequisite for eligibility.

It is, however, also crucial to recognize that FDA's efforts to enhance listing data quality remain limited by certain other regulatory constraints. For example, currently section 510(j) of the Act only requires certain changes for listings of products to be reported to FDA twice per year (in June and December), which means listing information can fall quickly out of date unless firms voluntarily provide more timely updates. FDA's traditional enforcement mechanisms – such as injunction or seizure actions – are extremely resource-intensive, and for this and other reasons are impractical to rely on for promoting listing compliance on a large-scale. Clarifying FDA authority to remove from its databases those listings that are incorrect or out-of-date would give the Agency an efficient yet powerful tool for prompting compliance, and correcting errors or omissions. The quality of FDA's drug listing data might also be improved by:

- Promulgation of FDA regulations addressing the assignment and use of NDCs.
- Increasing timing and frequency of drug listing submissions, rather than once each June and December as required under current law.
- Requiring submission of additional drug listing elements to help ensure that FDA has the type of information it needs to maintain a comprehensive, accurate, up-to-date inventory

of marketed drugs and require that drug listings be submitted to FDA prior to a drug's introduction into interstate commerce.

- Providing for cancellation of establishment registrations and drug listings (removal from FDA's electronic systems), if information is not updated as required, or otherwise contains false, incomplete, or inaccurate information, and for suspension of establishment registrations and drug listings for a violation of the Act that could result in serious adverse health consequences or death to humans or animals.

Finally, FDA is concerned about marketed unapproved drugs. The challenges FDA and CMS face stem in part from provisions in current law that still theoretically allow continued marketing of, and reimbursement for certain unapproved prescription drugs. For FDA, even though "new drugs" are generally required to obtain FDA approval prior to marketing, there is a limited definitional exclusion if a drug is "generally recognized as safe and effective," and narrow "grandfather" exemptions for older drugs. Although FDA believes it is unlikely that any currently marketed prescription drugs are actually entitled to "grandfather" status or otherwise not new drugs, it is theoretically possible. (More information is available at www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsonUnapprovedDrugs/default.htm). This also means that approval cannot be a prerequisite for drug listing and FDA can not reject a listing submission simply because it lacks an approved application number. For CMS, the definition of a "covered outpatient drug" also allows for reimbursement of certain unapproved drugs and even differs from the FDCA in ways that allow for CMS reimbursement of drugs that could be unlawfully marketed unapproved drugs under the FDCA. As one example, the category of "pre-1962" drugs eligible for coverage under the Social Security Act (SSA) is broader than the potential pool of "pre-1962" drugs that might be lawfully exempt from FDA's new drug approval requirements under the FDCA. Improving consistency between FDA approval requirements and CMS reimbursement criteria would strengthen the Agency's ability to address a variety of issues relating to marketed unapproved drugs, including drug listing data quality.

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APPENDIX C

Centers for Medicare & Medicaid Services Comments

DEPARTMENT OF HEALTH & HUMAN SERVICES

Centers for Medicare & Medicaid Services

Administrator
Washington, DC 20201

2010 AUG 27 AM 10:17

GENERAL

DATE: AUG 25 2010

TO: Daniel R. Levinson
Inspector General

/S/

FROM: Donald M. Berwick, M.D.
Administrator

SUBJECT: Office of Inspector General (OIG) Draft Report: FDA's Approval Status of Drugs Paid for by Medicaid (OEI-03-08-00500)

Thank you for the opportunity to review and comment on the OIG Draft Report entitled, "FDA's Approval Status of Drugs paid for by Medicaid" (OEI-03-08-00500). The OIG was asked to determine the Food and Drug Administration's (FDA) approval status of drugs paid for by Medicaid in 2008. The OIG found that 62 percent of drugs paid for by Medicaid in 2008 had an approved application number in the National Drug Code (NDC) Directory; the remaining 38 percent either did not have an approved application number listed or were not in the NDC Directory at all. This report highlights the fact that the NDC Directory cannot be readily used to verify the approval and listing status of drugs under the Medicaid drug rebate program. The OIG had one recommendation that we address below.

OIG Recommendation

The OIG recommends that the FDA continue to improve the completeness and accuracy of the NDC Directory. OIG suggests that the FDA could take the following steps to ensure that the NDC Directory is accurate and complete:

- Conduct frequent reviews of its NDC Directory to ensure its completeness and accuracy.
- Work with the Centers for Medicare & Medicaid Services (CMS) and Congress to seek a legislative or regulatory change that compels manufacturers to list all approved products with FDA before the products become eligible for Medicaid payment. By making payment under Medicaid contingent upon listing, manufacturers would have increased incentives to ensure that FDA has the most complete and timely information on the products in the NDC Directory.

CMS Response

CMS defers the response to this recommendation to the FDA. CMS will continue to work with the FDA on these important issues to ensure protection of Medicaid payments and beneficiaries. CMS looks forward to providing input on any legislative or regulatory change that the FDA implements in order to compel manufacturers to list all of their approved products with the FDA.

CMS thanks the OIG for the opportunity to review and comment on this draft report.

ACKNOWLEDGMENTS

This report was prepared under the direction of Robert A. Vito, Regional Inspector General for Evaluation and Inspections in the Philadelphia regional office, and David E. Tawes, Director, Prescription Drug Pricing Unit.

Edward K. Burley served as the team leader for this study. Other principal Office of Evaluation and Inspections staff from the Philadelphia regional office who contributed to the report include Roman Strakovsky; other central office staff who contributed include Kevin Manley.

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