Center for Drug Evaluation and Research

Food and Drug Administration

10903 New Hampshire Avenue
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MAY 12 2016

Mr. Louis J. Milione
Deputy Assistant Administrator
Office of Diversion Control
Drug Enforcement Administration
8701 Morrissette Drive
Springfield, Virginia 22152

Dear Mr. Milione:

This document is in response to your letter dated January 8, 2016, 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 2016 and 2017, 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.

Currently, we are providing forecasts on the usage of twenty-six Schedule II substances for the years 2016 and 2017. The Schedule II substances to be evaluated in this memorandum are: alfentanil, amobarbital, amphetamine, cocaine, codeine, dihydrocodeine, diphenoxylate, fentanyl, hydrocodone, hydromorphone, levorphanol, 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 and Table 2**, usage for most opioids is predicted to decline in 2016 and 2017. The exceptions are buprenorphine, oxycodone, oxymorphone as well as tapentadol which show predictions of minor increases in 2016 and 2017.

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 the non-controlled mu-opioid antagonists, 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, clobazam, clonazepam, diazepam, diethylpropion, lorazepam, midazolam, temazepam and zolpidem.

We recognize that there can be significant differences between the estimates FDA provides and the actual published Aggregate Production Quota (APQ). We continue to be interested in more fully understanding the process that DEA uses to set the APQ.

I. **Tabular Data**

The *observed* usage (purchases in kilograms) of Schedule II substances in 2013, 2014, and 2015, 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 2016 and 2017. Each predicted value is an estimate subject to variation.

The *observed* usage for 2013, 2014, and 2015, and *predicted* usage (purchases, in kilograms) for 2016 and 2017 for substances controlled under the Psychotropic Convention are provided in **Table 2.** The *observed* usage for 2013, 2014 and 2015, and *predicted* usage (purchases, in kilograms) for 2015 and 2016 for ephedrine and pseudoephedrine are provided in **Table 3.**

Among the substances for reporting requested by DEA, we are not providing forecasted usage for the following: cannabidiol, gamma-hydroxybutyric acid, marijuana, noroxymorphone, phenylpropanolamine, and tetrahydrocannabinols because the data regarding the usage of these substances were limited or not available.

- Comments on *Observed* usages in 2015 (See Table 1, Table 2 and Table 3).

In 2015, there was an increase in the *observed* usage (relative to 2014) for amobarbital, amphetamine, codeine, dihydrocodeine, diphenoxylate, lisdexamfetamine, opium, oxycodone, oxymorphone, pentobarbital, remifentanil, tapentadol, buprenorphine, clobazam, diethylpropion, midazolam, naloxone, and naltrexone. Amobarbital, amphetamine, codeine, dihydrocodeine, clobazam, and naltrexone all demonstrated an increase of ≥ 10% in their *observed* usage for 2015. In contrast, hydrocodone, meperidine, methadone, methamphetamine, and nabilone showed a decrease of ≥ 10% in their *observed* use in 2015.

In 2015, hydrocodone usage decreased significantly, in contrast to the significant increase in usage for **codeine** and **dihydrocodeine.** Several NDAs and manufacturing supplements were approved in 2015, which may account for the increase in usage for codeine and dihydrocodeine (See Reports from FDA's Office of New Drugs below).

(b) (4), (b) (5)

Even though data is not available for **marijuana, cannabidiol,** and **tetrahydrocannabinols,** it must be noted here as reported from FDA's Office of New Drugs that in addition to the on-going studies conducted under IND for cannabidiol; that there are (b) (4) expanded access INDs, resulting in potentially (b) (4) patients receiving the drug.

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 2017 (See Table 1, Table 2, and Table 3).

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

II. Reports from FDA's Office of New Drugs, Office of Generic Drugs, Center for Veterinary Medicine, National Institute on Drug Abuse (NIDA) and the Substance Abuse and 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, substances derived from thebaine as well as substances controlled under the Psychotropic Convention. The reports originate from the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP), the Division of Metabolism and Endocrinology Products, the Division of Neurology Products, the Division of Pulmonary, Allergy, and Rheumatology Products, and the Division of Psychiatry Products.

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: buprenorphine, codeine, fentanyl, hydromorphone, methadone, morphine, naloxone, naltrexone, oxycodone, and oxymorphone. Additionally, DAAAP reports that it has (b) (4) for oxycodone and naltrexone combination and one pending NDA for oxycodone single ingredient.

In 2015, the **Division of Metabolism and Endocrinology Products (DMEP)** approved two manufacturing supplements for Contrave (naltrexone and bupropion) capsules.

The **Division of Neurology Products (DNP)** reports the approval of NDA manufacturing supplements for gamma-hydroxybutyric acid, clonazepam, and zolpidem in 2015. DNP also reports that in addition to the (b) (4) INDs they have for cannabidiol, that there are (b) (4) expanded access INDs, resulting in potentially (b) (4) patients receiving the drug. Regarding GHB, DNP reports that approximately (b) (4) units of GHB were distributed in approved marketed products in the United States from July 1, 2014 to June 30, 2015 (Note: One unit = one 180 mL bottle).

In 2015, the **Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)** reports the approval of NDAs for codeine phosphate and chlorpheniramine maleate; codeine polistirex and chlorpheniramine polistirex; hydrocodone bitartrate and guaifenesin; and hydrocodone, guaifenesin and pseudoephedrine. Also, DPARP reports the approval of manufacturing

supplements in the past year for codeine polistirex and chlorpheniramine polistirex; hydrocodone and guaifenesin oral solution; and desloratadine and pseudoephedrine sulfate.

The **Division of Psychiatry Products (DPP)** reports the approval of NDAs or Efficacy Supplements in 2015, for the following substances: lisdexamfetamine dimesylate, methylphenidate, and amphetamine. DPP also reports pending NDAs or Efficacy Supplements for methylphenidate, and lisdexamfetamine.

The **Drug Shortage Staff (DSS)** reports that controlled drug products are stable and that they did not see much increase in demand for Schedule II controlled substances in 2015. However, DSS did note a spike in demand for the nasal naloxone product, probably due to its preferred use by first responders during emergency events.

The CDER **Office of Generic Drugs** provides listings of products containing Schedule II, thebaine-derived or internationally controlled substances approved in 2015 **(Table 4)**, products discontinued in 2015 **(Table 5)**, and products that may be approved in 2016 **(Table 6)**.

The **Center for Veterinary Medicine (CVM)** reports that there are no changes from what CVM reported last year.

The **National Institute on Drug Abuse (NIDA)'s Division of Therapeutics and Medical Consequences of Drug Abuse** reports that in 2015, their contractor, the University of Mississippi manufactured (b) (4) kg of plant material, (b) (4) kg of delta-9-THC, (b) (4) kg of extract and (b) (4) g of all other cannabinoids. For the same year, their contractor RTI produced (b) (4) kg of plant material.

For 2016, NIDA predicts that the University of Mississippi will produce (b) (4) kg of plant material, (b) (4) g of delta-9-THC, (b) (4) kg of extract, and (b) (4) kg of all other cannabinoids. RTI is predicted to produce (b) (4) kg of plant material.

Additionally, NIDA reports that currently there are no plans to grow marijuana in 2017.

The **Substance Abuse and Mental Health Services Administration (SAMHSA)** provides information about the usage of methadone and buprenorphine in maintenance treatment of opioid addiction. Data on the use of methadone in Opioid Treatment Programs (OTPs) are not available from IMS Health, Inc.; therefore, **Table 1** most likely comprises methadone usage for treatment of pain.

SAMHSA reports that the 2015 data from the National Survey of Substance Abuse Treatment Services (N-SSATS) is not yet available. The 2014 N-SSATS data did not include patient counts. However, in 2014, a total of 1,475 facilities responded to the survey that indicated that they were SAMHSA-certified OTPs; 1,751 additional facilities responded to the survey that they were *NOT* SAMHSA-certified OTPs, but prescribed buprenorphine for the treatment of opioid addiction; and 10,926 facilities did not use methadone or buprenorphine to treat opioid

addiction (although many of these facilities accepted patients who received their medication elsewhere).

Also, SAMHSA reports that they do not collect dosage information in N-SSATS (or any other regularly occurring survey). The last time these data were collected was in 2011; therefore, these data are the same as reported last year.

We hope these data prove useful to the Drug Enforcement Administration in making quota determinations. If you have any questions or need additional clarifications, please contact Corinne P. Moody, Science Policy Analyst, Controlled Substance Staff, at 301-796-5402.

Sincerely,

Corinne P. Moody

for 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 Director for regulatory Programs
Center for Drug Evaluation and Research

Enclosures:

Attachment I: Description of Forecasting Methodology

Table 1: Forecast Uses (Purchases, in Kg) for 2016 and 2017, and Observed Use for 2013, 2014, and 2015 of Schedule II Controlled Substances

Table 2: Forecast Uses (Purchases, in Kg) for 2016 and 2017, and Observed Use in substances controlled under the Psychotropic Convention

Table 3: Forecast Uses (Purchase, in Kg) for 2016 and 2017, Observed Use in 2013, 2014, and 2015 of ephedrine and pseudoephedrine

Table 4: Generic Drug Products Containing Schedule II, Thebaine-Derived or Internationally Controlled Substances **Approved** in 2015

Table 5: Generic Drug Products Containing Schedule II, Thebaine-Derived or Internationally Controlled Substances **Discontinued** in 2015

Table 6: Generic Drug Products Containing Schedule II, Thebaine-Derived or Internationally Controlled Substances With Action Dates in 2016

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, IMS National Sales Perspectives™ measures the volume of drug products, both prescription and over-the-counter, and selected diagnostic products moving from manufacturers into various outlets within the retail and non-retail markets. Volume is expressed in terms of sales dollars, eaches, extended units, and share of market. These data are based on national projections. Outlets within the retail market include the following pharmacy settings: chain drug stores, independent drug stores, mass merchandisers, food stores, and mail service. Outlets within the non-retail market include clinics, 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 patient use but do provide a national estimate of units sold from the manufacturers to various channels of distribution. The amount of product purchased by these retail and non-retail channels of distribution may be a possible surrogate for use, if we assume that facilities purchase drugs in quantities reflective of actual patient use. The estimates provided are national estimates, but no statistical tests were performed to determine statistically significant changes over time or between products.

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 2016 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. To minimize errors in forecasting, the predictions are based on one of three smoothing methods:

- Simple Exponential Smoothing (SES)
- Brown's exponential smoothing (Brown)
- Damped-trend exponential smoothing (Damp)

The decision to use one smoothing method over the other to make projections depends on the characteristic of the time-series. Time-series smoothing methods were applied to annual time-series data in order to predict the amount of Schedule I/II and List I controlled substances required to meet the legitimate medical, scientific, and stock needs of the United States for 2016 and 2017. Simple exponential smoothing is generally applied to series that either do not have any apparent recent trend or to series with a recent trend but is currently experiencing erratic behavior. Brown's linear exponential smoothing or damp-trend exponential or damp-trend exponential smoothing is applied to series characterized by increasing or decreasing trend. For substances in which SES is applied, predictions are made only for 2016 – a reflection of uncertainty. For substances in which the Brown or damp methods are appropriate, predictions are provided for 2016 *and* 2017 for some substances while only 2016 predictions are provided for others. The latter reflects either the small number of data points used for the series or the low stability in the observed increasing or decreasing trend or both. For substances in which 2016 and 2017 projections are provided, the 2017 projections are more uncertain than the 2016 projections and should be interpreted with caution.

Table 1: Forecast (*Predicted*) uses (Purchases, in Kg) for 2016 and 2017, and observed use for 2013, 2014, and 2015, 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.

SUBSTANCE	2013 Observed	2014 Observed (%CHANGE[1])	2015 Observed (%CHANGE[2])	2016 Predicted (%CHANGE[3])	2017 Predicted (%CHANGE[4])
ALFENTANIL	0.34	0.35 (2.94)	0.35 (0.0)	0.35 (0.0)	N/A
AMOBARBITAL	1.61	**0.93 (-42.2)**	**1.17 (25.8)**	**1.03 (-12.0)**	N/A
AMPHETAMINE	10701.67	**11820.09 (10.5)**	**13074.41 (10.6)**	13755.61(5.2)	14638.56 (6.4)
COCAINE	38.88	35.52 (-8.6)	34.21(-3.7)	30.88 (-9.7)	28.36 (-8.2)
CODEINE	21345.28	21350.03 (0.0)	**26485.41(24.0)**	24559.37 (-7.2)	N/A
DIHYDROCODEINE	33.88	**3.07 (-90.9)**	**19.82 (545.6)**	**11.90 (-40.0)**	N/A
DIPHENOXYLATE	378.69	358.72(-5.3)	369.61(3.0)	356.83 (-3.5)	N/A
FENTANYL	536.41	525.16 (-2.1)	500.36 (-4.7)	479.96 (-4.1)	464.09 (-3.3)
HYDROCODONE	60684.14	55701.63 (-8.2)	**48488.43 (-12.9)**	**41514.97 (-14.4)**	**34233.29 (-17.5)**
HYDROMORPHONE	1905.80	1812.93 (-4.9)	1642.55 (-9.4)	1498.14 (-8.8)	1375.55 (-8.2)
LEVORPHANOL	2.29	**2.66 (16.2)**	2.57 (-3.4)	2.48 (-3.5)	N/A
LISDEXAMFETAMINE	13082.75	13741.08 (5.0)	14675.42 (6.8)	15371.49 (4.7)	16022.83 (4.2)
MEPERIDINE	1504.15	**1228.87 (-18.3)**	**1058.33 (-13.9)**	**893.72 (-15.6)**	**759.30 (-15.0)**
METHADONE	5761.31	5212.48 (-9.5)	**4674.55 (-10.3)**	4212.43 (-9.9)	3823.88 (-9.2)
METHAMPHETAMINE	11.76	10.77 (-8.4)	**9.20 (-14.6)**	9.27 (0.8)	8.55 (-7.8)
METHYLPHENIDATE	17095.22	17283.32 (1.1)	17224.22 (-0.3)	17234.35 (0.1)	N/A
MORPHINE	25873.51	24257.14 (-6.2)	23138.73 (-4.6)	22261.25 (-3.8)	21573.04 (-3.1)
NABILONE	0.03	**0.04 (33.3)**	**0.02 (-50.0)**	**0.03 (50.0)**	N/A
OPIUM	73.20	73.37 (0.2)	73.48 (0.1)	73.48 (0.0)	N/A
OXYCODONE	59482.85	58204.25 (-2.1)	58702.64 (0.9)	59081.36 (0.6)	59371.10 (0.5)
OXYMORPHONE	1825.05	1891.52 (3.6)	1921.88 (1.6)	**2141.51 (11.42)**	2345.15 (9.5)
PENTOBARBITAL	24.23	**16.54 (-31.7)**	17.65 (6.7)	19.29 (9.3)	**22.62 (17.3)**
REMIFENTANIL	1.16	1.23 (6.0)	1.35 (9.8)	1.44 (6.7)	1.53 (6.3)
SECOBARBITAL	11.50	11.13 (-3.2)	10.11 (-9.2)	9.55 (-5.5)	9.40 (-1.6)
SUFENTANIL	0.05	**0.04 (-20.0)**	0.04 (0.0)	**0.03 (-25.0)**	N/A
TAPENTADOL	5843.62	5510.73 (-5.7)	5579.61 (1.2)	5636.85 (1.0)	5685.50 (0.9)

[1] 100 x [Observed (2014) – Observed (2013)/Observed (2013)]
[2] 100 x [Observed (2015) – Observed (2014)/Observed (2014)]
[3] 100 x [Forecast (2016) – Observed (2015)/Observed (2015)]
[4] 100 x [Forecast (2017) – Forecast (2016)/Forecast (2016)]

Source: FDA/CDER/Office of Biostatistics VII

Table 2: Forecast (*Predicted*) uses (Purchases, in Kg) for 2016 and 2017, and observed use for 2013, 2014, and 2015 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	2013 Observed	2014 Observed (%CHANGE[1])	2015 Observed (%CHANGE[2])	2016 Predicted (%CHANGE[3])	2017 Predicted (%CHANGE[4])
ALPRAZOLAM	2277.63	2243.14 (-1.5)	2215.64 (-1.2)	2193.29 (-1.0)	2175.29 (-0.8)
BUPRENORPHINE	2276.09	2527.71 (11.1)	2760.58 (9.2)	2993.49 (8.4)	3226.40 (7.8)
CLOBAZAM	153.84	**220.25 (43.2)**	**281.03 (27.6)**	**350.99 (24.9)**	N/A
CLONAZEPAM	1485.64	1497.40 (0.8)	1476.82 (-1.4)	1492.83 (1.1)	1488.93 (-0.3)
DIAZEPAM	4841.79	4644.97 (-4.1)	4570.84 (-1.6)	4476.55 (-2.1)	N/A
DIETHYLPROPION	487.31	466.24 (-4.3)	480.33 (3.0)	488.13 (1.6)	500.20 (2.5)
LORAZEPAM	1384.84	1335.94 (-3.5)	1278.31 (-4.3)	1315.89 (2.9)	N/A
MIDAZOLAM	422.31	**351.32 (-16.8)**	352.73 (0.4)	**285.20 (-19.1)**	N/A
NALOXONE	479.32	520.50 (8.6)	564.50 (8.5)	608.49 (7.8)	652.49 (7.2)
NALTREXONE	694.51	**866.45 (24.8)**	**1548.33 (78.7)**	1547.64 (-0.0)	N/A
TEMAZEPAM	6442.27	6209.57 (-3.6)	6023.82 (-3.0)	5854.49 (-2.8)	5655.76 (-3.4)
ZOLPIDEM	11504.52	10826.76 (-5.9)	10184.54 (-5.9)	9581.84 (-5.9)	9031.26 (-5.7)

[1] 100 x [Observed (2014) – Observed (2013)/Observed (2013)]
[2] 100 x [Observed (2015) – Observed (2014)/Observed (2014)]
[3] 100 x [Forecast (2016) – Observed (2015)/Observed (2015)]
[4] 100 x [Forecast (2017) – Forecast (2016)/Forecast (2016)]

Source: FDA/CDER/Office of Biostatistics VII

Table 3: Forecast (*Predicted)* uses (Purchases, in Kg) for 2016 and 2017, and observed use for 2013, 2014, and 2015 of ephedrine and pseudoephedrine.

SUBSTANCE	2013 Observed	2014 Observed (%CHANGE[1])	2015 Observed (%CHANGE[2])	2016 Predicted (%CHANGE[3])	2017 Predicted (%CHANGE[4])
EPHEDRINE	2078.62	2235.17 (7.5)	2135.92 (-4.4)	2199.80 (3.0)	2238.18 (1.7)
PSEUDOEPHEDRINE	92649.82	90289.81 (-2.5)	90147.22 (-0.2)	89956.70 (-0.2)	90166.80 (0.2)

[1]100 x [Observed (2014) – Observed (2013)/Observed (2013)]
[2]100 x [Observed (2015) – Observed (2014)/Observed (2014)]
[3]100 x [Forecast (2016) – Observed (2015)/Observed (2015)]
[4]100 x [Forecast (2017) – Forecast (2016)/Forecast (2016)]

Source: FDA/CDER/Office of Biostatistics VII

Table 4: Generic Drug Products Containing Schedule II, Thebaine-Derived or Internationally Controlled Substances Approved in 2015

DRUG PRODUCT	ANDA #	SPONSOR
ALPRAZOLAM Extended Release Tablets	078449	Apotex, Inc
ALPRAZOLAM Tablets	200739	Natco Pharma, LTD
ALPRAZOLAM Tablets	203346	Aurobindo Pharma, LTD
AMPHETAMINE ASPARTATE; AMPHETAMINE SULFATE; DEXTROAMPHETAMINE SACCHARATE; DEXTROAMPHETAMINE SULFATE Tablets	206721	Mylan Pharmaceuticals, Inc
ASPIRIN; BUTALBITAL; CAFFEINE; CODEINE PHOSPHATE Capsules	203335	Coastal Pharmaceuticals
BUPRENORPHINE HYDROCHLORIDE Sublingual Tablets	090279	Sandoz, Inc
BUPRENORPHINE HYDROCHLORIDE Sublingual Tablets	090819	Actavis Elizabeth, LLC
BUPRENORPHINE HYDROCHLORIDE Sublingual Tablets	201066	Mylan Pharmaceuticals, Inc
BUPRENORPHINE HYDROCHLORIDE Injectable	206586	Par Sterile Products, LLC
BUPRENORPHINE HYDROCHLORIDE; NALOXONE HYDROCHLORIDE Sublingual Tablets	204431	Ethypharma USA Corp
CHLORPHENIRAMINE MALEATE; HYDROCODONE BITARTRATE Oral Solution	206438	Tris Pharma, Inc
CHLORPHENIRAMINE MALEATE; HYDROCODONE BITARTRATE; PSEUDOEPHEDRINE HYDROCHLORIDE Oral Solution	205657	Coastal Pharmaceuticals
CODEINE PHOSPHATE; PHENYLEPHRINE HYDROCHLORIDE; PROMETHAZINE HYDROCHLORIDE Syrup	200963	Amneal Pharmaceuticals
DEXMETHYLPENIDATE HYDROCHLORIDE Extended Release Capsules	079108	Watson Laboratories, Inc
DEXMETHYLPHENIDATE HYDROCHLORIDE Tablets	201231	Sun Pharmaceutical Industries, LTD
DEXMETHYLPHENIDATE HYDROCHLORIDE Extended Release Capsules	204266	Mylan Pharmaceuticals, Inc
DEXMETHYLPHENIDATE HYDROCHLORIDE Tablets	204534	Novel Laboratories, Inc
DEXMETHYLPHENIDATE HYDROCHLORIDE Tablets	206931	Abhai, Inc
DEXTROAMPHETAMINE SULFATE Tablets	203548	Avanthi, Inc
FENTANYL Extended Release Transdermal Film	077154	Mallinckrodt, Inc
FEXOFENADINE HYDROCHLORIDE; PSEUDOEPHEDRINE HYDROCHLORIDE Extended Release Tablets	090818	Sun Pharma Global FZE
GUAIFENESIN; PSEUDOEPHEDRINE HYDROCHLORIDE Extended Release Tablets	091071	Actavis Laboratories FL, Inc
HYDROCODONE BITARTRATE; PSEUDOEPHEDRINE HYDROCHLORIDE Oral Solution	205658	Coastal Pharmaceuticals
HYDROMORPHONE HYDROCHLORIDE Extended Release Tablets	204278	Paddock Laboratories, LLC
METHADONE HYDROCHLORIDE Tablets	090065	Corepharma, LLC
METHADONE HYDROCHLORIDE Tablets	203502	Aurolife Pharma, LLC
METHAMPHETAMINE HYDROCHLORIDE Tablets	203846	Roxane Laboratories, Inc
METHYLPHENIDATE HYDROCHLORIDE Extended Release Capsules	203583	Mallinckrodt, Inc

METHYLPHENIDATE HYDROCHLORIDE Chewable Tablets	204115	Novel Laboratories, Inc
METHYLPHENIDATE HYDROCHLORIDE Oral Solution	204602	Novel Laboratories, Inc
METHYLPHENIDATE HYDROCHLORIDE Tablets	207416	Ascent Pharmaceuticals, Inc
METHYLPHENIDATE HYDROCHLORIDE Extended Release Tablets	207488	Abhai, LLC
METHYLPHENIDATE HYDROCHLORIDE Tablets	207884	Novel Laboratories, Inc.
MORPHINE SULFATE Oral Solution	202309	Vintage Pharmaceuticals, LLC
MORPHINE SULFATE Oral Solution	202310	Vintage Pharmaceuticals, LLC
MORPHINE SULFATE Extended Release Capsules	202718	Teva Pharmaceuticals USA
MORPHINE SULFATE Oral Solution	203518	Tris Pharma, Inc
MORPHINE SULFATE Extended Release Tablets	203602	Novel Laboratories, Inc
MORPHINE SULFATE Extended Release Tablets	203849	Actavis Elizabeth, LLC
MORPHINE SULFATE Injectable	205758	Eurohealth International SARL
OXYCODONE HYDROCHLORIDE Tablets	076636	Actavis Elizabeth, LLC
OXYCODONE HYDROCHLORIDE Tablets	077712	Vintage Pharmaceuticals, Inc
OXYCODONE HYDROCHLORIDE Tablets	202662	Epic Pharma, LLC
OXYCODONE HYDROCHLORIDE Capsules	202773	Avanthi, Inc
OXYCODONE HYDROCHLORIDE Oral Solution	204603	Novel Laboratories, Inc
OXYCODONE HYDROCHLORIDE Capsules	204752	Novel Laboratories, Inc
OXYCODONE HYDROCHLORIDE Oral Solution	204979	Ani Pharmaceuticals, Inc
OXYCODONE HYDROCHLORIDE Oral Solution	206456	Wockhardt Bio AG
OXYMORPHONE HYDROCHLORIDE Extended Release Tablets	203506	Sun Pharmaceutical Industries, LTD
TEMAZEPAM Capsules	201781	Vintage Pharmaceuticals, Inc
ZOLPIDEM TARTRATE Sublingual Tablets	204299	Novel Laboratories, Inc

(b) (4), (b) (5)

Table 5: Generic Drug Products Containing Schedule II, Thebaine-Derived or Internationally Controlled Substances Discontinued in 2015

DRUG PRODUCT	ANDA #	SPONSOR
MIDAZOLAM HYDROCHLORIDE Injectable	078141	Wockhardt, LTD
MIDAZOLAM HYDROCHLORIDE Injectable	078511	Wockhardt, LTD

Table 6: Generic Drug Products Containing Schedule II, Thebaine-Derived or Internationally Controlled Substances with Action Dates in 2016

DRUG PRODUCT	ANDA #	SPONSOR
DEXTROAMPHETAMINE SULFATE; AMPHETAMINE SULFATE Extended Release Capsules	76852	Impax Laboratories, Inc
DEXTROAMPHETAMINE SULFATE; AMPHETAMINE SULFATE Extended Release Tablets	206340	Actavis Elizabeth LLC
BUPRENORPHINE Sublingual Tablets	201760	Sun Pharmaceutical Industries, LTD
DEXTROAMPHETAMINE SULFATE Extended Release Capsules	206735	Mylan Pharmaceuticals, Inc
(b) (4)		
MORPHINE SULFATE Injection, USP	204393	Mallinckrodt, Inc
(b) (4)		
DEXMETHYLPHENIDATE HYDROCHLORIDE Tablets	207901	Tris Pharma, Inc
DEXTROAMPHETAMINE SULFATE; AMPHETAMINE SULFATE Extended Release Capsules	206159	Par Pharmaceutical, Inc
HYDROMORPHONE HYDROCHLORIDE Tablets, USP	205814	Aurolife Pharma, LLC
METHYLPHENIDATE Controlled Release Tablets	76772	Actavis Laboratories FL, Inc
METHYLPHENIDATE HYDROCHLORIDE Tablets, USP	206840	Tedor Pharma, Inc
METHYLPHENIDATE HYDROCHLORIDE Tablets, USP	207587	Nostrum Laboratories, Inc
METHYLPHENIDATE HYDROCHLORIDE Chewable Tablets	204954	Nostrum Laboratories, Inc

(b) (4), (b) (5)

(b) (4), (b) (5)