

Director, Office of Trade Agreements Negotiations and Compliance	Deputy Assistant Secretary for Trade Policy and Analysis	Head of Contracting Offices, Acquisition and Grants Office
Director, Office of Accounting	Director, Office of Standards and Investment Policy	Director, Workforce Management Office
Director, Office of Policy	Director, Office of Trade and Economic Analysis	Senior Advisor for International Affairs
<i>Global Markets</i>	Director, Office of Trade Negotiations and Analysis	Director, Office of Legislation & Intergovernmental Affairs
Assistant Secretary of Global Markets and Director General for the US&FCS	Director, Office of Intellectual Property Rights	Freedom of Information Officer
Deputy Director General	Deputy Assistant Secretary for Manufacturing	<b>National Technical Information Service</b>
Principal Deputy Assistant Secretary	Director, Office of Energy and Environmental Industries	Director
Executive Director, Advocacy Center	Director, Office of Transportation and Machinery	Deputy Director
Director, Business Information and Technology Office	Director, Office of Health and Information Technologies	Chief Financial Officer/Associate Director for Finance and Administration
Director, Global Knowledge Center	Deputy Assistant Secretary for Textiles, Consumer Goods, and Materials	<b>National Telecommunications and Information Administration</b>
Director, Office of Budget	Director, Office of Textiles and Apparel	Deputy Assistant Secretary
Director, Office of Foreign Service Human Capital	Director, Office of Materials	Chief Counsel
Director, Office of Strategic Planning	Director, Office of Consumer Goods	Deputy Chief Counsel
Director, Office of Administrative Services	<b>Minority Business Development Agency</b>	[FR Doc. 2014-03633 Filed 2-26-14; 8:45 am]
Executive Director, SelectUSA	Chief Counsel	<b>BILLING CODE 3510-17-P</b>
Deputy Assistant Secretary for U.S. Field National U.S. Field Director	Freedom of Information Officer	
Deputy Assistant Secretary for Asia	<b>National Institute of Standards and Technology</b>	
Executive Director for Asia	Director for Administration and Chief Financial Officer	<b>DEPARTMENT OF JUSTICE</b>
Director, Office of the ASEAN and Pacific Basin	Chief, Management and Organization Office	<b>Drug Enforcement Administration</b>
Director, Office of East Asia and APEC	NIST Counsel	<b>21 CFR Part 1308</b>
Director, Office of South Asia	<b>National Oceanic and Atmospheric Administration</b>	[Docket No. DEA-389]
Deputy Assistant Secretary for China, Hong Kong, and Mongolia	Under Secretary	<b>Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products From Schedule III to Schedule II</b>
Executive Director for China, Hong Kong, and Mongolia	Deputy Under Secretary for Operations	<b>AGENCY:</b> Drug Enforcement Administration, Department of Justice.
Director, Office of China, Hong Kong, and Mongolia	Chief, Resource and Operations Management	<b>ACTION:</b> Notice of proposed rulemaking.
Deputy Assistant Secretary for Western Hemispheres	Director, Office of Communications and External Affairs	<b>SUMMARY:</b> The Drug Enforcement Administration (DEA) proposes to reschedule hydrocodone combination products from schedule III to schedule II of the Controlled Substances Act. This proposed action is based on a rescheduling recommendation from the Assistant Secretary for Health of the Department of Health and Human Services and an evaluation of all other relevant data by the DEA. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule II controlled substances on persons who handle (manufacture, distribute, dispense, import, export, engage in research, conduct instructional activities, or possess) or propose to handle hydrocodone combination products.
Executive Director for Western Hemispheres	Director, Office of Marine and Aviation Operations	<b>DATES:</b> Interested persons may file written comments on this proposal pursuant to 21 CFR 1308.43(g).
Director, Office of North and Central America	General Counsel	Electronic comments must be submitted, and written comments must be postmarked, on or before April 28, 2014. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after midnight Eastern Time on the last day of the comment period.
Director, Office of South America	Deputy General Counsel	
Deputy Assistant Secretary for Europe, Middle East, and Africa	Assistant Administrator for National Ocean Services	
Executive Deputy Assistant Secretary for Europe, Middle East, and Africa	Deputy Assistant Administrator for National Ocean Services	
Executive Director for Europe and Eurasia	Assistant Administrator for National Marine Fisheries Service	
Director, Office of Europe Country Affairs	Deputy Assistant Administrator for Regulatory Programs for National Marine Fisheries Service	
Director, Office of the European Union	Assistant Administrator for National Weather Services	
Director, Office of Russia, Ukraine, and Eurasia	Deputy Assistant Administrator for National Weather Services	
Executive Director for Africa and Middle East	Assistant Administrator for National Environmental Satellite, Data, and Information Service	
Director, Office of the Middle East and North Africa	Deputy Assistant Administrator for National Environmental Satellite, Data, and Information Service	
Director, Office of Sub-Saharan Africa	Assistant Administrator for Oceanic and Atmospheric Research	
<i>Industry and Analysis</i>	Deputy Assistant Administrator for Programs & Administration (Oceanic and Atmospheric Research)	
Assistant Secretary for Industry and Analysis	Assistant Administrator for Program, Planning and Integration	
Deputy Assistant Secretary for Industry and Analysis	Chief Administrative Officer	
Trade Agreements Secretariat	Chief Financial Officer	
Executive Director, Office of Trade Programs and Strategic Partnerships	Chief Information Officer	
Director, Trade Promotion Programs	Director, Acquisition and Grants Office	
Director, Strategic Partnerships	Deputy Director, Acquisition and Grants Office	
Director, Office of Advisory Committees and Industry Outreach	Office	
Director, Office of Planning, Coordination and Management		
Deputy Assistant Secretary for Services		
Director, Office of Financial and Insurance Industries		
Director, Office of Digital Service Industries		
Director, Office of Supply Chain, Professional and Business Services		
Executive Director for National Travel and Tourism Office		
Director, Office of Travel and Tourism Industries		

Interested persons, defined as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811)," 21 CFR 1300.01, may file a request for hearing or waiver of an opportunity for a hearing or to participate in a hearing pursuant to 21 CFR 1308.44 and in accordance with 21 CFR 1316.45, 1316.47, 1316.48 or 1316.49, as applicable. Requests for hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before March 31, 2014.

**ADDRESSES:** To ensure proper handling of comments, please reference "Docket No. DEA-389" on all electronic and written correspondence. The DEA encourages that all comments be submitted electronically through the Federal eRulemaking Portal which provides the ability to type short comments directly into the comment field on the Web page or attach a file for lengthier comments. Please go to [www.regulations.gov](http://www.regulations.gov) and follow the on-line instructions at that site for submitting comments. Paper comments that duplicate electronic submissions are not necessary. Should you, however, wish to submit written comments, in lieu of electronic comments, they should be sent via regular or express mail to: Drug Enforcement Administration, Attention: DEA Federal Register Representative/ODW, 8701 Morrissette Drive, Springfield, Virginia 22152. All requests for a hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attention: Hearing Clerk/LJ, 8701 Morrissette Drive, Springfield, Virginia 22152.

**FOR FURTHER INFORMATION CONTACT:**  
Ruth A. Carter, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152, Telephone: (202) 598-6812.

**SUPPLEMENTARY INFORMATION:**

**Posting of Public Comments**

Please note that all comments received in response to this docket are considered part of the public record and will be made available for public inspection online at [www.regulations.gov](http://www.regulations.gov). Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter.

The Freedom of Information Act (FOIA) applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your

comment, but do not want it to be made publicly available, you must include the phrase "PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment. If a comment has so much confidential business information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments containing personal identifying information or confidential business information identified as directed above will be made publicly available in redacted form.

An electronic copy of this document and supplemental information to this proposed rule are available at [www.regulations.gov](http://www.regulations.gov) for easy reference. If you wish to personally inspect the comments and materials received or the supporting documentation the DEA used in preparing the proposed action, these materials will be available for public inspection by appointment. To arrange a viewing, please see the "For Further Information Contact" paragraph above.

**Request for Hearing, Notice of Appearance at Hearing, or Waiver of an Opportunity for a Hearing or To Participate in a Hearing**

Pursuant to the provisions of the Controlled Substances Act (CSA), 21 U.S.C. 811(a), this action is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551-559. 21 CFR 1308.41-1308.45; 21 CFR Part 1316 subpart D. In accordance with 21 CFR 1308.44(a)-(c), requests for a hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing may be submitted only by interested persons, defined as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811)." 21 CFR 1300.01. Requests for hearing and notices of appearance must conform to the requirements of 21 CFR 1308.44(a) or

(b), and 1316.47 or 1316.48 as applicable, and include a statement of the interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver must conform to the requirements of 21 CFR 1308.44(c) and 1316.49, including a written statement regarding the interested person's position on the matters of fact and law involved in any hearing.

Please note that pursuant to 21 U.S.C. 811(a)(1), the purpose and subject matter of a hearing held in relation to this rulemaking is restricted to: "(A) find[ing] that such drug or other substance has a potential for abuse, and (B) mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of section 812 of [title 21] for the schedule in which such drug is to be placed \* \* \*." Requests for a hearing, notices of appearance at a hearing, and waivers of an opportunity for a hearing or to participate in a hearing must be submitted to the DEA using the address information provided above.

**Legal Authority**

The DEA implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. 21 U.S.C. 801-971. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), parts 1300 to 1321. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, controlled substances are classified into one of five schedules based upon their potential for abuse, their currently accepted medical use, and the degree of dependence the substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at 21 CFR Part 1308. 21 U.S.C. 812(a).

Pursuant to 21 U.S.C. 811(a)(1), the Attorney General may, by rule, “add to such a schedule or transfer between such schedules any drug or other substance if he (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by [21 U.S.C. 812(b)] for the schedule in which such drug is to be placed \* \* \*.” Pursuant to 28 CFR 0.100(b), the Attorney General has delegated this scheduling authority to the Administrator of the DEA.

The CSA provides that the scheduling of any drug or other substance may be initiated by the Attorney General (1) on his own motion; (2) at the request of the Secretary of the Department of Health and Human Services (HHS); or (3) on the petition of any interested party. 21 U.S.C. 811(a). This proposed action was initiated by a petition to reschedule hydrocodone combination products (HCPs)<sup>1</sup> from schedule III to schedule II of the CSA, and is supported by, *inter alia*, a recommendation from the Assistant Secretary for Health of the HHS.<sup>2</sup> If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions of schedule II controlled substances on any person who handles, or proposes to handle, HCPs.

## Background

Hydrocodone was listed in schedule II of the CSA upon the enactment of the CSA in 1971. Public Law 91–513, 84 Stat. 1236, sec. 202(c), schedule II, paragraph (a), clause (1) (codified at 21 U.S.C. 812(c)); initially codified at 21 CFR 308.12(b)(1)(x) (36 FR 7776, April 24, 1971) (currently codified at 21 CFR 1308.12(b)(1)(vi)). At that time, HCPs in specified doses (containing no greater than 15 milligrams (mg) hydrocodone per dosage unit or not more than 300 mg hydrocodone per 100 milliliters) were listed in schedule III of the CSA when formulated with specified amounts of an isoquinoline alkaloid of opium or one or more therapeutically active nonnarcotic ingredients. Public Law 91–513, 84 Stat.

<sup>1</sup> Hydrocodone combination products (HCPs) are pharmaceuticals containing specified doses of hydrocodone in combination with other drugs in specified amounts. These products are approved for marketing for the treatment of pain and for cough suppression.

<sup>2</sup> As set forth in a memorandum of understanding entered into by the HHS, the Food and Drug Administration (FDA), and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of the NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations.

1236, sec. 202(c), schedule III, paragraph (d), clauses (3) and (4) (codified at 21 U.S.C. 812(c)); initially codified at 21 CFR 308.13(e)(3) and (4) (36 FR 7776, April 24, 1971) (currently codified at 21 CFR 1308.13(e)(1)(iii) and (iv)). Any other products that contain single-entity hydrocodone or combinations of hydrocodone and other substances outside the range of specified doses are listed in schedule II of the CSA.<sup>3</sup>

## Proposed Determination To Transfer HCPs to Schedule II

Pursuant to 21 U.S.C. 811(a), proceedings to add a drug or substance to those controlled under the CSA, or to transfer a drug between schedules, may be initiated on the petition of any interested party. In response to a petition the DEA had received requesting that HCPs be controlled in schedule II of the CSA, in 2004 the DEA submitted a request to the HHS to provide the DEA with a scientific and medical evaluation of available information and a scheduling recommendation for HCPs, pursuant to 21 U.S.C. 811(b) and (c). In 2008 the HHS provided to the DEA its recommendation that HCPs remain controlled in schedule III of the CSA. In response, in 2009, the DEA requested that the HHS re-evaluate their data and provide another scientific and medical evaluation and scheduling recommendation based on additional data and analysis.

On July 9, 2012, President Obama signed the Food and Drug Administration Safety and Innovation Act (Pub. L. 112–144) (FDASIA). Section 1139 of the FDASIA<sup>4</sup> directed

<sup>3</sup> In the United States there are currently no approved, marketed, products containing hydrocodone in combination with other active ingredients that fall outside schedule III of the CSA. Further, until recently, there were no approved hydrocodone single-entity schedule II products. In Oct. 2013, the FDA approved Zohydro<sup>TM</sup> ER, a single-entity, extended release schedule II product. The sponsor of this product in a press release dated Oct. 25, 2013, stated that Zohydro<sup>TM</sup> ER will be launched in approximately four months. Accordingly, all of the historical data regarding hydrocodone from different national and regional databases that support this proposal should refer to HCPs only, regardless of whether the database utilizes the term “hydrocodone” or “hydrocodone combination products.”

<sup>4</sup> FDASIA, SEC1139. SCHEDULING OF HYDROCODONE. (a) IN GENERAL.—Not later than 60 days after the date of enactment of this Act, if practicable, the Secretary of Health and Human Services (referred to in this section as the “Secretary”) shall hold a public meeting to solicit advice and recommendations to assist in conducting a scientific and medical evaluation in connection with a scheduling recommendation to the Drug Enforcement Administration regarding drug products containing hydrocodone, combined with other analgesics or as an antitussive. (b)

the Food and Drug Administration (FDA) to hold a public meeting to “solicit advice and recommendations” pertaining to the scientific and medical evaluation in connection with its scheduling recommendation to the DEA regarding drug products containing hydrocodone, combined with other analgesics or as an antitussive.

Additionally the Secretary was required to solicit stakeholder input “regarding the health benefits and risks, including the potential for abuse” of hydrocodone combination products and the impact of up-scheduling of these products.

Accordingly, on January 24–25, 2013, the FDA held a public Advisory Committee meeting at which the DEA made a presentation. The Advisory Committee included members with scientific and medical expertise in the subject of opioid abuse, and a patient representative. Members included representatives from National Institute on Drug Abuse (NIDA) and the Centers for Disease Control (CDC). There was also an opportunity for the public to provide comment. The Advisory Committee voted 19 to 10 in favor of recommending that hydrocodone combination products be placed into schedule II. According to the FDA, 768 comments were submitted by patients, patient groups, advocacy groups, and professional societies to the FDA.

Upon evaluating the scientific and medical evidence, along with the above considerations (e.g., recommendation of the Advisory Committee, the public comments, consideration of the health benefits and risks, and information about the impact of rescheduling) mandated by the FDASIA, the HHS on December 16, 2013, submitted to the Administrator of the DEA its scientific and medical evaluation (henceforth called HHS review) entitled, “Basis for the Recommendation to Place Hydrocodone Combination Products in Schedule II of the Controlled Substances Act.” Pursuant to 21 U.S.C. 811(b), this document contained an eight-factor analysis of the abuse potential of HCPs, along with the HHS’s recommendation to control HCPs under schedule II of the CSA.

The HHS stated that the comments received during the open public hearing, to the docket, and the discussion of the Advisory Committee

STAKEHOLDER INPUT.—In conducting the evaluation under subsection (a), the Secretary shall solicit input from a variety of stakeholders including patients, health care providers, harm prevention experts, the National Institute on Drug Abuse, the Centers for Disease Control and Prevention, and the Drug Enforcement Administration regarding the health benefits and risks, including the potential for abuse and the impact of up-scheduling of these products.

members of the FDA Advisory Committee meeting provided support for its conclusion that individuals are taking HCPs in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community; that there is significant diversion of HCPs; and that individuals are taking HCPs on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs. The HHS stated it has also given careful consideration to the fact that the members of the Advisory Committee voted 19 to 10 in favor of rescheduling HCPs from schedule III to schedule II under the CSA. The HHS considered the increasing trends, the public comments, the recommendation of the Advisory Committee, the health benefits and risks, and the information available about the impact of rescheduling, and concluded that HCPs have high potential for abuse.

### Summary of Eight Factor Analyses

The DEA has reviewed the scientific and medical evaluation and scheduling recommendation provided by the HHS, and all other relevant data, and completed its own eight-factor review document pursuant to 21 U.S.C. 811(c). Included below is a brief summary of each factor as considered by the DEA in its proposed rescheduling action. Both the DEA and HHS analyses are available in their entirety in the public docket for this proposed rule (Docket No. DEA-389) at [www.regulations.gov](http://www.regulations.gov) under “Supporting and Related Material.” Full analysis of, and citations to, information referenced in this summary may also be found in the supporting material.

#### 1. The Drug’s Actual or Relative Potential for Abuse

The term “abuse” is not defined in the CSA. However, the legislative history of the CSA provides the following criteria to determine whether a particular drug or substance has a potential for abuse:<sup>5</sup>

(a) Individuals are taking the drug or other substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community; or

(b) There is a significant diversion of the drug or other substance from legitimate drug channels; or

(c) Individuals are taking the drug or other substance on their own initiative rather than on the basis of medical

advice from a practitioner licensed by law to administer such drugs; or

(d) The drug is so related in its action to a drug or other substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

The DEA considered the HHS’s evaluation and all other relevant data, including data related to the above mentioned criteria, and finds that:

(a) *Individuals are using HCPs in amounts sufficient to create a hazard to their health, to the safety of other individuals, or to the community.*

The HHS states that there are increasing trends in the adverse effects from abuse of HCPs, including emergency department (ED) visits, admissions to addiction treatment centers, and deaths in selected States. In 2011, HCPs were listed in 3,376 admissions for drug treatment as the primary drug of abuse and in 6,601 admissions listing HCPs in addition to other drugs in the Treatment Episode Data Set (TEDS).<sup>6</sup> HCPs are prescribed in an unprecedented manner and their total prescriptions exceed prescriptions for any other opioid analgesic; this characteristic drives their abuse potential and sets them apart from other opioid analgesics in terms of abuse risks.

Drug Abuse Warning Network (DAWN)<sup>7</sup> data indicate that abuse of HCPs, similar to oxycodone products<sup>8</sup> (schedule II), has been associated with large numbers of admissions to the ED.

<sup>6</sup> TEDS is a program coordinated and managed by the SAMHSA. This database includes information on treatment admissions that are routinely collected by states to monitor their individual substance abuse treatment systems. Thus, TEDS includes data primarily from treatment facilities that receive public funds. TEDS includes information on demographic variables including age, gender, race and ethnicity. TEDS also reports on the top three drugs of abuse at the time of admission. TEDS does not include all drugs that may have been abused prior to admission. States and jurisdictions can choose whether or not to report the detailed listing.

<sup>7</sup> The Drug Abuse Warning Network (DAWN) is a nationally representative public health surveillance system that continuously monitors drug-related visits to hospital EDs. The DAWN data are used to monitor trends in drug misuse and abuse in the United States. DAWN captures both ED visits that are directly caused by drugs and those in which drugs are a contributing factor but not the direct cause of the ED visit.

<sup>8</sup> Unless otherwise specified, for purposes of this document “oxycodone products” refers to both its single-entity and its combination products. All oxycodone products are schedule II controlled substances.

For example, in 2011 the total number of ED visits related to nonmedical use of HCPs and oxycodone products were 82,479 and 151,218, respectively.<sup>9</sup> The American Association of Poison Control Centers’ National Poison Data System<sup>10</sup> (NPDS; formerly known as Toxic Exposure Surveillance System or TESS) reported that HCPs were involved in 30,792 and 29,391 annual toxic exposures in 2011 and 2012, respectively. The corresponding data for oxycodone products was 19,423 and 18,495. The majority of exposures for both drug products were for intentional reasons.<sup>11</sup>

The HHS mentions that nationwide estimates of overdose deaths due to HCPs cannot be quantified, but the available data for a limited number of States suggest that HCPs contribute to a substantial number of overdose deaths each year. According to the HHS, DAWN medical examiner (ME) data for five States from 2004 through 2010 reported an increase of 63% and 133% in deaths related to HCPs and oxycodone products, respectively. According to the Florida Department of Law Enforcement (FDLE),<sup>12</sup> HCPs have

<sup>9</sup> In DAWN, nonmedical use of pharmaceuticals includes taking more than the prescribed dose of a prescription pharmaceutical or more than the recommended dose of an over-the-counter pharmaceutical or supplement; taking a pharmaceutical prescribed for another individual; deliberate poisoning with a pharmaceutical by another person; and documented misuse or abuse of a prescription drug, an over-the-counter pharmaceutical, or a dietary supplement.

<sup>10</sup> The American Association of Poison Control Centers (AAPCC) maintains the national database of information logged by the United States’ 57 Poison Control Centers (PCCs). Case records in this database are from self-reported calls: they reflect only information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure, etc.), or request information/educational materials. Exposures do not necessarily represent a poisoning or overdose. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to PCCs and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

<sup>11</sup> According to the AAPCC’s NPDS database, “intentional reasons” include suspected suicide, misuse, abuse, and intentional unknown.

<sup>12</sup> The Florida Department of Law Enforcement Medical Examiners Commission publishes an Annual Medical Examiners Report, the Annual and Interim Drugs in Deceased Persons Report. In order for a death to be considered “drug-related” at least one drug identified must be in the decedent; each identified drug is a drug occurrence. The State’s medical examiners were asked to distinguish between whether the drugs were the “cause” of death or merely “present” in the body at the time of death. A drug is only indicated as the cause of death when, after examining all evidence and the autopsy and toxicology results, the medical examiner determines the drug played a causal role in the death. It is not uncommon for a decedent to have multiple drugs listed as a cause of death.

<sup>5</sup> Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No 91-1444, 91st Cong., Sess.1 (1970) reprinted in U.S.C.C.A.N. 4566, 4601.

been associated with large numbers of deaths in Florida. For example, in 2012, HCPs were associated with 777 deaths, while oxycodone products were associated with 1,426.

As summarized below, a review of drug abuse indicators for HCPs over the past several years further indicates that these products, similar to oxycodone products, are among the most widely diverted and abused drugs in the country and have high potential for abuse.

*(b) There is a significant diversion of HCPs from legitimate drug channels.*

According to forensic laboratory data as reported by the National Forensic Laboratory System<sup>13 14</sup> (NFLIS) and the System to Retrieve Information from Drug Evidence<sup>15</sup> (STRIDE), HCPs, similar to oxycodone products, are among the top 10 most frequently encountered drugs. From 2002 through 2010, total cases (from both NFLIS and STRIDE) for both HCPs and oxycodone products gradually increased with some decline in 2011 and 2012. From 2002 through 2008, annual total cases involving HCPs (range: 9,106 in 2002 to 33,611 in 2008) consistently exceeded those for oxycodone products (range: 7,993 in 2002 to 28,343 in 2008). In 2009, total cases for HCPs (37,894) were similar to that for oxycodone products (37,680). From 2010 through 2012, total cases for oxycodone products (47,238 in 2010 and 41,915 in 2012) exceeded those for HCPs (39,261 in 2010 and 34,832 in 2012). The DEA has documented a large number of diversion and trafficking cases involving HCPs. DEA investigations conducted from 2005 through 2007 determined that HCPs were diverted from rogue Internet pharmacies.

Although a medical examiner may determine a drug is present or detected in the decedent, the drug may not have played a causal role in the death. A decedent may have multiple drugs listed as present.

<sup>13</sup> The NFLIS is a program of the DEA, Office of Diversion Control. NFLIS systematically collects drug identification results and associated information from drug cases submitted to and analyzed by State and local forensic laboratories. NFLIS represents an important resource in monitoring illicit drug abuse and trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. NFLIS is a comprehensive information system that includes data from forensic laboratories that handle approximately 90% of an estimated 1.0 million distinct annual State and local drug analysis cases. NFLIS includes drug chemistry results from completed analyses only.

<sup>14</sup> While NFLIS data is not direct evidence of abuse, it can lead to an inference that a drug has been diverted and abused. See 76 FR 77330, 77332, Dec. 12, 2011.

<sup>15</sup> STRIDE is a database of drug exhibits sent to DEA laboratories for analysis. Exhibits from the database are from the DEA, other federal agencies, and local law enforcement agencies.

*(c) Individuals are using HCPs on their own initiative rather than on the basis of medical advice.*

According to the data from the National Survey on Drug Use and Health<sup>16</sup> (NSDUH), the lifetime (i.e., ever used) users of HCPs for nonmedical purposes exceeded those for oxycodone products in the United States. For example, in 2004, over 17.7 million Americans age 12 years or older reported lifetime nonmedical use of HCPs as compared to over 11.9 million reported for oxycodone products. In 2012, the corresponding data for HCPs and oxycodone products were over 25.6 and 16 million, respectively. The NSDUH also reported large increases from 2004 through 2012 in the number of individuals using HCPs and oxycodone products for nonmedical purposes.

The past year initiates (i.e., the first use of a substance within the 12 months prior to the interview date) of HCPs exceeded those of oxycodone products from 2002 through 2005. Past year initiates for HCPs were over 1.3, 1.4, 1.3 and 1.3 million in 2002, 2003, 2004 and 2005, respectively. The corresponding data for oxycodone products were over 0.47, 0.5, 0.6 and 0.45 million. According to a report by the NSDUH, the combined data from 2002 through 2005 indicate that 57.7% of persons who first used pain relievers nonmedically in the past year used HCPs while 21.7% used oxycodone products. The NSDUH data from 2002 through 2006 also indicate that the lifetime users of HCPs have a higher propensity than that of lifetime users of oxycodone immediate release products (single-entity and combination products combined) to have used for nonmedical purposes any pain relievers in the past year.

According to the Monitoring the Future<sup>17</sup> (MTF) survey, from 2002 through 2011 the annual prevalence of

<sup>16</sup> The National Survey on Drug Use and Health, formerly known as the National Household Survey on Drug Abuse (NHSDA), is conducted annually by the Department of Health and Human Service's Substance Abuse and Mental Health Services Administration (SAMHSA). It is the primary source of estimates of the prevalence and incidence of nonmedical use of pharmaceutical drugs, illicit drugs, alcohol, and tobacco use in the United States. The survey is based on a nationally representative sample of the civilian, non-institutionalized population 12 years of age and older. The NSDUH provides yearly national and state level estimates of drug abuse, and includes prevalence estimates by lifetime (i.e., ever used), past year, and past year abuse or dependence.

<sup>17</sup> Monitoring the Future (MTF) is a national survey conducted by the Institute for Social Research at the University of Michigan under a grant from the NIDA that tracks drug use trends among American adolescents among the 8th, 10th, and 12th grades.

nonmedical use of Vicodin<sup>®</sup>, an HCP, ranged from about 8% to 10.5% among high school seniors (12th graders) and exceeded that of OxyContin<sup>®</sup> (4% to 5.5%), an oxycodone extended release product. In 2012, the annual prevalence rate for nonmedical use of OxyContin<sup>®</sup> was 1.6%, 3.0%, and 4.3% among 8th, 10th and 12th graders, respectively. The corresponding rates for Vicodin<sup>®</sup> were 1.3%, 4.4% and 7.5%. According to the MTF, the annual prevalence of nonmedical use of Vicodin<sup>®</sup> in college students and young adults was 3.8% and 6.3% in 2012. The corresponding data for OxyContin<sup>®</sup> were 1.2% and 2.3%. The aforementioned data from drug abuse surveys (NSDUH and MTF) collectively indicate high prevalence of abuse of HCPs among Americans including students thereby indicating their high abuse potential.

*(d) HCPs are so related in their action to a drug or other substance already listed as having a potential for abuse to make it likely that they will have the same potential for abuse as such substance, thus making it reasonable to assume that there may be significant diversion from legitimate channels, significant use contrary to or without medical advice, or that they have a substantial capability of creating hazards to the health of the user or to the safety of the community.*

Hydrocodone possesses abuse liability effects substantially similar to morphine (schedule II) in both animals and humans. Hydrocodone, similar to morphine, is a  $\mu$  opioid receptor agonist and shares pharmacological properties with morphine. Hydrocodone substitutes for morphine in animals trained to discriminate the presence and absence of morphine. Hydrocodone, similar to morphine, is self-administered by animals. Hydrocodone substitutes for morphine in opioid-dependent subjects. Clinical abuse liability studies have also demonstrated that HCPs (Hycodan<sup>®</sup> or hydrocodone in combination with acetaminophen) are similar to morphine with respect to physiological effects, subjective effects, and drug "liking" scores.

Hydrocodone/acetaminophen and oxycodone/acetaminophen combination products at equi-miotic doses, in general, produce similar profiles of psychopharmacological effects. These two opioid products produced prototypic opiate-like effects and psychomotor impairment of similar magnitudes.

Collectively these data demonstrate that HCPs have a high potential for abuse similar to other schedule II opioid analgesic drugs such as morphine and oxycodone products.

## 2. Scientific Evidence of the Drug's Pharmacological Effects, if Known

The HHS states that hydrocodone's pharmacological effects are similar to other  $\mu$  opioid receptor agonists. It is effective as an antitussive agent and as an analgesic drug. Opioid analgesics have an important role in the management of pain. HCPs contain other nonnarcotic active ingredients such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs) (aspirin and ibuprofen), chlorpheniramine or homatropine methylbromide. The mechanism of analgesic and antitussive effects of HCPs are different from those of nonnarcotic active ingredients present in HCPs. Acetaminophen and NSAIDs are less effective against severe pain, but have a recognized role in a variety of pain settings.

HCPs, similar to other opioid analgesics such as oxycodone products, are associated with a substantial number of overdose, suicide, abuse, and dependence reports. Overdose of HCPs, similar to other opioid analgesics, can lead to respiratory depression and death. Common adverse effects of NSAIDs include gastrointestinal, cardiovascular, renal and renovascular adverse events, and hepatic injury. Acetaminophen has low incidence of gastrointestinal side effects and is a common household analgesic available over the counter. Overdoses of acetaminophen can cause severe hepatic damage and death. Opioid/acetaminophen combination products are linked to numerous liver injuries.

## 3. The State of Current Scientific Knowledge Regarding the Drug or Other Substance

The HHS provided additional scientific information with focus on chemical and toxicological properties of hydrocodone and nonnarcotic components of HCPs. Hydrocodone is a semisynthetic opioid. The bitartrate salt form of hydrocodone is the main active component in all currently marketed HCPs. Nonnarcotic drugs present as co-ingredients are acetaminophen, aspirin, ibuprofen, chlorpheniramine or homatropine methylbromide. Hydrocodone and nonnarcotic drugs present in HCPs have potential to produce adverse effects.

## 4. Its History and Current Pattern of Abuse

Soon after introduction for clinical use, there were reports of hydrocodone abuse and addiction. By the 1950s, it was established that hydrocodone has an abuse liability similar to that of

morphine. Data regarding the pharmacological effects of hydrocodone and its high potential for abuse were available prior to the enactment of the CSA and the placement of hydrocodone in schedule II reflects that knowledge base. In the United States, popularity of hydrocodone as a drug of abuse increased in the 1990s coinciding with its increased use as an analgesic. Currently HCPs are widely diverted and abused throughout the United States as demonstrated in national and regional drug-abuse-related databases. HCPs and oxycodone products (schedule II) are the two most common opioid analgesic products encountered by law enforcement.

Data from DEA field offices indicate that HCPs are diverted and are among the most sought after licit drugs in every geographic region of the country. DEA case investigations document numerous methods of diversion of HCPs. These methods involve drug theft, doctor shopping, fraudulent oral (call-in) prescriptions, fraudulent prescriptions, diversion by registrants, and various other drug trafficking schemes. HCPs are abused by individuals of diverse ages from adolescents to older populations. According to the NSDUH, in 2012, of the 37 million people in the United States who used pain relievers nonmedically in their lifetime, over 25.6 million (representing 9.9% of the United States population age 12 years or older) reported lifetime nonmedical use of HCPs. The MTF surveys indicate that from 2002 through 2012, 8.1% to 10.5% of high school seniors used Vicodin®, an HCP, for nonmedical purposes. In 2012, the annual prevalence of nonmedical use of Vicodin® in college students and young adults was 3.8% and 6.3%, respectively.

Several published epidemiological studies indicate that HCPs are widely abused. For example, a published epidemiological study reviewed prescription opioid abuse data collected by drug abuse experts (representatives of the nation's methadone programs, treatment centers, impaired health care professional programs, NIDA grantees and high-prescribing physicians) and found that HCPs are one of the most commonly abused prescription opioid drugs. Rates of abuse, expressed as cases per 100,000 population, were the highest for hydrocodone and extended release oxycodone products, while the rest of the opioid analgesics, including immediate release oxycodone products, had lower rates. Another published epidemiological study also indicates that the rate of intentional exposure (abuse, intentional misuse, suicide or intentional unknown) was highest for

HCPs at 3.75 per 100,000 population followed by oxycodone products at 1.81 per 100,000. HCPs were involved in 55% of all of the intentional exposure cases, whereas oxycodone products were involved in 27%. In addition, published data on toxic exposure calls received by Texas poison centers from 1998 through 2009 showed that toxic exposure calls related to ingestion of the combination of HCPs, carisoprodol and alprazolam (commonly referred under street names such as "Holy Trinity," "Houston Cocktail," or "Trio") have increased from 2000 through 2007 with some decline in 2009.

## 5. The Scope, Duration, and Significance of Abuse

The HHS mentions that abuse of HCPs is considerable and is associated with considerable negative public health impact. The extent of nonmedical use of HCPs by adolescents is higher than for oxycodone products. These data are of significant concern as this may reflect particular risk for younger individuals. The HHS also states that because of the large number of prescriptions, large amounts of HCPs are potentially available for illicit use. Large numbers of adversely affected individuals and the severity of the adverse effects related to abuse of HCPs suggest that individuals are taking these products in amounts sufficient to create a hazard to their health and to the safety of other individuals and the community. Abuse of HCPs is associated with progressively increasing trends in serious adverse effects, including ED visits, admissions for abuse treatment, and in mortality data in selected States. The HHS cites the widespread prescriptions for HCPs as one of the reasons for these adverse outcomes. According to the HHS, data suggests that HCPs have high potential for abuse.

The DEA notes that initial reports of abuse of HCPs in the U.S. were published in the 1960s. Since the 1990s, the diversion and abuse of HCPs has escalated in the country. By the late 1990s, there were large increases in the diversion and abuse of HCPs. HCPs, similar to oxycodone products, are widely diverted and abused pharmaceutical opioid analgesics. HCPs are associated with significant illicit activity and abuse. Federal, State and local forensic laboratory data rank HCPs as one of the two most frequently encountered opioid pharmaceuticals in submissions to the laboratories. For example, in 2012, there were over 34,000 exhibits for HCPs (NFLIS). All DEA field divisions across the U.S. have reported that HCPs are among the most sought after pharmaceuticals.

In 2012, according to the poison control centers data (NPDS), there were over 29,390 toxic exposures involving HCPs. In 2002, there were over 25,000 DAWN ED visits associated with HCPs and it was ranked sixth among all controlled substances. According to DAWN, the nonmedical use related ED visits for HCPs were 86,258; 95,972; and 82,480 in 2009, 2010, and 2011, respectively. A number of data sources indicate that abuse of HCPs is associated with a large number of deaths.

According to NSDUH, there were large numbers of lifetime and past year initiates of HCPs for nonmedical purposes and these numbers exceeded those of oxycodone. According to the MTF, about 8% to 10% of high school seniors reported nonmedical use of Vicodin®, an HCP, in recent years.

DEA case investigations document numerous methods of diversion of HCPs. These methods involve drug theft, doctor shopping, fraudulent oral (call-in) prescriptions, fraudulent prescriptions, diversion by registrants, and various other drug trafficking schemes.

#### 6. What, if Any, Risk There Is to the Public Health

Despite the medical value of HCPs as antitussive and analgesic drugs, the misuse and abuse of these products present numerous risks to the public health. Many of the risk factors associated with these products are common risks shared with other  $\mu$  opioid receptor agonists. These include the risks of developing tolerance, dependence and addiction, and the attendant problems associated with these risks including death. According to the CDC, from 1999 to 2010, the number of drug poisoning deaths<sup>18</sup> involving any opioid analgesic (e.g., oxycodone, methadone, or hydrocodone) markedly increased (over four-fold), from 4,030 to 16,651, and accounted for 43% of the 38,329 drug poisoning deaths and 39% of the 42,917 total poisoning deaths<sup>19</sup> in 2010. In 1999, opioid analgesics were involved in 24% of the 16,849 drug poisoning deaths and 20% of the 19,741 total poisoning deaths.

The HHS reviewed the HCPs related adverse events that were reported to the

<sup>18</sup> Drug poisoning deaths include unintentional and intentional poisoning deaths resulting from overdoses of a drug, being given the wrong drug, using the drug in error, or using a drug inadvertently.

<sup>19</sup> Total poisoning deaths include those resulting from drugs, and those associated with solid or liquid biologics, gases or vapors, or other substances. Poisoning deaths are from all manners, including unintentional, suicide, homicide, and undetermined intent.

FDA Adverse Events Reporting System (FAERS)<sup>20</sup> from 1969 through 2012 and compared them to those associated with oxycodone products. The most common adverse events reported for HCPs included terms such as *complete suicide, intentional overdose, drug abuse, drug dependence, and drug abuser*.<sup>21</sup> The HHS found that both HCPs and oxycodone products are associated with substantial numbers of reports of overdose, suicide, abuse, and dependence reports. Both products have large numbers of adverse events reported that reflect abuse, misuse and injury due to inappropriate use. HCPs had fewer such reports than oxycodone products.

According to the DAWN, ED mentions associated with HCPs and oxycodone products are the highest among all opioid analgesics suggesting that both HCPs and oxycodone products have a great adverse risk to the public health. According to the HHS, DAWN ME data for five States from 2004 through 2010 reported an increase of 63% and 133% in deaths related to HCPs and oxycodone products, respectively. According to the FDLE, HCPs have been associated with large numbers of deaths in Florida in recent years. According to the NPDS annual reports, since 2002, annual figures for toxic exposures (within the category of opioid analgesic drugs) were the largest for HCPs, followed by oxycodone products (see summary of Factor 1 above). From 2006 through 2012, NPDS reported a total of 84,798 single substance exposures related to HCPs resulting in 195 deaths. The corresponding data for oxycodone products is 57,219 exposures and 173 deaths.

<sup>20</sup> FAERS is a computerized information database designed to support FDA's surveillance program for the post-marketing safety of all drug and therapeutic biologic products. FDA receives adverse drug reaction reports from manufacturers as required by regulation. Health care professionals and consumers voluntarily submit reports through the MedWatch program. All reported adverse terms are coded according to standardized international terminology, MedDRA (the Medical Dictionary for Regulatory Activities). These numbers are crude reports and may include duplicates. These reports were not individually reported to determine the association between the drug and the adverse event reported and may contain concomitant use of other medications.

<sup>21</sup> The top 20 most frequently reported adverse event terms associated with all hydrocodone reports (a report may contain more than one adverse event) received from 1969 to 2012 in the FAERS, in decreasing frequency, were: Completed suicide, overdose, cardio-respiratory arrest, toxicity to various agents, cardiac arrest, respiratory arrest, drug ineffective, intentional overdose, nausea, intentional drug misuse, vomiting, death, drug abuse, accidental overdose, pain, dizziness, medication error, drug dependence, headache, and drug abuser.

#### 7. Its Psychic or Physiological Dependence Liability

According to the HHS, data from animal and human studies indicate the dependence potential of hydrocodone. The severe dependence potential is reflected by the number of individuals admitted to addiction treatment centers citing HCPs as their substance of abuse. The HHS also states that the treatment admissions linked to abuse of HCPs are increasing. The HHS concluded that abuse of HCPs may lead to severe psychological or physical dependence.

The DEA notes that as evident from the NSDUH data from 2002 through 2006, the propensity of the lifetime users of HCPs to develop substance use disorders on any pain relievers is higher than that of lifetime users of any pain relievers, as well as lifetime users of oxycodone products other than OxyContin® (i.e., oxycodone immediate release single-entity products and immediate release combination products). The FAERS data (from 1969 through August 28, 2008) indicate that the abuse and dependence reports associated with HCPs expressed as a percentage of all its adverse events (13.3%) were similar (both in magnitude and temporal distribution) to that for oxycodone products other than OxyContin® (13.6%).

The DEA also notes that according to several published epidemiological surveys and retrospective review of medical records of addiction treatment populations, HCPs are among the most abused opioid pharmaceuticals in prescription opioid dependent individuals in the country and are frequently mentioned as the primary drug of abuse in these subjects.

The above data collectively indicate that HCPs, similar to oxycodone products, have high potential to cause severe psychological or physiological dependence.

#### 8. Whether the Substance Is an Immediate Precursor of a Substance Already Controlled Under the CSA

HCPs are not immediate precursors of a substance already controlled under the CSA, as defined in 21 U.S.C. 811(e).

#### Conclusion

Based on consideration of the scientific and medical evaluation and accompanying recommendation of the HHS, and based on the DEA's consideration of its own eight-factor analysis, the DEA finds that these facts and all other relevant data constitute substantial evidence of high potential for abuse of HCPs. As such, the DEA hereby proposes to transfer HCPs from

schedule III to schedule II under the CSA.

#### Proposed Determination of Appropriate Schedule

The CSA outlines the findings required to transfer a drug or other substance between schedules (I, II, III, IV, or V) of the CSA. 21 U.S.C. 811(a); 21 U.S.C. 812(b). After consideration of the analysis and rescheduling recommendation of the Assistant Secretary for Health of the HHS and review of available data, the Administrator of the DEA, pursuant to 21 U.S.C. 811(a) and 21 U.S.C. 812(b)(2), finds that:

1. HCPs have a high potential for abuse similar to that of schedule II substances;

2. HCPs have a currently accepted medical use in treatment in the United States. According to the HHS, several pharmaceutical products containing hydrocodone in combination with acetaminophen, aspirin, NSAIDS, and homatropine are approved by FDA for use as analgesics for pain relief and for the symptomatic relief of cough and upper respiratory symptoms associated with allergies and colds; and

3. Abuse of HCPs may lead to severe psychological or physical dependence similar to that of schedule II substances.

Based on these findings, the Administrator of the DEA concludes that HCPs warrant control in schedule II of the CSA. 21 U.S.C. 812(b)(2).

#### Requirements for Handling HCPs

If this rule is finalized as proposed, persons who handle HCPs would be subject to the CSA's schedule II regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, dispensing, importing, exporting, research, and conduct of instructional activities, including the following:

**Registration.** Any person who handles (manufactures, distributes, dispenses, imports, exports, engages in research, or conducts instructional activities with) HCPs, or who desires to handle HCPs, would be required to be registered with the DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312.

**Security.** HCPs would be subject to schedule II security requirements and would need to be handled and stored pursuant to 21 U.S.C. 821, 823, 871(b) and in accordance with 21 CFR 1301.71–1301.93.

**Labeling and Packaging.** All labels and labeling for commercial containers of HCPs would need to comply with 21

U.S.C. 825, 958(e), and be in accordance with 21 CFR part 1302.

**Quotas.** A quota assigned pursuant to 21 U.S.C. 826 and in accordance with 21 CFR part 1303 would be required in order to manufacture HCPs.

**Inventory.** Any person who becomes registered with the DEA after the effective date of the final rule would be required to take an initial inventory of all stocks of controlled substances (including HCPs) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to 21 U.S.C. 827, 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11(a) and (b).

After the initial inventory, every DEA registrant would be required to take a new inventory of all stocks of controlled substances on hand every two years, pursuant to 21 U.S.C. 827, 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

**Records.** Every DEA registrant would be required to maintain records with respect to HCPs pursuant to 21 U.S.C. 827, 958, and in accordance with 21 CFR parts 1304, 1307, and 1312.

**Reports.** Every DEA registrant would be required to submit reports regarding HCPs to the Automation of Reports and Consolidated Order System (ARCOS) pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.33.

**Orders for HCPs.** Every DEA registrant who distributes HCPs would be required to comply with order form requirements, pursuant to 21 U.S.C. 828, and in accordance with 21 CFR part 1305.

**Prescriptions.** All prescriptions for HCPs would need to comply with 21 U.S.C. 829, and would be required to be issued in accordance with 21 CFR part 1306, and part 1311 subpart C.

**Importation and Exportation.** All importation and exportation of HCPs would need to be in compliance with 21 U.S.C. 952, 953, 957, 958, and in accordance with 21 CFR part 1312.

**Liability.** Any activity involving HCPs not authorized by, or in violation of, the CSA, would be unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

#### Regulatory Analyses

##### Executive Orders 12866 and 13563

In accordance with 21 U.S.C. 811(a), this proposed scheduling action is subject to formal rulemaking procedures performed “on the record after opportunity for a hearing,” which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the procedures and criteria for scheduling a drug or other substance.

Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to Section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

##### Executive Order 12988

This proposed regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 Civil Justice Reform to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

##### Executive Order 13132

This proposed rulemaking does not have federalism implications warranting the application of Executive Order 13132. The proposed rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or the distribution of power and responsibilities among the various levels of government.

##### Executive Order 13175

This proposed rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

##### Regulatory Flexibility Act

The Administrator, in accordance with the Regulatory Flexibility Act (5 U.S.C. 601–612) (RFA), has reviewed this proposed rule, and by approving it, certifies that it will not have a significant economic impact on a substantial number of small entities. The purpose of this proposed rule is to place HCPs into schedule II of the CSA. No less restrictive measures (i.e., non-control or control in a lower schedule) would enable the DEA to meet its statutory obligation under the CSA.

HCPs are widely prescribed drugs for the treatment of pain and cough suppression. Handlers of HCPs primarily include manufacturers, distributors, exporters, pharmacies, practitioners, mid-level practitioners, and hospitals/clinics.<sup>22</sup> It is possible

<sup>22</sup> For purposes of performing regulatory analysis, the DEA uses the definition of a “practitioner” as a physician, veterinarian, or other individual licensed, registered, or otherwise permitted, by the United States or the jurisdiction in which he/she practices, to dispense a controlled substance in the

that other registrants, such as importers, researchers, analytical labs, teaching institutions, etc., also handle HCPs. However, based on its understanding of its registrant population, the DEA assumes for purposes of this analysis that for all business activities other than manufacturers, distributors, exporters, pharmacies, practitioners, mid-level practitioners, and hospitals/clinics, that the volume of HCPs handled is nominal, and therefore *de minimis* to the economic impact determination of this proposed rescheduling action.

Because HCPs are so widely prescribed, for the purposes of this analysis, the DEA conservatively assumes all distributors, exporters, pharmacies, practitioners, mid-level practitioners, and hospitals/clinics currently registered with the DEA to handle schedule III controlled substances are also handlers of HCPs. The DEA estimated the number of manufacturers and exporters handling HCPs directly from DEA records. In total, the DEA estimates that nearly 1.5 million controlled substance registrations, representing approximately 376,189 entities, would be affected by this rule.

The DEA does not collect data on company size of its registrants. The DEA used DEA records and multiple subscription-based and public data sources to relate the number of registrations to the number of entities and the number of entities that are small entities. The DEA estimates that of the 376,189 entities that would be affected by this rule, 366,351 are “small entities” in accordance with the RFA and Small Business Administration size standards. 5 U.S.C. 601(6); 15 U.S.C. 632.<sup>23</sup>

The DEA examined the registration, security (including storage), labeling and packaging, quota, inventory, recordkeeping and reporting, ordering, prescribing, importing, exporting, and disposal requirements for the 366,351 small entities estimated to be affected by the proposed rule. The DEA estimates that only the physical security requirements will have material economic impact and such impacts will be limited to manufacturers, exporters, and distributors. Many manufacturers and exporters are likely to have sufficient space in their existing vaults to accommodate HCPs. However, the DEA understands that some manufacturers, exporters, and

course of professional practice, but does not include a pharmacist, pharmacy, or hospital (or other person other than an individual).

<sup>23</sup> The estimated break-down is as follows: 50 manufacturers, 4 exporters, 683 distributors, 50,774 pharmacies, and 314,840 practitioners/mid-level practitioners/hospitals/clinics.

distributors will need to build new vaults or expand existing vaults to store HCPs in compliance with schedule II controlled substance physical security requirements. Due to the uniqueness of each business, the DEA made assumptions based on research and institutional knowledge of its registrant community to quantify the costs associated with physical security requirements for manufacturers, exporters and distributors.

The DEA estimates there will be significant economic impact on 1 (2.0%) of the affected 50 small business manufacturers, and 54 (7.9%) of the affected 683 small business distributors. The DEA estimates no significant impact on the remaining affected 4 small business exporters, 50,774 small business pharmacies, or 314,840 small business practitioners/mid-level practitioners/hospitals/clinics. In summary, 55 of the 366,351 (0.015%) affected small entities are estimated to experience significant impact, (i.e., incur costs greater than 1% of annual revenue) if the proposed rule were finalized. The percentage of small entities with significant economic impact is below the 30% threshold for all registrant business activities. The DEA’s assessment of economic impact by size category indicates that the proposed rule will not have a significant effect on a substantial number of these small entities.

The DEA’s assessment of economic impact by size category indicates that the proposed rule to reschedule HCPs as schedule II controlled substances will not have a significant economic impact on a substantial number of small entities. The DEA will consider written comments regarding the DEA’s economic analysis of the impact of such rescheduling, including this certification, and requests that commenters describe the specific nature of any impact on small entities and provide empirical data to illustrate the extent of such impact.

#### *Unfunded Mandates Reform Act of 1995*

On the basis of information contained in the “Regulatory Flexibility Act” section above, the DEA has determined and certifies pursuant to the Unfunded Mandates Reform Act (UMRA) of 1995 (2 U.S.C. 1501 *et seq.*), that this action would not result in any Federal mandate that may result “in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted for inflation) in any one year \* \* \*.” Therefore, neither a Small Government Agency Plan nor any other

action is required under provisions of the UMRA of 1995.

#### *Paperwork Reduction Act of 1995*

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

#### **List of Subjects in 21 CFR Part 1308**

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, 21 CFR part 1308 is proposed to be amended to read as follows:

#### **PART 1308—SCHEDULES CONTROLLED SUBSTANCES**

- 1. The authority citation for 21 CFR part 1308 continues to read as follows:

**Authority:** 21 U.S.C. 811, 812, 871(b) unless otherwise noted.

#### **§ 1308.13 [Amended]**

- 2. Amend § 1308.13 by removing paragraphs (e)(1)(iii) and (iv) and redesignating paragraphs (e)(1)(v) through (viii) as (e)(1)(iii) through (v), respectively.

Dated: February 21, 2014.

**Michele M. Leonhart,**  
*Administrator.*

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#### **DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT**

#### **24 CFR Parts 50 and 58**

**[Docket No. FR-5616-P-01]**

**RIN 2506-AC34**

#### **Environmental Compliance Recordkeeping Requirements**

**AGENCY:** Office of Secretary, HUD.  
**ACTION:** Proposed rule.

**SUMMARY:** This proposed rule would revise the regulations governing the format used for conducting the required environmental reviews for HUD program and policy actions. HUD’s current regulations require that HUD staff document part 50 environmental review compliance using form HUD-