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# Fax

**To:** Chris Sannerud **From:** Corinne P Moody

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**Phone:** (b)(6) **Date:** 05-30-14

**Re:** 2014 Quota Response **cc:** Joseph Rannazzisi

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• **Comments:**

DEPARTMENT OF HEALTH & HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION & RESEARCH

MAY 30 2014

Mr. Joseph T. Rannazzisi
Deputy Assistant Administrator
Office of Diversion Control
Drug Enforcement Administration
600 Army-Navy Drive
Arlington, Virginia 22202

Dear Mr. Rannazzisi:

This document is in response to your letter dated February 12, 2014, to the Food and Drug Administration, Center for Drug Evaluation and Research (FDA/CDER), requesting estimates of medical, scientific, and reserve stock needs for calendar years 2014 and 2015, for Schedule I and II substances, pursuant to 21 CFR Part 1303 (21 United States Code [U.S.C.] 826 and 42 U.S.C., Section 242). The Controlled Substance Staff in the Office of the Center Director, FDA/CDER, has been requested to respond.

We provide forecasts on the usage of twenty-five Schedule II substances for the years 2014 and 2015. The Schedule II substances to be evaluated in this memorandum are: alfentanil, amobarbital, amphetamine, cocaine, codeine, dihydrocodeine, diphenoxylate, fentanyl, hydrocodone, hydromorphone, lisdexamfetamine, meperidine, methadone, methamphetamine, methylphenidate, morphine, nabilone, opium, oxycodone, oxymorphone, pentobarbital, remifentanil, secobarbital, sufentanil, and tapentadol.

In general, according to the forecasted data in **Table 1**, usage for most opioids are predicted to decline in 2014 and 2015.

We also provide forecasts for the same years for ephedrine and pseudoephedrine. As in previous years, we are including the predicted usage of drug substances synthesized from the Schedule II precursor, thebaine. Production of these substances determines the quantities of thebaine produced. The drug substances derived from thebaine include naloxone and naltrexone. At the additional request of the DEA, we are providing forecasts on the usage of substances that are internationally controlled under the Psychotropic Convention. These drugs include: alprazolam, buprenorphine, clonazepam, diazepam, diethylpropion, lorazepam, midazolam, temazepam, and zolpidem.

## I. Tabular Data

The *observed* usage (purchases in kilograms) of Schedule II substances in 2011, 2012, and 2013, and percent changes based on the *observed* values from the previous year are presented in **Table 1**. *Predicted* usage (purchases in kilograms) of the Schedule II substances are also provided for 2014 and 2015. Each predicted value is an estimate

subject to variation.

The *observed* usage for 2011, 2012, and 2013, and *predicted* usage (purchases, in kilograms) for 2014 and 2015 for substances controlled under the Psychotropic Convention are provided in **Table 2**. The *observed* usage for 2011, 2012, and 2013 and *predicted* usage (purchases, in kilograms) for 2014 and 2015 for ephedrine and pseudoephedrine are provided in **Table 3.**

Among the substances requested by DEA, we are not providing forecasted usage for the following Schedule I and II substances: difenoxin, etorphine, gamma-hydroxybutyrate (GHB or sodium oxybate), levorphanol, marijuana, noroxymorphone, propiram, psilocybin, synthetic cannabinoids, synthetic cathinones, and tetrahydrocannabinols because data regarding the usage of these substances were limited or not available. Data was also unavailable for phenylpropanolamine. The Schedule IV substance clobazam was also not included in this analysis because data are only available for 2012, since the drug was approved in October 2011. There were data gaps for difenoxin and levorphanol in which no sales data were available for varying time periods.

- Comments on *Observed* usages in 2012 (See **Table 1, Table 2 and Table 3**).

In 2013, there was an increase in the *observed* usage (relative to 2012) for both hydromorphone and remifentanil. The increase is also *predicted* for 2014.

Most of the predicted usage data for drugs data received this year were similar to usage data from previous years. In contrast, alfentanil, dihydrocodeine, meperidine, methadone, nabilone, pentobarbital, and secobarbital all demonstrated a *decrease* of ≥ 10% in their observed use. Further, alfentanil, dihydrocodeine, meperidine, methadone, oxymorphone, and sufentanil are *predicted* to have a decrease of ≥ 10% in 2014. Dihydrocodeine and pentobarbital displayed relatively large decreases in both *observed* usage in 2013, and *predicted* usage in 2014.

The *observed* retail and non-retail sales values for some substances were inconsistent with previous years. This is a result of regular data corrections and updates by the IMS data investigation team. As stated in previous reports, most of these corrections were minor (e.g., ≤0.5%) and should not be an influencing factor in the current forecasting. Similar discrepancies were also noted and resolved in previous reports.

- Forecasted (*Predicted*) Increases for 2014 (See **Table 1, Table 2, and Table 3**).

The *predicted* usage of these substances does not take under consideration specific needs of some manufacturers due to recent recalls of defective products or drug shortages.

**II. Reports from FDA Office of New Drugs, Office of Generic Drugs, Center for Veterinary Drugs, and the Substance Abuse Mental Health Services Administration (SAMHSA)**

The CDER Office of New Drugs review divisions reported the approvals and pending actions of products with Schedule I and II controlled substances, as well as substances controlled under the Psychotropic Convention. The reports originate from the Division of Metabolism and Endocrinology Products (DMEP), Division of Anesthesia, Analgesia, and Addiction Products (DAAAP), Division of Psychiatry Products (DPP), Division of Neurology Products (DNP), and the Division of Pulmonary, Allergy and Rheumatology Products (DPARP). Information on drug shortages and manufacturing delays were reported by the CDER Drug Shortages Staff. The CDER Office of Generic Drugs provides listings of Schedule I and II containing products that were approved in 2013 (**Table 4**), products discontinued in 2013 (**Table 5**), and products that may be approved in 2014 (**Table 6**).

The Center for Veterinary Medicine (CVM) reports that thiopental is no longer available.

SAMHSA provides information about the usage of methadone and buprenorphine in maintenance treatment of opioid addiction. Data on the use of methadone in OTPs is not available from IMS; therefore, **Table 1** most likely refers to usage of methadone for pain treatment.

The Division of Metabolism and Endocrinology Products (DMEP) notes that they have received the resubmission of the NDA for Contrave (naltrexone + bupropion). The Sponsor currently has an ongoing trial (under IND) for this product that may affect quota demands for naltrexone.

The Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) reports the approval of NDAs or Efficacy and Manufacturing Supplements in the past year for the following substances: alfentanil, cocaine, codeine, dihydrocodeine, fentanyl, gamma-hydroxybutyrate, hydrocodone, hydromorphone, ketamine, levorphanol, meperidine, methadone, morphine, oxycodone, oxymorphone, remifentanil, sufentanil, tapentadol, tetrahydrocannabinols, tramadol, and buprenorphine.

In 2013, the Division of Psychiatry Products (DPP) approved an efficacy supplement for Vyvanse (lisdexamfetamine). DPP has pending NDAs/efficacy supplements for Amphetamine Polistirex Extended-Release Orally Disintegrating Tablets and a methylphenidate patch. DPP also expects the continued development of a new, methylphenidate transdermal patch.

DPP has also received the following INDS that may require the manufacturing of commercial-type batches of products containing the following substances: (b) (4)

(b) (4)

The Division of Neurology Products (DNP) reports the receipt of NDAs and efficacy and manufacturing supplements for the following substances in 2013: (b) (4)

(b) (4) clobazam, and zolpidem. In addition, DNP reports receiving

INDs for cannabidiol and Sativex (tetrahydrocannabinol and cannabidiol), and notes that Klonopin (clonazepam) orally disintegrating tablet will no longer be marketed. Finally, DNP reports distributing approximately (b) (4) units of GHB from July 1, 2012 through June 30, 2013 (one unit = 180 mL bottle).

The Division of Pulmonary, Allergy and Rheumatology Products (DPARP) reports the approval of an NDA for hydrocodone bitartrate and chlorpheniramine in 2013, along with INDs for the following:

- (b) (4)
- 
- 
- 

Based on increased demand, manufacturing delays, and shortages in 2013, the Drug Shortages Division predicted additional quota demands in 2014 for the following substances: alfentanil, amphetamine, fentanyl, hydromorphone, ketamine, meperidine, methadone, methamphetamine, methylphenidate, morphine, sufentanil, diazepam, lorazepam, midazolam, naloxone, naltrexone, and ephedrine.

The Center for Veterinary Medicine (CVM) reports that thiopental is no longer available as an unapproved animal drug. Veterinarians are interested in using alternative anesthetic agents.

The Substance Abuse Mental Health Services Administration (SAMHSA) reports that based on data from the National Survey of Substance Abuse Treatment Services (N-SSATS), on March 30, 2012, there were 306,512 patients that received methadone via Outpatient Treatment Programs (OTP). N-SSATS does not collect data for the number of physicians prescribing methadone.

SAMHSA also reports that according to the 2011 Opioid Treatment Survey, the most current dosage data for patients receiving methadone maintenance are as follows:

- Less than 40 mg: 26,252 patients (10.3%)
- 40-79 mg: 67,237 patients (26.3%)
- 80-119 mg: 82,519 patients (32.3%)
- 120 mg or more: 45,070 patients (17.6%)
- Unknown: 34,357 patients (13.5%)

These dosages are for patients in maintenance treatment and do not include dosages that may have been used for detoxification.

Finally, based on the 2012 N-SSATS data, there were 7,409 patients receiving buprenorphine in OTPs and an additional 31,814 patients receiving buprenorphine in specialty substance abuse treatment facilities that were not OTPs. These numbers do not include patients that received buprenorphine from office-based practicing physicians who were not attached with a specialty substance abuse treatment facility. Per the Drug Abuse Treatment Act (DATA) of 2000, these physicians have waivered authority to dispense or prescribe certain narcotic drugs for maintenance or detoxification treatment.

We hope that these data prove useful to the Drug Enforcement Administration in making

quota determinations. If you have any questions or need additional clarification, please contact Chad Reissig, Ph.D., Controlled Substance Staff, at 301-796-5402.

Sincerely,

Michael Klein, Ph.D.
Director, Controlled Substance Staff
Office of the Center Director
Center for Drug Evaluation and Research

Concur:

Douglas C. Throckmorton, M.D.
Deputy Center Director
Center for Drug Evaluation and Research

**Attachments:**

**Attachment I:** Description of Forecasting Methodology

**Table 1:** Forecast Uses (Purchases, in Kg) for 2014 and 2015, and Observed Use for 2011, 2012, and 2013 of Schedule II Controlled Substances.

**Table 2:** Forecast Uses (Purchases, in Kg) for 2014 and 2015, and Observed Use for 2011, 2012, and 2013, of substances derived from thebaine and for substances controlled under the Psychotropic Convention.

**Table 3:** Forecast Uses (Purchases in Kg) for 2014, and 2015, and Observed Use for 2011, 2012, and 2013 of the substance ephedrine and pseudoephedrine

**Table 4:** Recently Approved Generic Drug Products Containing Schedule II Controlled Substances Approved in 2013.

**Table 5:** Generic Products Containing Schedule II Controlled Substances Discontinued in 2013.

**Table 6:** Generic Drug Products Containing That May be Approved in 2014.

**Attachment I. Description of Forecasting Methodology**

Monthly purchase data comprised of retail and non-retail sales are extracted from the IMS Health, National Sales Perspectives™ database. The IMS Health, National Sales Perspectives™ database measures the volume of drug products and selected diagnostic products moving from manufacturers into various outlets within the retail and non-retail markets. The retail market includes the following pharmacy settings: chain drug stores, independent pharmacies, mass merchandisers, grocery stores, and mail order pharmacies. The non-retail market includes clinics, federal and non-federal hospitals, federal facilities, HMOs, long-term care facilities, home health care and other miscellaneous settings.

The accuracy of the usage data provided depends on a variety of factors, including sampling and non-sampling errors. The IMS Health, National Sales Perspectives™ does not provide a direct estimate of use but does provide a national estimate of units (in kilograms) sold from the manufacturer to various channels of distribution. The quantities of products purchased by retail and non-retail channels of distribution may be a possible surrogate for use, assuming that facilities purchase drugs in quantities reflective of actual consumer use.

As in past years, accuracy of the forecast is affected by unexpected changes in consumption, supply, data collection, or IMS Health's drug categorization and sampling plan. The mathematical modeling process involves only objective factors. Deterministic factors may affect the reliability of the forecasted values. Predictions of usage for 2015 should be carefully interpreted because the precision of the forecast reduces with time into the future.

Each year, IMS Health adjusts the complete database by applying correction factors to update product usage data. Such factors may include a "re-calibration" of reported values or shifts in series reflecting new use of a drug containing the substance of interest. Such changes can result in the forecasted estimate for a given year that differs from the estimate given in previous years. Fortunately, the correction factors for most substances are small.

The forecasting method relies on a mathematical model that is accurate only to the extent that the environment of the drug use system remains essentially unchanged from previous years. This year, three smoothing approaches are used to minimize errors in forecasting:

1. Simple exponential smoothing (SES)
2. Brown's exponential smoothing (Brown)
3. Damped-trend exponential smoothing (damp)

The decision to use one approach over the other is based on the characteristics of the data used to make the projections. For substances that exhibited no apparent usage trend or a trend that is characterized by abrupt changes or recent inconsistencies, simple exponential smoothing (SES) is used and forecasts are only provided for 2014. These substances are usually characterized by either a small number of data points or low stability in an increasing or decreasing trend or both.

For substances with a well-defined increasing or decreasing trend, Brown's Linear Exponential Smoothing is used. Brown's method is applied to series where the recent behavior is characterized by an increasing or decreasing trend. For these series, the decision to provide predictions of one or two years into the future depends on the number of data points used in the model and on the degree of stability of the trend. For stable series with 10 or more data points, predictions of two years into the future are provided. For series with fewer than 10 data points, the decision to provide one or two years forecasts is examined on a case by case basis.

In settings where there's a stable and smooth linear trend, an application of the Brown method is appropriate. However, when a trend is characterized by a recent sharp increase or a sharp decrease, the Brown method can lead to extreme forecasts. In these situations, the damp method provides a useful alternative to the Brown method because it often leads to less extreme forecasts.

**Table 1:** Forecast (*Predicted*) uses (Purchases, in Kg) for 2014 and 2015, and observed use for 2011, 2012, and 2013, of Schedule II Controlled Substances. (*Note*: Substances and years for which either *observed* or *predicted* increases are equal to or exceed 10% appear in **bold.**) Percent changes reflect the change from the previous year.
Source: FDA/CDER/ Office of Biostatistics VII.

| SUBSTANCE | 2011 Observed | 2012 Observed (%CHANGE[1]) | 2013 Observed (%CHANGE[2]) | 2014 Predicted (%CHANGE[3]) | 2015 Predicted (%CHANGE[4]) |
|---|---|---|---|---|---|
| **ALFENTANIL** | 0.49 | **0.40 (-18.4)** | **0.34 (-15.0)** | **0.27 (-20.6)** | N/A |
| AMOBARBITAL | 1.41 | 1.55 (9.9) | 1.60 (3.2) | 1.55 (-3.1) | N/A |
| **AMPHETAMINE** | 9402.50 | **10647.40 (13.2)** | 10612.60 (-0.3) | 11286.71 (6.4) | 11957.40 (5.9) |
| **COCAINE** | 48.70 | **43.80 (-10.1)** | 39.50 (-9.8) | 36.40 (-7.8) | **32.55 (-10.6)** |
| **CODEINE** | 25200.70 | **22295.30 (-11.5)** | 21332.50 (-4.3) | 21383.00 (0.2) | 20533.05 (-4.0) |
| **DIHYDROCODEINE** | 102.70 | **71.30 (-30.6)** | **33.81(-52.6)** | **19.36 (-42.7)** | N/A |
| **DIPHENOXYLATE** | 423.80 | **381.40 (-10.0)** | 378.60 (-0.7) | 353.91(-6.5) | N/A |
| FENTANYL | 528.30 | 560.20 (6.0) | 534.70 (-4.6) | 560.37 (4.8) | 568.62 (1.5) |
| HYDROCODONE | 62551.20 | 61997.30 (-0.9) | 60585.30 (-2.3) | 59708.95 (-1.4) | 58400.02 (-2.2) |
| **HYDROMORPHONE** | 1659.60 | **1885.10 (13.6)** | 1897.00 (0.6) | 2033.20 (7.2) | 2168.95 (6.7) |
| **LISDEXAMFETAMINE** | 11749.60 | **13402.60 (14.1)** | 12952.70 (-3.4) | 12567.85 (-3.0) | N/A |
| **MEPERIDINE** | 2283.10 | **1858.10 (-18.6)** | **1514.30 (-18.5)** | **1251.34 (-17.4)** | **1035.94 (-17.2)** |
| **METHADONE** | 7590.40 | **6733.90 (-11.3)** | **5762.20 (-14.4)** | **5065.40 (-12.1)** | N/A |
| METHAMPHETAMINE | 12.45 | 12.74 (2.3) | 11.85 (-7.0) | 11.08 (-6.5) | N/A |
| METHYLPHENIDATE | 18218.90 | 18595.80 (2.1) | 17082.60 (-8.1) | 17562.87 (2.8) | N/A |
| MORPHINE | 29989.70 | 28229.20 (-5.9) | 25759.40 (-8.7) | 23628.23 (-8.3) | 21788.42 (-7.8) |
| **NABILONE** | 0.05 | **0.04 (-20.0)** | **0.03 (-25.0)** | 0.03 (0.0) | N/A |
| OPIUM | 80.60 | 77.0 (-4.5) | 72.90 (-5.3) | 70.26 (-3.6) | N/A |
| OXYCODONE | 69926.80 | 65718.00 (-6.0) | 59336.70 (-9.7) | 53969.54 (-9.0) | 49451.04 (-8.4) |
| **OXYMORPHONE** | 2604.70 | **1916.10 (-26.4)** | 1826.00 (-4.7) | **1488.39 (-18.5)** | N/A |
| **PENTOBARBITAL** | 79.20 | **46.80 (-40.9)** | **24.17 (-48.4)** | 22.26 (-7.9) | N/A |
| REMIFENTANIL | 1.05 | 1.11(5.7) | 1.15 (3.6) | 1.21 (5.2) | 1.27 (5.0) |
| **SECOBARBITAL** | 19.60 | **15.40 (-21.4)** | **11.64 (-24.4)** | 10.54 (-9.5) | N/A |
| **SUFENTANIL** | 0.05 | 0.05 (0.0) | 0.05 (0.0) | **0.04 (-20.0)** | N/A |
| **TAPENTADOL** | 4923.20 | **6255.60 (27.1)** | 5833.50 (-6.7) | 5478.46 (-6.1) | N/A |

[1] 100 x [Observed (2012) - Observed (2011)]/Observed (2011)
[2] 100 x [Observed (2013) - Observed (2012)] /Observed (2012)
[3] 100 x [Observed (2014) - Forecast (2013)]/Observed (2013)
[4] 100 x [Forecast (2015) - Forecast (2014)]/Forecast (2014)

**Table 2:** Forecast (*Predicted*) uses (Purchases, in Kg) for 2014 and 2015, and observed use for 2011, 2012, and 2013 of substances derived from thebaine and for substances controlled under the Psychotropic Convention (*Note*: Substances and years for which either *observed* or *predicted* increases are equal to or exceed 10 percent appear in **bold**).

| SUBSTANCE | 2011 Observed | 2012 Observed (%CHANGE[1]) | 2013 Observed (%CHANGE[2]) | 2014 Predicted (%CHANGE[3]) | 2015 Predicted (%CHANGE[4]) |
|---|---|---|---|---|---|
| ALPRAZOLAM | 2342.50 | 2278.20 (-2.7) | 2277.60 (0.0) | 2269.49 (0.4) | N/A |
| **BUPRENORPHINE** | **1746.40** | **1981.50 (13.5)** | **2251.80 (13.6)** | **2522.03 (12.0)** | **2792.26 (10.7)** |
| CLONAZEPAM | 1406.90 | 1417.80 (0.8) | 1485.40 (4.8) | 1507.40 (1.5) | 1536.20 (1.9) |
| DIAZEPAM | 5109.80 | 4888.20 (-4.3) | 4833.30 (-1.1) | 4833.36 (0.0) | N/A |
| **DIETHYLPROPION** | 601.50 | 545.80 (-9.3) | **487.70 (-10.6)** | **433.62 (-11.1)** | **387.61 (-10.6)** |
| LORAZEPAM | 1387.20 | 1344.70 (-3.1) | 1380.90 (2.7) | 1362.21 (-1.4) | N/A |
| **MIDAZOLAM** | 675.80 | **314.00 (-53.5)** | **431.20 (37.3)** | **315.12 (-26.9)** | N/A |
| **NALOXONE** | 390.90 | **430.80 (10.2)** | 473.20 (9.8) | 515.60 (9.0) | 557.99 (8.2) |
| **NALTREXONE** | 622.60 | 605.20 (-2.8) | **685.90 (13.3)** | 721.90 (5.2) | 763.26 (5.7) |
| TEMAZEPAM | 6584.30 | 6397.60 (-2.8) | 6441.50 (0.7) | 6438.90 (0.0) | N/A |
| ZOLPIDEM | 12230.10 | 12141.00 (-0.7) | 11501.30 (-5.3) | 10897.60 (-5.2) | 10293.32 (-5.5) |

Source: FDA/CDER/ Office of Biostatistics VII.

[1] 100 x [Observed (2012) - Observed (2011)]/Observed (2011)
[2] 100 x [Observed (2013) - Observed (2012)] /Observed (2012)
[3] 100 x [Observed (2014) - Forecast (2013)]/Observed (2013)
[4] 100 x [Forecast (2015) - Forecast (2014)]/Forecast (2014)

**Table 3:** Forecast (*Predicted*) uses (Purchases, in Kg) for 2014 and 2015, and observed use for 2011 and 2012, and 2013 of ephedrine and pseudoephedrine (*Note*: Substances for which either *observed* or *predicted* increases are equal to or exceed 10 percent are in bold).

| SUBSTANCE | 2011 | 2012 Observed (%CHANGE[1]) | 2013 Predicted (%CHANGE[2]) | 2014 Predicted (%CHANGE[3]) | 2015 Predicted (%CHANGE[4]) |
|---|---|---|---|---|---|
| **EPHEDRINE** | 1534.40 | **1972.30 (28.5)** | 2076.90 (5.3) | 2094.29 (0.8) | NA |
| **PSEUDOEPHEDRINE** | 101110.70 | 92869.90 (-8.2) | 92333.80 (-0.6) | **78533.25 (-14.9)** | 70755.93 (-9.9) |

Source: FDA/CDER/ Office of Biostatistics VII.

[1] 100 x [Observed (2012) - Observed (2011)]/Observed (2011)
[2] 100 x [Observed (2013) - Observed (2012)] /Observed (2012)
[3] 100 x [Observed (2014) - Forecast (2013)]/Observed (2013)
[4] 100 x [Forecast (2015) - Forecast (2014)]/Forecast (2014)

**Table 4**: Generic drug products containing controlled substances approved in 2013.

| DRUG PRODUCT | ANDA # | SPONSOR |
|---|---|---|
| AMPHETAMINE ASPARTATE; AMPHETAMINE SULFATE; DEXTROAMPHETAMINE SACCHARATE; DEXTROAMPHETAMINE SULFATE, EXTENDED RELEASE CAPSULES | 077488 | Teva |
| AMPHETAMINE ASPARTATE; AMPHETAMINE SULFATE; DEXTROAMPHETAMINE SACCHARATE; DEXTROAMPHETAMINE SULFATE, EXTENDED RELEASE CAPSULES | 076536 | Barr |
| AMPHETAMINE ASPARTATE; AMPHETAMINE SULFATE; DEXTROAMPHETAMINE SACCHARATE; DEXTROAMPHETAMINE SULFATE, TABLETS | 202424 | Aurolife |
| DEXTROAMPHETAMINE SULFATE, ORAL SOLUTION | 203644 | Tris Pharma |
| DEXTROAMPHETAMINE SULFATE, TABLETS | 202893 | Aurolife |
| CODEINE PHOSPHATE; PROMETHAZINE HYDROCHLORIDE, ORAL SYRUP | 200894 | Amneal |
| ACETAMINOPHEN; CODEINE PHOSPHATE, TABLETS | 202800 | Aurolife |
| HYDROCODONE BITARTRATE; IBUPROFEN, TABLETS | 091633 | Caraco |
| ACETAMINOPHEN; HYDROCODONE BITARTRATE, ORAL SOLUTION | 040838 | Pharmaceutical Associates |
| ACETAMINOPHEN; HYDROCODONE BITARTRATE, TABLETS | 202214 | Tris |
| DEXMETHYLPHENIDATE HYDROCHLORIDE, EXTENDED RELEASE CAPSULES | 078992 | Intellipharm |
| DEXMETHYLPHENIDATE HYDROCHLORIDE, EXTENDED RELEASE CAPSULES | 202580 | Mylan |
| DEXMETHYLPHENIDATE HYDROCHLORIDE, EXTENDED RELEASE CAPSULES | 078908 | Teva |
| DEXMETHYLPHENIDATE HYDROCHLORIDE, EXTENDED RELEASE CAPSULES | 202731 | Teva |

| | | |
|---|---|---|
| DEXMETHYLPHENIDATE HYDROCHLORIDE, EXTENDED RELEASE CAPSULES | 079108 | Watson |
| METHYLPHENIDATE HYDROCHLORIDE, ORAL SOLUTION | 201466 | Caraco |
| METHYLPHENIDATE HYDROCHLORIDE, EXTENDED RELEASE TABLETS | 091695 | Kudco |
| MORPHINE SULFATE, EXTENDED RELEASE CAPSULES | 202104 | Upsher Smith |
| OXYCODONE HYDROCHLORIDE, ORAL SOLUTION | 204037 | ROXANE |
| OXYCODONE HYDROCHLORIDE, ORAL SOLUTION | 203208 | ROXANE |
| ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE, TABLETS | 201447 | ACTAVIS |
| ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE, TABLETS | 201972 | AUROLIFE |
| ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE, TABLETS | 090535 | CARACO |
| ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE, TABLETS | 090733 | VINTAGE |
| ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE, TABLETS | 090734 | VINTAGE |
| OXYMORPHONE HYDROCHLORIDE, TABLETS | 203601 | AVANTHI |
| OXYMORPHONE HYDROCHLORIDE, TABLETS | 202321 | MALLINCKRODT |
| OXYMORPHONE HYDROCHLORIDE, EXTENDED RELEASE TABLETS | 079046 | ACTAVIS |
| OXYMORPHONE HYDROCHLORIDE, EXTENDED RELEASE TABLETS | 200822 | ROXANE |
| TRAMADOL HYDROCHLORIDE, TABLETS | 202390 | ACCORD |

| | | |
|---|---|---|
| TRAMADOL HYDROCHLORIDE, TABLETS | 091498 | CSPS OUYI |
| BUPRENORPHINE HYDROCHLORIDE; NALOXONE HYDROCHLORIDE DIHYDRATE, SUBLINGUAL TABLETS | 091422 | ACTAVIS |
| BUPRENORPHINE HYDROCHLORIDE; NALOXONE HYDROCHLORIDE DIHYDRATE, SUBLINGUAL TABLETS | 203136 | AMNEAL |
| LORAZEPAM, ORAL CONCENTRATE | 091407 | LUPIN |
| ZOLPIDEM TARTRATE, EXTENDED RELEASE TABLETS | 200266 | APOTEX |
| ZOLPIDEM TARTRATE, EXTENDED RELEASE TABLETS | 078970 | LUPIN |
| ZOLPIDEM TARTRATE, EXTENDED RELEASE TABLETS | 090153 | WATSON |
| DEXBROMPHENIRAMINE MALEATE; PSEUDOEPHEDRINE SULFATE, EXTENDED RELEASE | 078648 | AVANTHI |

**Table 5:** Generic drug products containing controlled substances discontinued in 2013.

| DRUG PRODUCT | NDA/ ANDA# | SPONSOR |
|---|---|---|
| AMPHETAMINE ASPARTATE; AMPHETAMINE SULFATE; DEXTROAMPHETAMINE SACCHARATE; DEXTROAMPHETAMINE SULFATE, TABLETS | 040472 | TEVA |
| CARISOPRODOL, TABLETS | 040397 | COREPHARMA |
| CARISOPRODOL, TABLETS | 040188 | PROSAM |
| CARISOPRODOL, TABLETS | 040124 | WEST WARD |
| CODEINE PHOSPHATE; PROMETHAZINE HYDROCHLORIDE, ORAL SYRUP | 089647 | PHARMACEUITCAL ASSOC |
| ACETAMINOPHEN; CAFFEINE; DIHYDROCODEINE BITARTRATE, CAPSULES | 040109 | MIKART |
| ACETAMINOPHEN; CAFFEINE; DIHYDROCODEINE BITARTRATE, CAPSULES | 040688 | WRASER |
| ACETAMINOPHEN; CAFFEINE; DIHYDROCODEINE BITARTRATE, TABLETS | 040316 | MIKART |
| ACETAMINOPHEN; CODEINE PHOSPHATE, TABLETS | 089238 | MIKART |
| ACETAMINOPHEN; CODEINE PHOSPHATE, TABLETS | 089231 | MIKART |
| ACETAMINOPHEN; CODEINE PHOSPHATE, TABLETS | 089363 | MIKART |
| ACETAMINOPHEN; HYDROCODONE BITARTRATE, CAPSULES | 081067 | MIKART |
| ACETAMINOPHEN; HYDROCODONE BITARTRATE, CAPSULES | 089008 | MIKART |
| ACETAMINOPHEN; HYDROCODONE BITARTRATE, TABLETS | 087757 | UCB |
| ACETAMINOPHEN; HYDROCODONE BITARTRATE, TABLETS | 089698 | MIKART |
| ACETAMINOPHEN; HYDROCODONE BITARTRATE, TABLETS | 040849 | MIKART |
| ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE, TABLETS | 040679 | MIKART |
| ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE, TABLETS | 089775 | ROXANE |
| ALPRAZOLAM, EXTENDED RELEASE TABLETS | 077979 | TEVA |
| CLONAZEPAM, TABLETS | 075468 | APOTEX |
| DIAZEPAM, INJECTION | 070296 | WATSON |
| LORAZEPAM, INJECTION | 074276 | WATSON |
| LORAZEPAM, TABLETS | 071193 | SANDOZ |

| | | |
|---|---|---|
| LORAZEPAM, TABLETS | 071194 | SANDOZ |
| LORAZEPAM, TABLETS | 071195 | SANDOZ |
| MIDAZOLAM HYDROCHLORIDE, INJECTION | 75637 | APOTEX |
| MIDAZOLAM HYDROCHLORIDE, INJECTION | 076144 | INTERNATIONAL MEDICATED SYSTEMS |
| MIDAZOLAM HYDROCHLORIDE, INJECTION | 076020 | INTERNATIONAL MEDICATED SYSTEMS |
| MIDAZOLAM HYDROCHLORIDE, ORAL SYRUP | 077115 | APOTEX |
| NALTREXONE HYDROCHLORIDE, TABLETS | 075434 | SANDOZ |
| ZOLPIDEM TARTRATE, TABLETS | 077985 | DR REDDY'S |
| LORATADINE; PSEUDOEPHEDRINE SULFATE, EXTENDED RELEASE TABLETS | 076208 | WATSON |

**Table 6:** Generic drug products that may be approved in 2014.

| DRUG PRODUCT | NDA/ ANDA# | SPONSOR |
|---|---|---|
| (b) (4) | | |
| (b) (4) | | |
| MORPHINE SULFATE, EXTENDED RELEASE TABLETS | 203849 | ACTAVIS |
| OXYMORPHONE HYDROCHLORIDE, EXTENDED RELEASE TABLETS | 202946 | MALLINCKRODT |
| NALOXONE HYDROCHLORIDE, INJECTION | 205014 | MYLAN |
| NALOXONE HYDROCHLORIDE, INJECTION | 204997 | MYLAN |