Billing Code 4410-09-P

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

[Docket No. DEA-1228E]

Established Aggregate Production Quotas for Schedule I and II Controlled Substances and Assessment of Annual Needs for the List I Chemicals Ephedrine, Pseudoephedrine, and Phenylpropanolamine for 2024

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final order.

SUMMARY: This final order establishes the initial 2024 aggregate production quotas for controlled substances in schedules I and II of the Controlled Substances Act and the assessment of annual needs for the list I chemicals ephedrine, pseudoephedrine, and phenylpropanolamine.

DATE: This Notice is effective [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

FOR FURTHER INFORMATION CONTACT: Scott A. Brinks, Regulatory Drafting and Policy Support Section, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, VA 22152, Telephone: (571) 776-3882.

SUPPLEMENTARY INFORMATION:

I. Legal Authority

Section 306 of the Controlled Substances Act (CSA) (21 U.S.C. 826) requires the

Attorney General to establish aggregate production quotas for each basic class of controlled substance listed in schedule I and II and for the list I chemicals ephedrine, pseudoephedrine, and phenylpropanolamine. The Attorney General has delegated this function to the Administrator of the Drug Enforcement Administration (DEA) pursuant to 28 CFR 0.100.

II. Background

The 2024 aggregate production quotas (APQ) and assessment of annual needs (AAN) represent those quantities of schedule I and II controlled substances and the list I chemicals ephedrine, pseudoephedrine, and phenylpropanolamine that may be manufactured in the United States in 2024, in order to provide for the estimated medical, scientific, research, and industrial needs of the U.S., lawful export requirements, and the establishment and maintenance of reserve stocks. These quotas include imports of ephedrine, pseudoephedrine, and phenylpropanolamine, but do not include imports of controlled substances for use in industrial processes.

On November 2, 2023, a notice titled "Proposed Aggregate Production Quotas for Schedule I and II Controlled Substances and Assessment of Annual Needs for the List I Chemicals Ephedrine, Pseudoephedrine, and Phenylpropanolamine for 2024" was published in the *Federal Register*. 88 FR 75312. This notice proposed the 2024 APQ for each basic class of controlled substance listed in schedules I and II and the 2024 AAN for the list I chemicals ephedrine, pseudoephedrine, and phenylpropanolamine. All interested persons were invited to comment on or object to the proposed APQ and the proposed AAN on or before December 4, 2023.

III. Comments Received

Within the public comment period, DEA received 4,699 comments from DEA registrants, people with chronic pain, patients with attention deficit/hyperactivity disorder (ADHD), pain advocacy associations, U.S. professional associations, U.S. nurses, the Royal Australian and New Zealand College of Psychiatrists, the Australian ADHD Professionals Association, the ADHD Foundation Australia, and others. The comments included concerns about potential domestic opioid drug shortages due to further quota reductions; stimulant drug shortages in the United States and Australia; concerns that medical professionals might be impeded from exercising their medical expertise regarding opioid prescriptions; two requests for a public hearing; concerns with the implementation of quarterly quota allotments, and comments not pertaining to DEA regulated activities. DEA restricted seven comments from public view due to confidential business information and/or confidential personal identifying information.

Opioid Adequacy

Issue (Medication Out of Stock at Pharmacy Level): Commenters questioned whether the 2024 proposed APQs for Schedule II opioids will be adequate to meet legitimate medical needs of patients. Commenters said that because of decreases in aggregate production quotas for specific opioids, they have had difficulty filling legitimate prescriptions at pharmacies. These issues have negatively impacted their quality of life and caused mental health-related issues, possibly leading to suicide.

DEA Response: DEA is committed to ensuring an adequate and uninterrupted supply of controlled substances in order to meet legitimate medical, scientific, and export needs of

the United States. DEA sets the APQs for controlled substances based on the available data and information received at that specific point in time set by the regulations, however, subsequent factors and manufacturers' business practices may arise afterwards and potentially contribute to a temporary lack of inventory of controlled substances at the point of dispensation. In recent years, this has included labor shortages and a lack of production capacity. In such circumstances, DEA, in coordination with the Food and Drug Administration (FDA), can utilize tools under the CSA to prevent or alleviate drug shortages and ensure that patients are able to fill legitimate prescriptions for controlled substances without undue delay. Additionally, if a patient is faced with a delay in receiving their medications, the patient may request a one-time transfer of initial dispensing of an electronic prescription for Schedules II – V controlled substances from one retail pharmacy to another retail pharmacy. If the medication is a controlled substance in Schedules III – V and includes authorized refills, the refills can also be transferred with the initial prescription to the receiving pharmacy.

Issue (Nationwide Shortages): Some commenters stated that there is a nationwide shortage of opioid medication because their local pharmacies were often out of stock. One commenter also stated that the American Society of Health-System Pharmacists (ASHP) has warned about shortages of immediate release oxycodone and hydrocodone medications, but shortages have not been publicly acknowledged by DEA or FDA.

DEA Response: DEA utilizes the available, reliable data and information received by the agency at the time APQs are proposed and proactively monitors drug production, distribution and supply during the year. However, drug shortages may occur

subsequently due to factors outside of DEA control such as manufacturing and quality problems, processing delays, supply chain disruptions, or discontinuations. In such circumstances, if the drug manufacturer notifies the FDA Drug Shortage Staff, FDA will coordinate with DEA to address and minimize the impact of drug shortages if both agencies believe action is warranted. Currently, FDA has not issued any nationwide shortages of oxycodone and hydrocodone products.

Issue (Patients Switching to Illicit Fentanyl or Medications Obtained from Illegal Sources): Several commenters expressed concerns that because of DEA's reduction of quotas for pain relieving controlled substances, patients with chronic pain who were unable to fill their legitimate prescriptions eventually turned to illegal fentanyl or medications obtained from illegitimate sources as a substitute relief that could increase the risk of overdose death. These commenters stated that overdose deaths in the United States continue to rise because of illegal fentanyl or illegitimate medications, not from pharmaceutical medications prescribed to patients with chronic pain.

DEA Response: In proposing and establishing APQs for opioids, DEA considers rates of overdose deaths. Congress, in 21 U.S.C. 826(i), mandates DEA to estimate diversion for five controlled substances—fentanyl, hydrocodone, hydromorphone, oxycodone, and oxymorphone. This estimation must consider the rates of overdose deaths, among other factors. While overdose deaths may occur as a result of use of illicit substances, DEA's quotas help prevent misuse and diversion of pharmaceutical controlled substances. In this way, these quotas can reduce the occurrence of overdose and death from the use of legitimate controlled substances. Patients should work closely with their providers to

utilize other FDA-approved medications for their conditions and fill their prescriptions only from DEA-registered pharmacies. The only safe medications are ones prescribed by a trusted, DEA-registered medical professional and dispensed by a licensed pharmacist at a DEA-registered pharmacy. The medications received from unregistered internet sources may, in fact, be manufactured or laced with illicit substances including illicit fentanyl, which contributes to rates of overdose deaths.

Issue (Prescribing Hesitancy): Many commenters, mostly self-identified patients with chronic pain patients, expressed that the goal of the 2016 Centers for Disease Control and Prevention (CDC) Guidelines was to decrease opioid overdoses, but instead there has been an increase in overdoses nationwide of over 400 percent due to illegal fentanyl or illegally manufactured pain pills. Commenters stated that many patients with chronic pain patients have been harmed, and some have died by suicide, due to the inability to get prescriptions because of the APQ reductions made by DEA. Many commenters also stated that restrictions imposed by DEA have caused opioid medications to be under-prescribed due to fear of prosecution. Commenters said doctors should have latitude in making treatment decisions to prescribe opioid pain medications based on individual patient needs.

DEA Response: Pursuant to the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities (SUPPORT) Act, DEA is mandated to estimate diversion for 5 controlled substances – fentanyl, hydrocodone, hydromorphone, oxycodone and oxymorphone, and this estimation includes the consideration of rates of overdose deaths. While overdose deaths may occur as a result of

the use of illegal fentanyl or illegally manufactured pain medications, quotas are being set by the DEA to prevent misuse and diversion of pharmaceutical controlled substances, and thus reducing the occurrence of overdose and death from the use of legitimate controlled substances. Additionally, DEA's regulations do not impose restrictions on the amount and the type of medication that licensed practitioners can prescribe. DEA has consistently emphasized and supported the authority of individual practitioners under the CSA to administer, dispense, and prescribe controlled substances for the legitimate treatment of pain within acceptable medical standards, as outlined in DEA's policy statement published in the Federal Register on September 6, 2006, titled Dispensing Controlled Substances for the Treatment of Pain. 71 FR 52716.

Attention Deficit/Hyperactivity Disorder Medications Medication Shortages

Issue: DEA received comments expressing general concerns regarding the ongoing shortages experienced with ADHD medications produced from amphetamine and methylphenidate.

DEA Response: DEA is committed to ensuring an adequate and uninterrupted supply of controlled substances in order to meet the estimated legitimate medical, scientific, research, and industrial needs of the United States, for lawful export requirements, and for the establishment and maintenance of reserve stocks. DEA sets the APQs to provide for all legitimate medical purposes and for anticipated foreign demand. Additionally, DEA and FDA coordinate efforts to prevent or alleviate drug shortages. Such efforts may include the adjustment of the APQs and individual domestic manufacturers' quotas, FDA's approval of additional market competitors, and coordination between the agencies

to allow importation of foreign-manufactured drug products that meet FDA approval. Based on the data DEA considers in setting the APQs, including any new FDA approved drug products, as well as manufacturing issues that DEA considers under 21 CFR 1303.11(b)(7), DEA determined that the proposed APQs for amphetamine, lisdexamfetamine and methylphenidate are sufficient to supply legitimate medical needs, reserve stocks, and export requirements for 2024. If the actual prescribing rates of these substances are significantly higher than the 2024 estimates of medical needs, the Administrator has the authority to increase the aggregate production quota at any time. 21 CFR 1303.13(a). For example, in 2023, DEA adjusted the methylphenidate (for sale) APQ to address shortages of methylphenidate HCL extended release tablets upon consideration of the criteria in accordance with 21 CFR 1303.13. Adjustment of Aggregate Production Quota for Methylphenidate (for sale) for 2023, 88 FR 68147 (October 3, 2023).

Issue (Lisdexamfetamine Shortages in Australia): DEA received comments from The ADHD Foundation Australia, Australian ADHD Professionals Association and the Royal Australian and New Zealand College of Psychiatrists. The ADHD Foundation Australia stated that the Australian Therapeutic Goods Administration (TGA) has advised of current shortages of lisdexamfetamine, with more shortages predicted into 2024, under the current production quotas. This commenter also asserted that Australia's domestic prescriptions of lisdexamfetamine have increased by over 150% from 2020-2022 due to increased awareness and diagnosis of ADHD. The Royal Australian and New Zealand College of Psychiatrists commented that they endorse the guidelines from the Australian

ADHD Professionals Association. Both the ADHD Foundation Australia and Australian ADHD Professionals Association stated that Vyvanse (lisdexamfetamine) and methylphenidate are the only two extended-release medications approved by the TGA to treat ADHD in Australia. Although Vyvanse's patent expired in August 2023 in the United States, Vyvanse remains under patent in Australia and generic lisdexamfetamine products will not be available. The commenters are concerned that the proposed 2024 lisdexamfetamine APQ has not been increased from 2023 levels despite reports of shortages in both the United States and Australia. They are also concerned that any U.S. production quotas allocated for production of Vyvanse will decrease as U.S. production quotas will instead be allotted to manufacture domestic generic products instead. The commenters requested that DEA consider increasing 2024 lisdexamfetamine APQ to resolve shortages in Australia and Aotearoa New Zealand.

DEA Responses: DEA considered the comments, additional export data, recent domestic consumption data, and determined that the proposed APQ for lisdexamfetamine will remain at the level proposed based on its belief that inventory of bulk active pharmaceutical ingredient (API) and the quantities which will be produced in 2024 will be sufficient to meet the growing medical usage in domestic and foreign markets. DEA is closely monitoring manufacturing and distribution data from manufacturers of FDA-approved drug products as reported by the company, Automation of Reports and Consolidated Orders System (ARCOS) reports, prescription dispensing data from IQVIA, and estimated and actual inventories to ensure that there is an adequate and uninterrupted supply. In addition, DEA is pursuing the purchase of additional third-party

data to better understand market penetration and demand in foreign countries – such as Australia – where American-made API and/or pharmaceutical preparations are dispensed.

Market Entry of Generic Lisdexamfetamine Products

Issue: DEA received comments from one association representing manufacturers and one dosage form manufacturer. They stated that DEA generally allocates procurement quotas using a company's historical sales of a drug. They asserted that this practice denies greater quota allocation to generic drug manufacturers who are entering the market following the expiration of a patent, due to the fact that new entrants do not have an established sales history. The association claimed that DEA's application process does not solicit information tailored to this situation. The association said that DEA's practice hindered the competition of generic lisdexamfetamine products, with the patent holder of Vyvanse holding onto a high share of the market.

DEA Response: DEA typically grants individual commercial manufacturing procurement quotas based on the sales history of the drug as reported by the company, ARCOS and IQVIA data, inventory estimated and actual, inventory allowed by regulation, and manufacturing process loss of existing manufacturers. DEA has always been cognizant that new manufacturers entering the market for the first time would not have any established sales history, and thus the manufacturer's past sales history is not a factor when determining the amount of quota needed to launch a new product. Instead, DEA considers other data including the historic timelines of the shift in prescribing from a branded product to a generic product(s) for controlled substances. For example, when the patent for Vyvanse expired in August 2023, DEA solicited additional information from

each FDA-approved manufacturer and considered the following factors to determine the amount of quota a dosage form manufacturer needed to launch a new generic lisdexamfetamine product: (1) the overall patient utilization for the branded product for the past 3 years, (2) the current estimated patient utilization for the current year, (3) the remaining months in the current year needed to meet patient needs, (4) the amount of quota previously granted for saleable validation, (5) current inventory of finished goods, in-process material and API, and (6) the amount of finished goods already shipped into the distribution chain.

The assertion that DEA's practice allowed the patent holder of Vyvanse to hold onto a higher share of the market is incorrect. However, DEA did consider that the current year (2023) would only allow for 4 months of brand erosion when allocating quota necessary to launch the generic lisdexamfetamine products. Some manufacturers were denied additional quota because their current inventory of saleable products was sufficient for a product launch during the remaining four months of the calendar year.

Diversion Estimates

Issue (Impact of Diversion Estimate on Opioids): Several commenters stated that the APQs of prescription opioids should not be reduced from calendar year 2023 APQ levels, given that less than 1 percent of prescription opioids are diverted.

DEA Response: DEA not only considers the extent of diversion, but it also considers other factors, as required by regulation, when determining the APQ. 21 U.S.C. 826(a), 21 CFR 1303.11(b). These factors include total net disposal of the class by all manufacturers during the current and 2 preceding years, trends in the national rate of net disposal of the

class, total actual or estimated inventories of the class and of all substances manufactured from the class, information obtained from the Food and Drug Administration, and changes in the currently accepted medical use in treatment. Additional factors considered can be found in 21 CFR 1303.11(b). After considering all of the relevant factors, DEA has determined that the APQs of prescription opioids should be reduced from calendar year 2023 APQ levels and they are sufficient to meet the forecasted domestic and foreign medical needs.

Issue (Underestimation of Opioid Diversion): One pharmaceutical company suggested that DEA underestimated actual diversion of opioids. The commenter said nonmedical use of prescription opioids is not a legitimate medical purpose, but DEA rejected this point in calculating diversion, and thus the 2024 APQ must be reduced for nonmedical use of prescription opioids. The commenter also asserted that the estimate is incomplete because a number of states did not provide Prescription Drug Monitoring Program (PDMP) data for the five covered controlled substances. Additionally, the commenter asserted that DEA rejected CDC guidelines of not prescribing greater than 90 morphine milligram equivalence (MME) daily and used 240 MME to calculate diversion.

DEA Response: The cited 2016 report[1] provides insightful information regarding the relationship between nonmedical prescription-opioid use and heroin use. However, it does not provide data in a form which DEA could utilize to modify its nationwide estimate for the diversion of oxycodone. Additionally, as stated in the published 2024

[1] Compton WM, Jones CM, Baldwin J. *Relationship between nonmedical prescription-opioid use and heroin use.* N Engl J Med. 2016;374(2):154–63, accessed from https://www.nejm.org/doi/full/10.1056/NEJMra1508490

Proposed APQ, DEA used available data at wholesale distribution and retail dispensing channels, *i.e.,* DEA's Theft/Loss Reports and available individual state PDMP data.

The state PDMP data submitted was adequate to allow DEA to draw reliable inferences regarding the state and U.S. population. The sample is large enough to allow DEA to accurately generalize the data to the whole population of the United States for use in the calculation of estimated national levels of diversion of the covered controlled substances.

The 2022 CDC Clinical Practice Guideline includes information that updates and replaces the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain. The 2022 CDC guidelines no longer set rigid dosage thresholds or duration of opioid therapy. Although DEA accepts CDC guidelines for prescribing opioids, DEA believes that higher dosages place individuals at higher risk of overdose and death, and prescriptions involving dosages exceeding 240 MME daily may indicate diversion, such as illegal distribution of controlled substances or prescribing outside the usual course of professional practice.

Issue (Use of Diversion Estimate for all Controlled Substances): One commenter questioned why diversion estimates were not considered for the stimulants when proposing the initial 2024 APQ.

DEA Response: Pursuant to 21 CFR 1303.11(b)(5), DEA considered the extent of diversion of the basic class as a factor in setting each APQ for each respective basic class, as well as the extent of diversion for all other schedule I and II controlled substances in proposing the estimated APQ. Under 21 U.S.C. 826(i)(A), DEA is only required to

publish the diversion estimates for 5 specific opioids.

Data Collection and Analysis

Issue (Data Accuracy): Several commenters stated FDA's estimation of medical needs and DEA's data collection process are flawed and inaccurate.

DEA Response: FDA utilizes a variety of data sources in developing its estimates of domestic medical needs. When determining the 2024 APQs, DEA considered the estimation of domestic medical needs data provided by FDA, and also considered other data sources including prescriptions dispensed in prior and current years reported in IQVIA, research and clinical trials information from DEA-registered researchers and manufacturers, information provided in quota applications from DEA-registered manufacturers, as well as historic and current year export data and future estimations of export requirements. DEA is actively reevaluating and improving the data collection process to ensure the APQs are set at an adequate level to meet legitimate medical, scientific, research, and export needs while establishing and maintaining reserve stocks.

Issue (Lack of Real-Time Data): One commenter opined that DEA lacks real-time data on opioid production and distribution. The lack of real-time data makes it difficult to accurately assess legitimate medical needs of patients and ensure adequate supply of opioid pain medications.

DEA Response: DEA has access to sales data provided by manufacturers from the Quota and Year-end Reporting Management System (QMS), ARCOS reports, and monthly IQVIA data when determining legitimate medical needs to ensure an adequate supply of medications containing schedule II controlled substances. Additionally, DEA is

considering regulatory changes to gain access to more real-time data such as requiring manufacturers and distributors to report sales data into the ARCOS database on a monthly basis to improve the timeliness and accuracy of data points being used to estimate legitimate medical needs.

Issue (Lack of Data Transparency): Two commenters stated that there is a lack of transparency in the quota setting process.

DEA Response: DEA is considering methods that might increase transparency in its quota setting process. Future regulatory proposals may include steps such as public notification and an opportunity for public input when prescribing rates for controlled substances substantially deviate from FDA's estimate of medical needs. DEA must strike a balance between increasing transparency and complying with laws and regulations aimed at protecting confidential business and patient information.

Schedule I Controlled Substances

Issue (Religious Use of Schedule I Substances): Two commenters requested that DEA increase APQs for certain schedule I controlled substances, including: psilocin, psilocybin, mescaline, ibogaine, lysergic acid diethylamide (LSD), 2-(4-Iodo-2,5-dimethoxyphenyl)ethanamine (2CI), dimethyltryptamine (DMT), 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) for religious use. They also commented that the APQ for mescaline should be increased in order to allow access to members of the Native American Church, as well as replanting into the wild because of shortages. They opined that DEA has disregarded their legal religious use of psychedelics as a factor when setting the production quotas of these substances. They also requested a hearing with the

Administrator if DEA does not take their freedom of religion into consideration.

DEA Response: In the past, DEA held discussions with representatives of indigenous communities when requested and continued to welcome further engagement and input. The APQs are determined in part by the individual manufacturing quota requests submitted by DEA-registered manufacturers of these substances. DEA received quota applications from DEA-registered manufacturers for 5-MeO-DMT, psilocin, psilocybin, mescaline, LSD, 2CI, DMT and 5-MeO-DMT. DEA has considered these applications, along with the factors listed in 21 CFR 1303.11 (b) when determining the aggregate production quotas.

Issue: Two commenters commented that the APQs should include fruiting bodies containing psilocybin and psilocin and peyote buttons containing mescaline, rather than pure chemicals only.

DEA Response: Psilocybin and psilocin are schedule I controlled substances naturally occurring in psychedelic mushrooms, while mescaline is the schedule I controlled substance naturally occurring in peyote. Because the CSA controls psilocybin and psilocin specifically, DEA will continue to establish APQ for those two substances. The APQs apply to psilocybin and psilocin that is manufactured synthetically as well as to substances that are derived naturally. Peyote is controlled under 21 U.S.C. 812(e) Schedule I (c) as a separate controlled substance from mescaline. As noted below, the APQ for peyote was proposed and is established at zero

Comments and quota applications from DEA-Registered Manufacturers

Issue: DEA received comments from three DEA-registered manufacturers regarding 3

different schedule I and II controlled substances, requesting that the proposed APQ for dexmethylphenidate (for conversion), lisdexamfetamine, and psilocybin be established at sufficient levels to allow for manufacturers to meet medical and scientific needs. DEA also received additional or revised quota applications for 4-Anilino-N-phenethyl-4-piperidine (4-ANPP), all other tetrahydrocannabinol, delta-9- tetrahydrocannabinol, dimethyltryptamine, fentanyl and pentobarbital.

DEA Response: DEA considered the comments and quota applications from the DEA-registered manufacturers and determined that DEA's proposed APQs will be increased for the abovementioned controlled substances, except lisdexamfetamine. The increases are reflected below in the section titled Determination of 2024 Aggregate Production Quotas and Assessment of Annual Needs.

List 1 Chemical (Pseudoephedrine)

Issue: Several pharmaceutical companies and healthcare organizations asserted that at a recent advisory meeting convened by the FDA, the advisory committee voted that phenylephrine, a common ingredient found in many over-the counter (OTC) cold and cough medications, is a safe but is ineffective as a decongestant at the 10 mg dose. According to FDA's website[2], FDA has yet to make a final decision on the status of phenylephrine. In light of this information, the commenters suggested that DEA should re-evaluate whether the 2024 pseudoephedrine (for sale) AAN is adequate given potential repercussions on the supply of and demand for phenylephrine-containing products, should FDA no longer designate phenylephrine as "generally recognized as safe and

[2] FDA clarifies results of recent advisory committee meeting on oral phenylephrine | FDA

effective" (GRASE).

DEA Response: DEA considered the comments and consulted with the FDA and determined that an increase of the 2024 pseudoephedrine (for sale) AAN from its proposed value currently is appropriate, and will continue to monitor inventory and use to ensure that there will be sufficient supply to address a potential increase in consumer demand for pseudoephedrine products should FDA determine that products containing phenylephrine are ineffective. The increase finalized herein will ensure that there is sufficient pseudoephedrine API for the manufacturing of OTC medications that are commonly used to treat congestion from cold, flu, allergy and COVID.

Quarterly Quota Allotment Implementation

Issue: DEA received comments from DEA-registered manufacturers and an association representing manufacturers regarding how DEA will implement quarterly quota allotment. They expressed concerns that DEA did not give sufficient notice of this significant change to adjust their business planning and schedules. They also believe that the quarterly quota allotment will cause a bottleneck and exacerbate shortages of medications.

DEA Response: As part of its commitment to ensure that all Americans have access to appropriately prescribed medications, DEA studied the supply chain dynamics for controlled substances subject to quotas, especially for those schedule II controlled substances in shortage. Beyond the lack of real-time data and gaps in its understanding of production lead times which DEA is seeking to resolve in forthcoming proposed regulatory changes, DEA also concluded that its existing quota allocation model did not

allow it to remain nimble when patent exclusivity for Vyvanse expired and FDA authorized fourteen (14) generic manufacturers to begin marketing. DEA's challenges with its existing allocation model were exacerbated because the loss of patent exclusivity occurred late in the quota year, a time when DEA had already allocated significant authority to the manufacturer of Vyvanse and due to the Food and Drug Administration's (FDA) decision that it would not provide 6-months of patent exclusivity to the first applicant who files a substantially complete abbreviated new drug application (commonly referred to as "first filer exclusivity").

With regard to comments that quarterly quotas will create bottlenecks and exacerbate drug shortages, DEA disagrees. There are several reasons why manufacturers of drugs containing controlled substances subject to quotas either gain (or lose) market share in any given calendar year for which a quota applies and include: changes in demand and a manufacturer's ability to adjust to those changes relative to its competitors; inflationary pressures which impact a manufacturer's profit margin and subsequent decisions to either continue (or discontinue) marketing; labor shortages in certain geographic areas; and supply chain difficulties which impact access to API, excipients, equipment and packaging material. In order for DEA to ensure an adequate and uninterrupted supply of schedule II controlled substances necessary to meet legitimate medical, commercial, and scientific needs, DEA believes that changes in its approach to allocating procurement quotas will ensure that it is best positioned to respond appropriately to changes in market demand. Along similar lines, DEA does not believe that applying these changes to schedule II drugs only after they enter shortage would be

sufficient, as DEA would then need to gather data and information for those drugs, a process which would delay DEA's efforts to address shortages and potentially exacerbate them.

DEA has elected to make these changes at the beginning of the 2024 quota year and will be providing guidance to manufacturers. Information gained from its approach will inform rulemaking which it is currently pursuing.

Administrative Procedures Act

Issue: DEA received comments from DEA-Registered manufacturers, an association representing manufacturers and the generic public that the quarterly quota allotment implementation did not go through a notice-and-comment rulemaking procedure as required by the Administrative Procedure Act.

DEA Response: DEA has elected to make changes at the beginning of the 2024 quota year as it believes that information gained from its approach will inform rulemaking which is currently being pursued. In addition, as discussed above, DEA is undertaking these changes for the 2024 quota year to allow it to more quickly and nimbly respond to fast-changing market trends, including potential shortages, with respect to medications subject to quotas. While these changes to the quota allotment process will impact the adjudication of individual quota applications, they do not affect any APQs set pursuant to this final order.

Request for Public Hearing

Issue: One pharmaceutical company requested a public hearing prior to publishing the Final Order to establish the initial 2024 APQ. This company requested a public hearing

"to correct the omissions and inaccurate diversion calculation in the 2023 oxycodone Quota." The company asserted that these omissions led to an inaccurate diversion calculation for oxycodone and that the 2024 APQ requires a significant reduction from the 2023 APQ.

DEA Response: The decision whether to grant a hearing on the issues raised by the commenter lies solely within the discretion of the Administrator. 21 CFR 1303.11(c). While hearings are required when requested by states in certain situations, this commenter is not a state. This request does not present any evidence that would lead to the conclusion that a hearing is necessary or warranted. DEA has addressed specific points raised by the commenter in Issues and Responses above.

Out of Scope Comments

DEA received comments that are outside the scope of this order. The comments were general in nature and raised issues with respect to specific medical illnesses, medical treatments and medication costs. These comments do not impact the analysis involved in establishing the 2024 APQ.

IV. Determination of 2024 Aggregate Production Quotas and Assessment of Annual Needs

In determining the established 2024 aggregate production quotas and assessment of annual needs, DEA has considered the above comments along with the factors set forth in 21 CFR 1303.11 and 21 CFR 1315.11, in accordance with 21 U.S.C. 826(a). These factors include, but are not limited to, the 2023 manufacturing quotas, current 2023 sales and inventories, anticipated 2024 export requirements, industrial use, additional

applications for 2024 quotas, and information on research and product development requirements.

On July 19, 2023, DEA published a temporary scheduling order placing Etizolam, Flualprazolam, Clonazolam, Flubromazolam, and Diclazepam in schedule I of the CSA (88 FR 48112), making all regulatory controls pertaining to schedule I controlled substances applicable to the manufacture of these substances, including the requirement to establish an aggregate production quota pursuant to 21 U.S.C. 826 and 21 CFR part 1303.

On December 12, 2023, DEA published a temporary scheduling order placing 4F–MDMB–BUTICA, 5F–EDMB–PICA, ADB–4en–PINACA, CUMYL–PEGACLONE, MDMB–4en–PINACA, MMB–FUBICA in schedule I of the CSA (88 FR 86040), making all regulatory controls pertaining to schedule I controlled substances applicable to the manufacture of these substances, including the requirement to establish an aggregate production quota pursuant to 21 U.S.C. 826 and 21 CFR part 1303.

On December 13, 2023, DEA published a final rule placing N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-butyl-1H-indazole-3-carboxamide (ADB–BUTINACA), 4-methyl-1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one (α-PiHP or alpha-PiHP), and 2-(methylamino)-1-(3- methylphenyl)propan-1-one (3–MMC or 3-methylmethcathinone) in schedule I of the Controlled Substances Act (CSA) (88 FR 86266), making all regulatory controls pertaining to schedule I controlled substances applicable to the manufacture of these substances, including the requirement to establish an aggregate production quota pursuant to 21 U.S.C. 826 and 21 CFR part 1303. Based on all of the above, the

Administrator is establishing the 2024 APQs for Etizolam, Flualprazolam, Clonazolam, Flubromazolam, and Diclazepam, 4F–MDMB–BUTICA, 5F–EDMB–PICA, ADB–4en–PINACA, CUMYL–PEGACLONE, MDMB–4en–PINACA, MMB–FUBICA, N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-butyl-1H-indazole-3-carboxamide (ADB-BUTINACA), 4-methyl-1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one (a-PiHP or alpha-PiHP), and 2-(methylamino)-1-(3- methylphenyl)propan-1-one (3-MMC or 3-methylmethcathinone) at greater than zero; and 4-Anilino-N-phenethyl-4-piperidine (4-ANPP), all other tetrahydrocannabinol, dexmethylphenidate (for conversion), delta-9-tetrahydrocannabinol, dimethyltryptamine, fentanyl, pentobarbital and psilocybin at higher levels than previously proposed.

The Administrator establishes the 2024 AAN for pseudoephedrine (for sale) at a higher level than was proposed.

Estimates of Diversion Pursuant to the SUPPORT Act

As specified in the proposal, and as required by 21 U.S.C. 826(i), DEA calculated a national diversion estimate for each of the covered controlled substances.

This data, which remains unchanged, was published in the *Proposed Aggregate Production Quotas for Schedule I and II Controlled Substances and Assessment of Annual Needs for the List I Chemicals Ephedrine, Pseudoephedrine, and Phenylpropanolamine for 2024*. 88 FR 75312 (November 2, 2023).

In accordance with 21 U.S.C. 826, 21 CFR 1303.11, and 21 CFR 1315.11, the Administrator hereby establishes the 2024 APQ for the following schedule I and II controlled substances and the 2024 AAN for the list I chemicals ephedrine,

pseudoephedrine, and phenylpropanolamine, expressed in grams of anhydrous acid or base, as follows:

Basic Class	Established 2024 Quotas (g)
New Temporary Controlled Schedule I Substances	
4F–MDMB–BUTICA	30
5F–EDMB–PICA	30
ADB–4en–PINACA	30
Clonazolam	30
CUMYL–PEGACLONE	30
diclazepam	30
etizolam	30
flualprazolam	30
flubromazolam	30
MDMB–4en–PINACA	30
MMB–FUBICA	30
Schedule I	
-[1-(2-Thienyl)cyclohexyl]pyrrolidine	20
1-(1-Phenylcyclohexyl)pyrrolidine	30
1-(2-Phenylethyl)-4-phenyl-4-acetoxypiperidine	10
1-(5-Fluoropentyl)-3-(1-naphthoyl)indole (AM2201)	30
1-(5-Fluoropentyl)-3-(2-iodobenzoyl)indole (AM694)	30
1-[1-(2-Thienyl)cyclohexyl]piperidine	15
2'-fluoro 2-fluorofentanyl	30
1-Benzylpiperazine	25
1-Methyl-4-phenyl-4-propionoxypiperidine	10
2-(2,5-Dimethoxy-4-ethylphenyl)ethanamine (2C-E)	30
2-(2,5-Dimethoxy-4-methylphenyl)ethanamine (2C-D)	30
2-(2,5-Dimethoxy-4-nitro-phenyl)ethanamine (2C-N)	30
2-(2,5-Dimethoxy-4-n-propylphenyl)ethanamine (2C-P)	30
2-(2,5-Dimethoxyphenyl)ethanamine (2C-H)	100
2-(4-Bromo-2,5-dimethoxyphenyl)-N-(2-methoxybenzyl)ethanamine (25B-NBOMe; 2C-B-NBOMe; 25B; Cimbi-36)	30

2-(4-Chloro-2,5-dimethoxyphenyl)ethanamine (2C-C)	30
2-(4-Chloro-2,5-dimethoxyphenyl)-N-(2-methoxybenzyl)ethanamine (25C-NBOMe; 2C-C-NBOMe; 25C; Cimbi-82)	25
2-(4-Iodo-2,5-dimethoxyphenyl)ethanamine (2C-I)	30
2-(4-Iodo-2,5-dimethoxyphenyl)-N-(2-methoxybenzyl)ethanamine (25I-NBOMe; 2C-I-NBOMe; 25I; Cimbi-5)	30
2,5-Dimethoxy-4-ethylamphetamine (DOET)	25
2,5-Dimethoxy-4-n-propylthiophenethylamine	25
2,5-Dimethoxyamphetamine	25
2-[4-(Ethylthio)-2,5-dimethoxyphenyl]ethanamine (2C-T-2)	30
2-[4-(Isopropylthio)-2,5-dimethoxyphenyl]ethanamine (2C-T-4)	30
3,4,5-Trimethoxyamphetamine	30
3,4-Methylenedioxyamphetamine (MDA)	12,000
3,4-Methylenedioxymethamphetamine (MDMA)	12,000
3,4-Methylenedioxy-N-ethylamphetamine (MDEA)	40
3,4-Methylenedioxy-N-methylcathinone (methylone)	5,200
3,4-Methylenedioxypyrovalerone (MDPV)	35
3-FMC; 3-Fluoro-N-methylcathinone	25
3-Methylfentanyl	30
3-Methylmethcathinone	30
3-Methylthiofentanyl	30
4,4′-Dimethylaminorex	30
4-Bromo-2,5-dimethoxyamphetamine (DOB)	30
4-Bromo-2,5-dimethoxyphenethylamine (2-CB)	5,100
4-Chloro-alpha-pyrrolidinovalerophenone (4-chloro-alpha-PVP)	25
4-CN-Cumyl-Butinaca	25
4-Fluoroisobutyryl fentanyl	30
4F–MDMB–BINACA	30
4-FMC; Flephedrone	25
4-MEC; 4-Methyl-N-ethylcathinone	25
4-Methoxyamphetamine	150
4-methyl-1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one (alpha-PiHP)	30
4-Methyl-2,5-dimethoxyamphetamine (DOM)	25
4-Methylaminorex	25
4-Methyl-N-methylcathinone (mephedrone)	45

4-Methyl-alpha-ethylaminopentiophenone (4-MEAP)	25
4-Methyl-alpha-pyrrolidinohexiophenone (MPHP)	25
4′-Methyl acetyl fentanyl	30
4-Methyl-α-pyrrolidinopropiophenone (4-MePPP)	25
5-(1,1-Dimethylheptyl)-2-[(1R,3S)-3-hydroxycyclohexyl]-phenol	50
5-(1,1-Dimethyloctyl)-2-[(1R,3S)-3-hydroxycyclohexyl]-phenol (cannabicyclohexanol or CP-47,497 C8-homolog)	40
5F-AB-PINACA ; (1-Amino-3-methyl-1-oxobutan-2-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide	25
5F-ADB; 5F-MDMB-PINACA (methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate)	25
5F-CUMYL-P7AICA; 1-(5-Fluoropentyl)-N-(2-phenylpropan-2-yl)-1H-pyrrolo[2,3-b]pyridine-3carboximide	25
5F-CUMYL-PINACA	25
5F-EDMB-PINACA	25
5F-MDMB-PICA	25
5F-AMB (methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3-methylbutanoate)	25
5F-APINACA; 5F-AKB48 (N-(adamantan-1-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide)	25
5-Fluoro-PB-22; 5F-PB-22	25
5-Fluoro-UR144, XLR11 ([1-(5-fluoro-pentyl)-1Hindol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone	25
5-Methoxy-3,4-methylenedioxyamphetamine	25
5-Methoxy-N,N-diisopropyltryptamine	25
5-Methoxy-N,N-dimethyltryptamine	11,000
AB-CHMINACA	30
AB-FUBINACA	50
AB-PINACA	30
ADB-BUTINACA	30
ADB-FUBINACA (N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1H-indazole-3-carboxamide)	30
Acetorphine	25
Acetyl Fentanyl	100
Acetyl-alpha-methylfentanyl	30
Acetyldihydrocodeine	30
Acetylmethadol	25
Acryl Fentanyl	25

ADB-PINACA (N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-pentyl-1H-indazole-3-carboxamide)	50
AH-7921	30
All other tetrahydrocannabinol	1,166,130
Allylprodine	25
Alphacetylmethadol	25
alpha-Ethyltryptamine	25
Alphameprodine	25
Alphamethadol	25
alpha-Methylfentanyl	30
alpha-Methylthiofentanyl	30
alpha-Methyltryptamine (AMT)	25
alpha-Pyrrolidinobutiophenone (α-PBP)	25
alpha-pyrrolidinoheptaphenone (PV8)	25
alpha-pyrrolidinohexabophenone (alpha-PHP)	25
alpha-Pyrrolidinopentiophenone (α-PVP)	25
Amineptine	30
Aminorex	25
Anileridine	20
APINCA, AKB48 (N-(1-adamantyl)-1-pentyl-1H-indazole-3-carboxamide)	25
Benzethidine	25
Benzylmorphine	30
Betacetylmethadol	25
beta-Hydroxy-3-methylfentanyl	30
beta-Hydroxyfentanyl	30
beta-Hydroxythiofentanyl	30
beta-Methyl fentanyl	30
beta′-Phenyl fentanyl	30
Betameprodine	25
Betamethadol	4
Betaprodine	25
Brorphine	30
Bufotenine	15
Butonitazene	30
Butylone	25
Butyryl fentanyl	30
Cathinone	40
Clonitazene	25

Codeine methylbromide	30
Codeine-N-oxide	192
Crotonyl Fentanyl	25
Cyclopentyl Fentanyl	30
Cyclopropyl Fentanyl	20
Cyprenorphine	25
d-9-THC	1,523,040
Desomorphine	25
Dextromoramide	25
Diapromide	20
Diethylthiambutene	20
Diethyltryptamine	25
Difenoxin	9,300
Dihydromorphine	639,954
Dimenoxadol	25
Dimepheptanol	25
Dimethylthiambutene	20
Dimethyltryptamine	11,000
Dioxyaphetyl butyrate	25
Dipipanone	25
Drotebanol	25
Ethylmethylthiambutene	25
Ethylone	25
Etodesnitazene	30
Etonitazene	25
Etorphine	30
Etoxeridine	25
Eutylone	30
Fenethylline	30
Fentanyl carbamate	30
Fentanyl related substances	600
Flunitazene	30
FUB-144	25
FUB-AKB48	25
Fub-AMB, MMB-Fubinaca, AMB-Fubinaca	25
Furanyl fentanyl	30
Furethidine	25
gamma-Hydroxybutyric acid	29,417,000
Heroin	150

Hydromorphinol	40
Hydroxypethidine	25
Ibogaine	150
Isobutyryl Fentanyl	25
Isotonitazine	25
JWH-018 and AM678 (1-Pentyl-3-(1-naphthoyl)indole)	35
JWH-019 (1-Hexyl-3-(1-naphthoyl)indole)	45
JWH-073 (1-Butyl-3-(1-naphthoyl)indole)	45
JWH-081 (1-Pentyl-3-[1-(4-methoxynaphthoyl)]indole)	30
JWH-122 (1-Pentyl-3-(4-methyl-1-naphthoyl)indole)	30
JWH-200 (1-[2-(4-Morpholinyl)ethyl]-3-(1-naphthoyl)indole)	35
JWH-203 (1-Pentyl-3-(2-chlorophenylacetyl)indole)	30
JWH-250 (1-Pentyl-3-(2-methoxyphenylacetyl)indole)	30
JWH-398 (1-Pentyl-3-(4-chloro-1-naphthoyl)indole)	30
Ketobemidone	30
Levomoramide	25
Levophenyacylmorphan	25
Lysergic acid diethylamide (LSD)	1,200
MAB-CHMINACA; ADB-CHMINACA (N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide)	30
MDMB-CHMICA; MMB-CHMINACA(methyl 2-(1-(cyclohexylmethyl)-1H-indole-3-carboxamido)-3,3-dimethylbutanoate)	30
MDMB-FUBINACA (methyl 2-(1-(4-fluorobenzyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate)	30
MMB-CHMICA-(AMB-CHIMCA); Methyl-2-(1-(cyclohexylmethyl)-1H-indole-3-carboxamido)-3-methylbutanoate	25
Mesocarb	30
Metodesnitazene	30
Metonitazene	30
Marijuana	6,675,000
Marijuana extract	1,000,000
Mecloqualone	30
Mescaline	1,200
Methaqualone	60
Methcathinone	25
Methiopropamine	30

Methoxetamine	30
Methoxyacetyl fentanyl	30
Methyldesorphine	5
Methyldihydromorphine	25
Morpheridine	25
Morphine methylbromide	5
Morphine methylsulfonate	5
Morphine-N-oxide	150
MT-45	30
Myrophine	25
NM2201: Naphthalen-1-yl 1-(5-fluorpentyl)-1H-indole-3-carboxylate	25
N,N-Dimethylamphetamine	25
Naphyrone	25
N-Ethyl-1-phenylcyclohexylamine	25
N-Ethyl-3-piperidyl benzilate	10
N-Ethylamphetamine	24
N-Ethylhexedrone	25
N-Ethylpentylone, ephylone	30
N-Hydroxy-3,4-methylenedioxyamphetamine	24
Nicocodeine	25
Nicomorphine	25
N-methyl-3-piperidyl benzilate	30
N-Pyrrolidino Etonitazene	30
Noracymethadol	25
Norlevorphanol	2,550
Normethadone	25
Normorphine	40
Norpipanone	25
Ocfentanil	25
ortho-Fluoroacryl fentanyl	30
ortho-Fluorobutyryl fentanyl	30
Ortho-Fluorofentanyl,2-Fluorofentanyl	30
ortho-Fluoroisobutyryl fentanyl	30
ortho-Methyl acetylfentanyl	30
ortho-Methyl methoxyacetyl fentanyl	30
Para-Chlorisobutyrl fentanyl	30
Para-flourobutyryl fentanyl	25
Para-fluorofentanyl	25

para-Fluoro furanyl fentanyl	30
Para-Methoxybutyrl fentanyl	30
Para-methoxymethamphetamine	30
para-Methylfentanyl	30
Parahexyl	5
PB-22; QUPIC	20
Pentedrone	25
Pentylone	25
Phenadoxone	25
Phenampromide	25
Phenomorphan	25
Phenoperidine	25
Phenyl fentanyl	30
Pholcodine	5
Piritramide	25
Proheptazine	25
Properidine	25
Propiram	25
Protonitazene	30
Psilocybin	20,000
Psilocin	24,000
Racemoramide	25
SR-18 and RCS-8 (1-Cyclohexylethyl-3-(2-methoxyphenylacetyl)indole)	45
SR-19 and RCS-4 (1-Pentyl-3-[(4-methoxy)-benzoyl]indole)	30
Tetrahydrofuranyl fentanyl	15
Thebacon	25
Thiafentanil	25
Thiofentanyl	25
Thiofuranyl fentanyl	30
THJ-2201 ([1-(5-fluoropentyl)-1H-indazol-3-yl](naphthalen-1-yl)methanone)	30
Tilidine	25
Trimeperidine	25
UR-144 (1-pentyl-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone	25
U-47700	30
Valeryl fentanyl	25
Zipeprol	30

Schedule II	
1-Phenylcyclohexylamine	15
1-Piperidinocyclohexanecarbonitrile	25
4-Anilino-N-phenethyl-4-piperidine (ANPP)	937,874
Alfentanil	5,000
Alphaprodine	25
Amobarbital	20,100
Bezitramide	25
Carfentanil	20
Cocaine	60,492
Codeine (for conversion)	942,452
Codeine (for sale)	19,262,957
d-amphetamine (for sale)	21,200,000
d,l-amphetamine	21,200,000
d-amphetamine (for conversion)	20,000,000
Dexmethylphenidate (for sale)	6,200,000
Dexmethylphenidate (for conversion)	5,374,683
Dextropropoxyphene	35
Dihydrocodeine	115,227
Dihydroetorphine	25
Diphenoxylate (for conversion)	14,100
Diphenoxylate (for sale)	770,800
Ecgonine	60,492
Ethylmorphine	30
Etorphine hydrochloride	32
Fentanyl	731,360
Glutethimide	25
Hydrocodone (for conversion)	1,250
Hydrocodone (for sale)	27,143,545
Hydromorphone	1,951,801
Isomethadone	30
L-amphetamine	30
Levo-alphacetylmethadol (LAAM)	25
Levomethorphan	30
Levorphanol	20,000
Lisdexamfetamine	26,500,000
Meperidine	681,184

Meperidine Intermediate-A	30
Meperidine Intermediate-B	30
Meperidine Intermediate-C	30
Metazocine	15
Methadone (for sale)	25,619,700
Methadone Intermediate	27,673,600
d,l-Methamphetamine	150
d-methamphetamine (for conversion)	485,020
d-methamphetamine (for sale)	47,000
l-methamphetamine	587,229
Methylphenidate (for sale)	53,283,000
Methylphenidate (for conversion)	19,975,468
Metopon	25
Moramide-intermediate	25
Morphine (for conversion)	2,393,200
Morphine (for sale)	20,805,957
Nabilone	62,000
Norfentanyl	25
Noroxymorphone (for conversion)	22,044,741
Noroxymorphone (for sale)	1,000
Oliceridine	25,100
Opium (powder)	250,000
Opium (tincture)	530,837
Oripavine	33,010,750
Oxycodone (for conversion)	437,827
Oxycodone (for sale)	53,658,226
Oxymorphone (for conversion)	28,204,371
Oxymorphone (for sale)	464,464
Pentobarbital	40,000,000
Phenazocine	25
Phencyclidine	35
Phenmetrazine	25
Phenylacetone	100
Piminodine	25
Racemethorphan	5
Racemorphan	5
Remifentanil	3,000
Secobarbital	172,100
Sufentanil	4,000

Tapentadol	10,390,226
Thebaine	57,137,944
List I Chemicals	
Ephedrine (for conversion)	41,100
Ephedrine (for sale)	3,933,336
Phenylpropanolamine (for conversion)	14,878,320
Phenylpropanolamine (for sale)	7,990,000
Pseudoephedrine (for conversion)	1,000
Pseudoephedrine (for sale)	186,617,466

The Administrator also establishes APQ for all other schedule I and II controlled substances included in 21 CFR 1308.11 and 1308.12 at zero. In accordance with 21 CFR 1303.13 and 21 CFR 1315.13, upon consideration of the relevant factors, the Administrator may adjust the 2024 APQ and AAN as needed.

Anne Milgram, DEC 28 2023
Administrator.