

DEPARTMENT OF JUSTICE

DRUG ENFORCEMENT ADMINISTRATION

21 CFR Part 1308

Docket No. DEA-1362; A.G. Order No. 5931-2024

Schedules of Controlled Substances: Rescheduling of Marijuana

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Department of Justice (“DOJ”) proposes to transfer marijuana from schedule I of the Controlled Substances Act (“CSA”) to schedule III of the CSA, consistent with the view of the Department of Health and Human Services (“HHS”) that marijuana has a currently accepted medical use as well as HHS’s views about marijuana’s abuse potential and level of physical or psychological dependence. The CSA requires that such actions be made through formal rulemaking on the record after opportunity for a hearing. If the transfer to schedule III is finalized, the regulatory controls applicable to schedule III controlled substances would apply, as appropriate, along with existing marijuana-specific requirements and any additional controls that might be implemented, including those that might be implemented to meet U.S. treaty obligations. If marijuana is transferred into schedule III, the manufacture, distribution, dispensing, and possession of marijuana would remain subject to the applicable criminal prohibitions of the CSA. Any drugs containing a substance within the CSA’s definition of “marijuana” would also remain subject to the applicable prohibitions in the Federal Food, Drug, and Cosmetic Act (“FDCA”). DOJ is soliciting comments on this proposal.

DATES: Comments must be submitted electronically or postmarked on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

Interested persons may file a request for a 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 1316.47 or 1316.49, as applicable. Requests for a hearing, and waivers of an opportunity for a hearing or to participate in a hearing, must be received or postmarked on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

To be considered as part of this rulemaking, comments and requests for a hearing must be submitted in response to this proposed rule within the timeframe specified above, regardless of whether the comment, hearing request, or other information was previously submitted to the Drug Enforcement Administration (“DEA”) in connection with any prior matter relating to the scheduling of marijuana.

Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 PM Eastern Time on the last day of the comment period.

ADDRESSES: To ensure proper handling of comments, please reference “Docket No. DEA-1362” on all correspondence, including any attachments.

- *Electronic comments:* DOJ encourages that all comments be submitted through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the web page or to attach a file for lengthier comments. Please go to <http://www.regulations.gov> and follow the online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on <http://www.regulations.gov>. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.

- *Paper comments:* Paper comments that duplicate electronic submissions are not necessary and are discouraged. Should you wish to mail a paper comment in lieu of submitting a comment electronically, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrisette Drive, Springfield, Virginia 22152.
- *Hearing requests:* All requests for a hearing and waivers, together with a written statement of position on the matters of fact and law asserted in the hearing, must be filed with DEA. Such requests must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrisette Drive, Springfield, Virginia 22152. For informational purposes, a courtesy copy of requests for hearing and waivers should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/OALJ, 8701 Morrisette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrisette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Drug & Chemical Evaluation Section, Diversion Control Division, Drug Enforcement Administration; Telephone: (571) 362-3249; Email: nprm@dea.gov.

SUPPLEMENTARY INFORMATION:

I. Posting of Public Comments

Please note that all comments received in response to this docket are considered part of the public record. DOJ will make comments available for public inspection online at <http://www.regulations.gov>. Such information includes personal or business identifiers (such as name, address, State or Federal identifiers, etc.) voluntarily submitted by the commenter. Generally, all information voluntarily submitted by the commenter, unless clearly marked as

“Confidential Information” in the method described below, will be publicly posted. Comments may be submitted anonymously. The Freedom of Information Act, 5 U.S.C. 552, applies to all comments received.

Commenters submitting comments that include personal identifying information (“PII”) or confidential or proprietary business information that the commenter does not want made publicly available should submit two copies of the comment. One copy must be marked “CONTAINS CONFIDENTIAL INFORMATION” and should clearly identify all PII or business information the commenter does not want to be made publicly available, including any supplemental materials. DOJ will review this copy, including the claimed PII and confidential business information, in its consideration of comments. The second copy should be marked “TO BE PUBLICLY POSTED” and must have all claimed confidential PII and business information already redacted. DOJ will post only the version of the comment with redactions on <http://www.regulations.gov> for public inspection.

An electronic copy of this document and supplemental information to this proposed rule are available at <http://www.regulations.gov> for easy reference. DOJ specifically solicits written comments regarding the economic analysis of the impact of these proposed changes. DOJ requests that commenters provide detailed descriptions in their comments of any expected economic impacts, especially to small entities. Commenters should provide empirical data to illustrate the nature and scope of such impact.

II. Request for Hearing, Notice of Appearance at, or Waiver of Participation in Hearing

Pursuant to 21 U.S.C. 811(a), this scheduling action is a formal rulemaking “on the record after opportunity for a hearing.” Such proceedings are conducted pursuant to the Administrative Procedure Act (“APA”), 5 U.S.C. 551–559. *See* 21 CFR 1308.41–1308.45; *id* part 1316, subpart D. Interested persons, as defined in 21 CFR 1300.01(b), may file requests for

a hearing in conformity with the requirements of 21 CFR 1308.44(a) and 1316.47(a), and such requests must:

(1) state with particularity the interest of the person in the proceeding;

(2) state with particularity the objections or issues concerning which the person desires to be heard; and

(3) state briefly the position of the person regarding the objections or issues.

All requests for a hearing and waivers of an opportunity for a hearing or participation, together with a written statement of position on the matters of fact and law involved in such hearing, must be sent to DEA using the address information provided above.

The decision whether an in-person hearing will be needed to address such matters of fact and law in the rulemaking will be made by the Administrator of DEA. Upon the Administrator's determination to grant an in-person hearing, DEA will publish a notice of hearing on the proposed rulemaking in the Federal Register. *See* 21 CFR 1308.44(b), 1316.53.

If the Administrator determines to grant an in-person hearing to address such matters of fact and law in this rulemaking, the Administrator will then designate an Administrative Law Judge ("ALJ") to preside over the hearing. The ALJ's functions shall commence upon designation, as provided in 21 CFR 1316.52. The ALJ will have all powers necessary to conduct a fair hearing, to take all necessary action to avoid delay, and to maintain order. *Id.* The ALJ's authorities include the power to hold conferences to simplify or determine the issues in the hearing or to consider other matters that may aid in the expeditious disposition of the hearing; require parties to state their position in writing; sign and issue subpoenas to compel the production of documents and materials to the extent necessary to conduct the hearing; examine witnesses and direct witnesses to testify; receive, rule on, exclude, or limit evidence; rule on procedural items; and take any action permitted by the presiding officer under DEA's hearing

procedures and the APA. *Id.*

Comments on or objections to the proposed rule submitted under 21 CFR 1308.43(g) will be offered as evidence at the hearing, but the presiding officer shall admit only evidence that is competent, relevant, material, and not unduly repetitive. 21 CFR 1316.59(a).

Any interested person may file a waiver of opportunity for a hearing or to participate in a hearing in conformity with the requirements of 21 CFR 1308.44(c), together with a written statement of position on the matters of fact and law involved in any hearing. 21 CFR 1316.49. Such statement, if admissible, will be included in the record and considered as described in 21 CFR 1308.44(c).

In accordance with 21 U.S.C. 811 and 812, the purpose of a hearing would be to “receiv[e] factual evidence and expert opinion regarding” whether marijuana should be transferred to schedule III of the list of controlled substances. 21 CFR 1308.42. Concurrent with this rulemaking, DEA will consider the marijuana-specific controls that would be necessary to comply with relevant treaty obligations in the event that, after the hearing, a final order reschedules marijuana, and, to the extent such controls are needed if marijuana is rescheduled, will seek to finalize any such regulations as soon as possible.

All requests for hearing and waivers of an opportunity for a hearing or participation must be sent to DEA using the address information above, on or before the date specified above.

III. Legal Authority

Under the CSA, 21 U.S.C. 801 *et seq.*, the Attorney General shall, before initiating proceedings to control, decontrol, or transfer between schedules a drug or other substance, request from the Secretary of HHS a scientific and medical evaluation, and the Secretary’s recommendations, as to whether such drug or other substance should be so controlled or removed as a controlled substance. 21 U.S.C. 811(b). The recommendations of the Secretary

shall include recommendations with respect to the appropriate schedule, if any, under which such drug or other substance should be listed. *Id.*

HHS recommended in August 2023 that marijuana be rescheduled to schedule III. *See* Letter for Anne Milgram, Administrator, DEA, from Rachel L. Levine, M.D., Assistant Secretary for Health, HHS (Aug. 29, 2023) (“August 2023 Letter”). The Attorney General then sought the legal advice of the Office of Legal Counsel (“OLC”) at DOJ on questions relevant to this rulemaking proceeding. Among other conclusions, OLC concluded that “HHS’s scientific and medical determinations must be binding until issuance of a notice of proposed rulemaking [(‘NPRM’)].” *Questions Related to the Potential Rescheduling of Marijuana*, 45 Op. O.L.C. ___, at *25 (Apr. 11, 2024) (“OLC Op.”).¹ After the issuance of a notice of rulemaking proceedings, HHS’s scientific and medical determinations are accorded “significant deference” through the rest of the rulemaking process.² OLC Op. at *26.

Under the CSA, when recommending or determining that a drug should be controlled (and if so, under which schedule), the Secretary and the Attorney General must consider eight factors set forth in 21 U.S.C. 811(c). The eight factors are:

1. The drug’s actual or relative potential for abuse;
2. Scientific evidence of its pharmacological effect, if known;
3. The state of current scientific knowledge regarding the drug or other substance;
4. Its history and current pattern of abuse;

¹ OLC’s opinion is available in its entirety under “Supporting and Related Material” of the public docket for this rule at <http://www.regulations.gov> under docket number DEA-1362.

² The CSA’s reliance on formal rulemaking for scheduling decisions indicates that HHS’s determinations do not bind DOJ for the entirety of the rulemaking process, because outside participants may submit additional scientific and medical evidence during the rulemaking that DOJ would need to consider. OLC Op. at *25. However, DOJ “may not simply cast aside HHS’s scientific and medical recommendations once it initiates rulemaking proceedings by issuing an NPRM,” since “[t]he categorical use of the word ‘binding’ in section 811(b) suggests that Congress intended HHS’s scientific and medical views to at least be a very significant input in the scheduling process,” and the legislative history of the CSA bolsters that conclusion. *Id.* at 25–26 (citing H.R. Rep. No. 91-1444, at 22–23 (1970)).

5. The scope, duration, and significance of abuse;
6. What, if any, risk there is to the public health;
7. Its psychic or physiological dependence liability; and
8. Whether the substance is an immediate precursor of a substance already controlled.

21 U.S.C. 811(c); *see also id.* 811(b) (specifying how HHS should consider each of the eight factors).

The United States is a party to the 1961 United Nations Single Convention on Narcotic Drugs, March 30, 1961, 18 U.S.T. 1407, 520 U.N.T.S. 151 (“Single Convention”), as amended by the 1972 Protocol, March 25, 1972, 26 U.S.T. 1439, 976 U.N.T.S. 3. Under 21 U.S.C. 811(d)(1), if control of a substance is required “by United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970,” the Attorney General must issue an order controlling such drug “under the schedule he deems most appropriate to carry out such obligations, without regard to the findings” required by 21 U.S.C. 811(a) or 812(b), “and without regard to the procedures” prescribed by 21 U.S.C. 811(a) and (b). Marijuana is a drug covered by the Single Convention. *See* Single Convention art. 1(1)(b); OLC Op. at *26 & n.7.

OLC and the United States Court of Appeals for the D.C. Circuit have explained that section 811(d)(1) does not supersede the scheduling procedures set forth in sections 811(a) through (b) and 812(b), including the requirement to consider the eight factors set forth in section 811(c). Instead, section 811(d)(1) allows the Attorney General to “identify which schedules would satisfy the United States’ international obligations with respect to a particular drug, and then—if more than one schedule would do so—select which schedule to use through the section 811(a) through (b) and 812(b) procedures.” OLC Op. at *29 n.8; *accord Nat’l Org. for Reform of Marijuana Laws (NORML II) v. DEA*, 559 F.2d 735, 747 (D.C. Cir. 1977). HHS performed the eight-factor analysis. *See* Memorandum for DEA, from HHS, *Re: Basis for the*

Recommendation to Reschedule Marijuana to Schedule III of the Controlled Substances Act (“HHS Basis for Rec.”). As noted above, HHS’s scientific and medical determinations are binding on DOJ until an NPRM is published, and, in addition, DOJ must accord “significant deference” to HHS’s scientific and medical determinations throughout the rulemaking process. OLC Op. at *25–26.

Once the determination is made that a particular drug or substance must be controlled under the CSA, the Attorney General must determine the level of control over the drug or substance under the CSA. *See* 21 U.S.C. 811(a), (b). The CSA divides controlled substances into five levels of control, or “schedules,” based on (1) a drug’s potential for abuse, (2) whether the drug has a currently accepted medical use in treatment in the United States (“CAMU”), and (3) whether there is a lack of accepted safety for use of the drug under medical supervision or the level of psychological or physical dependence that could result from abuse of the drug. *See id.* 812(b). Schedule I drugs have a high potential for abuse, no CAMU, and a lack of accepted safety for use under medical supervision. *Id.* 812(b)(1). Schedule II drugs also have a high potential for abuse but have a CAMU (or a CAMU with “severe restrictions”), and abuse of the drug may lead to severe psychological or physical dependence. *Id.* 812(b)(2). Schedule III drugs, meanwhile, have a lower potential for abuse when compared to drugs in schedules I and II, have a CAMU, and their abuse may lead to moderate or low physical dependence or high psychological dependence.³ 21 U.S.C. 812(b)(3). 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.

³ Schedule IV includes drugs that have a low potential for abuse relative to those in schedule III, that have a CAMU, and for which abuse may lead to limited physical or psychological dependence relative to those in schedule III. 21 U.S.C. 812(b)(4). Schedule V includes drugs that have a low potential for abuse relative to those in schedule IV, that have a CAMU, and for which abuse may lead to limited physical or psychological dependence relative to those in schedule IV. *Id.* 812(b)(5).

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. The CSA provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General on his own motion, at the request of the Secretary, or on the petition of any interested party. *Id.*

IV. Background

When Congress enacted the CSA in 1970, it placed marijuana in schedule I. Comprehensive Drug Abuse Prevention and Control Act of 1970, Pub. L. 91-513, tit. II, sec. 202(c), 84 Stat. 1236, 1249 (1970); 21 U.S.C. 812(c).⁴ The Attorney General is authorized to amend this initial placement. 21 U.S.C. 812(c); *see also id.* 811, 812(b). Other schedule I substances include heroin, lysergic acid diethylamide (commonly known as LSD), and 3,4-methylenedioxymethamphetamine (ecstasy). *See* 21 CFR 1308.11. Drugs controlled under schedule II include cocaine, methamphetamine, methadone, oxycodone, and fentanyl. *Id.* 1308.12. Drugs controlled under schedule III include products containing less than 90 milligrams of codeine per dosage unit, ketamine, and anabolic steroids. *Id.* 1308.13. Petitioners have requested that marijuana be rescheduled several times over the years. *See, e.g., Schedule of Controlled Substances: Petition To Remove Marihuana From Control or in the Alternative To Control Marihuana in Schedule V of the Controlled Substances Act*, 37 FR 18097 (Sept. 7,

⁴ The CSA refers to the drug as “marijuana” and “marihuana” interchangeably. *See, e.g.*, 21 U.S.C. 802(16)(A), 812(c). As used in this NPRM, “marijuana” means the term defined at 21 U.S.C. 802(16).

1972); *Notice of Denial of Petition*, 66 FR 20038 (Apr. 18, 2001); *Denial of Petition To Initiate Proceedings To Reschedule Marijuana*, 76 FR 40552 (July 8, 2011).

DEA and HHS last examined the issue of whether to reschedule marijuana eight years ago, in 2016, when DEA denied two petitions to reschedule marijuana.⁵ At the time, HHS concurred that marijuana should remain a schedule I drug because it met the three criteria for placement in schedule I. 81 FR at 53706–07. In accordance with the requirements for placement in schedule I, HHS found that: (1) marijuana had a high potential for abuse; (2) it did not have a CAMU; and (3) there was a lack of accepted safety for use of marijuana under medical supervision. *Id.* As discussed in detail below, in 2023, HHS conducted a scientific and medical evaluation of marijuana based on a comprehensive review of available data at that time and recommended that marijuana be transferred to schedule III.

Since 1996, 38 States, the District of Columbia, and 4 Federal Territories have legalized the use of medical marijuana. HHS Basis for Rec. at 30; OLC Op at *9. These laws typically allow the cultivation, sale, and use of marijuana by patients (or their caregivers) whose health care practitioners have recommended that they use marijuana to treat certain health conditions. *See, e.g.*, Ohio Rev. Code secs. 3796.01(A)(6)(a)–(v), 3796.01(A); N.Y. Cannabis Law secs. 3(18), 30, 31; N.M. Stat. secs. 26-2B-3(F)(1)–(23), 26-2B-3(N), 26-2B-4(A). Further, beginning in Fiscal Year 2015, Congress has adopted an appropriations rider every year that prohibits DOJ from using funds to prevent certain States, Territories, and the District of Columbia from implementing their own laws with respect to medical marijuana. *E.g.*, Consolidated Appropriations Act, 2024, Pub. L. 118-42, sec. 531, 138 Stat. 25; Consolidated

⁵ *Denial of Petition To Initiate Proceedings To Reschedule Marijuana*, 81 FR 53688 (Aug. 12, 2016); *Denial of Petition To Initiate Proceedings To Reschedule Marijuana*, 81 FR 53767 (Aug. 12, 2016).

Appropriations Act, 2023, Pub. L. 117-328, sec. 531, 136 Stat. 4459, 4561 (2022); *see also* Cong. Research Serv., R44782, *The Evolution of Marijuana as a Controlled Substance and the Federal-State Policy Gap* 26 & n.159 (updated Apr. 7, 2022) (collecting additional appropriations riders).

Marijuana is generally defined by statute to mean “the plant *Cannabis sativa* L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin.” 21 U.S.C. 802(16)(A). In 2018, Congress amended the CSA to remove “(i) hemp, as defined in section [1639o of title 7 of the U.S. Code]” from the definition of marijuana.⁶

Agricultural Improvement Act of 2018, Pub. L. 115-334, sec. 12619, 132 Stat. 4490, 5018.

Section 1639o(1) of title 7 in turn defines hemp as “the plant *Cannabis sativa* L. and any part of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or not, with a delta-9-tetrahydrocannabinol concentration of not more than 0.3 percent on a dry weight basis.” Delta-9-tetrahydrocannabinol (“ Δ 9-THC”) is the major psychoactive intoxicating cannabinoid in marijuana. *See* HHS Basis for Rec. at 10. This exclusion of hemp from the definition of marijuana had the effect of removing many products containing predominantly cannabidiol (“CBD”) derived from hemp and containing no more than 0.3 percent Δ 9-THC on a dry weight basis from control as marijuana.

On October 6, 2022, President Biden requested that the Attorney General and the Secretary of HHS “initiate the administrative process to review expeditiously how marijuana is

⁶ Marijuana under the CSA also does not include “the mature stalks of [the cannabis] plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of [the cannabis] plant which is incapable of germination.” 21 U.S.C. 802(16)(B)(ii).

scheduled under federal law.”⁷ HHS thereafter undertook a scientific and medical evaluation of marijuana as defined under the CSA in accordance with the President’s request.

In a letter dated August 29, 2023, Admiral Rachel L. Levine, M.D., HHS’s Assistant Secretary for Health, recommended to the Administrator of DEA that marijuana be controlled in schedule III of the CSA. August 2023 Letter. HHS found that marijuana has a potential for abuse less than the drugs or other substances in schedules I and II; that marijuana has a CAMU; and that the abuse of marijuana may lead to moderate or low physical dependence or high psychological dependence. HHS Basis for Rec. at 62–65. These findings correspond to the criteria for placement of a substance in schedule III. *See* 21 U.S.C. 812(b)(3). DEA has not yet made a determination as to its views of the appropriate schedule for marijuana.

V. Proposal to Reschedule Marijuana

The CSA vests the Attorney General with the authority to schedule, reschedule, or decontrol drugs. 21 U.S.C. 811(a). The Attorney General has delegated that authority to the DEA Administrator, *see* 28 CFR 0.100, but also retains the authority to schedule drugs under the CSA in the first instance, *see* 28 U.S.C. 509, 510. The HHS Assistant Secretary for Health has provided a recommendation for transferring marijuana to schedule III. In light of that recommendation, the Attorney General is exercising the Attorney General’s authority under 21 U.S.C. 811(a) to initiate a rulemaking that proposes the placement of marijuana in schedule III.

DEA believes that additional information arising from this rulemaking will further inform the findings regarding the appropriate schedule for marijuana. DEA has maintained an active review of the scientific literature addressing marijuana with a focus on how it relates to the

⁷ The White House, *Statement from President Biden on Marijuana Reform* (Oct. 6, 2022), <https://www.whitehouse.gov/briefing-room/statements-releases/2022/10/06/statement-from-president-biden-on-marijuana-reform/>.

scientific and medical evaluation and informs any updates to the eight-factor analysis. In addition to HHS’s scientific and medical determinations, which are binding until the issuance of this NPRM and which must be accorded significant deference throughout the rulemaking, DEA believes that factual evidence (including scientific data) and expert opinions, including additional data regarding different forms, formulations, and delivery methods for marijuana, as well as evidence regarding the effects of marijuana at various dosages or concentrations, may be relevant.

The HHS Basis for Recommendation, DEA’s analyses explaining its decisions to deny the petitions to reschedule marijuana in 2016, and the 2024 OLC opinion (cited throughout) are available in their entirety under “Supporting and Related Material” of the public docket for this rule at <http://www.regulations.gov> under docket number DEA-1362.

VI. Eight-Factor Analysis

DOJ has reviewed the scientific and medical evaluation and scheduling recommendation provided by HHS and has conducted a separate review of the eight factors identified in 21 U.S.C. 811(c). At this point in the proceedings, DOJ must treat HHS’s scientific and medical determinations as binding. *See* OLC Op. at *4, *25. HHS’s scientific and medical determinations are included below, as well as certain information from DEA.

1. Marijuana’s Actual or Relative Potential for Abuse

The first factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is the actual or relative potential for abuse of marijuana. The term “abuse” is not defined in the CSA. However, consistent with the legislative history of the CSA, DEA and HHS have typically weighed the

following factors in determining whether a particular drug or substance has a potential for abuse:⁸

A. Whether there is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.

As part of its analysis, HHS concluded that evidence shows that, although some individuals are taking marijuana in amounts sufficient to create a hazard to their health and to the safety of other individuals and the community, the vast majority of individuals who use marijuana are doing so in a manner that does not lead to dangerous outcomes to themselves or others. HHS Basis for Rec. at 6–7. The data supportive of this conclusion are discussed in detail in HHS’s analysis of Factors 4, 5, and 6. *See* HHS Basis for Rec. at 28–57.

In particular, HHS emphasized that an evaluation of various epidemiological databases of adverse outcomes from 2015 to 2021 involving marijuana or comparator drugs that are used nonmedically showed that the utilization-adjusted rate of adverse outcomes involving marijuana was consistently lower than the utilization-adjusted rates of adverse outcomes involving heroin, cocaine, and, for certain outcomes, other comparators, including alcohol. Also, alcohol or heroin typically ranked first or in immediately subsequent positions among the comparators in terms of incidence of adverse outcomes, with marijuana in a lower place in that ranking. This pattern also was observed for serious medical outcomes, including death, observed in Poison Center data, where marijuana was in the lowest ranking group. This suggests consistency across databases, across drugs, and over time. HHS thus concluded that although abuse of marijuana produces

⁸ *See, e.g.*, 81 FR at 53740; *see also* HHS Basis for Rec. at 6 (citing Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444 (1970), *reprinted in* 1970 U.S.C.C.A.N. 4566, 4603).

clear evidence of harmful consequences, these appear to be relatively less common and less severe than the consequences of some other comparator substances. HHS Basis for Rec. at 7–8.

Importantly, these comparisons of the prevalence of adverse outcomes were from descriptive analyses only, following the established practice in previous eight-factor analyses. Thus, differences in outcome frequency and severity, and the ranked order across comparators, may be attributable in part to underlying differences in the populations being compared (*e.g.*, age or pre-existing medical conditions), among other things. Despite these limitations, qualitative synthesis of descriptive analyses is the established practice in previous eight-factor analyses, and HHS determined that it is the most appropriate approach here. HHS Basis for Rec. at 7–8.

HHS also concluded that the public-health risks posed by marijuana are lower compared to those posed by other drugs of abuse (*e.g.*, heroin, oxycodone, cocaine), based on HHS’s evaluation of various epidemiological databases for emergency department (“ED”) visits, hospitalizations, unintentional exposures, and most importantly, overdose deaths. The rank order of the comparators in terms of greatest adverse consequences typically ranked heroin, benzodiazepines, and cocaine first or in immediately subsequent positions, with marijuana in a lower place in the ranking, especially when HHS adjusted for utilization. For overdose deaths, marijuana is always in the lowest ranking among comparator drugs. These evaluations demonstrate that there is consistency across databases, across substances, and over time. HHS thus concluded that although abuse of marijuana produces clear evidence of a risk to public health, that risk is relatively lower than that posed by most other comparator drugs. HHS Basis for Rec. at 7–8.

DEA notes that data provided by HHS in its recommendation included a 2023 national survey that tracks drug use trends among 8th-, 10th-, and 12th-grade students, and showed that

by 12th grade, 20.2 percent of students reported using marijuana in the past month.⁹ DEA also notes that the same study showed that the prevalence of ingesting marijuana by vaping is evidenced by students reporting vaping in the 30 days prior at the following rates: 4.2 percent for 8th graders, 10.3 percent for 10th graders, and 14.8 percent for 12th graders.¹⁰ In 2022, the Substance Abuse and Mental Health Services Administration’s (“SAMHSA”) Drug Abuse Warning Network (“DAWN”) reported that 11.9 percent of drug-related ED visits nationwide involved cannabis.¹¹ The rate of cannabis-related ED visits was highest in these demographic groups: 18 to 25 years old, male, Black or African American, and Not Hispanic or Latino.¹²

In addition to the data considered by the HHS Basis for Recommendation, the data considered by HHS and DEA in their 2015 eight-factor analysis, and the additional data discussed above, DEA anticipates that additional data on seizures of marijuana by law enforcement, cannabis-related ED visits, as well as updated epidemiological survey data since 2022, may be appropriate for consideration.

B. Whether there is significant diversion of the drug or drugs containing such a substance from legitimate drug channels.

HHS found that there is a lack of evidence of significant diversion of marijuana from legitimate drug channels. HHS Basis for Rec. at 8. It noted that marijuana is used by researchers for clinical research under investigational new drug (“IND”) applications, and that there are multiple DEA registrants that are approved to produce marijuana and derived formulations for use in DEA-authorized nonclinical and clinical research. HHS observed that

⁹ See HHS Basis for Rec. at 35 (discussing Richard A. Miech et al., Univ. of Mich. Inst. for Soc. Rsch., *Monitoring the Future: National Survey Results on Drug Use, 1975–2022: Secondary School Students* 71 (2023), <https://monitoringthefuture.org/wp-content/uploads/2022/12/mtf2022.pdf>).

¹⁰ Miech et al., *supra* note 9, at 75.

¹¹ Drug Abuse Warning Network, Substance Abuse & Mental Health Servs. Admin., *Findings from Drug-Related Emergency Department Visits, 2022*, at 1 (2023), <https://store.samhsa.gov/sites/default/files/pep23-07-03-001.pdf>.

¹² *Id.* at 27.

these authorizations represent the only federally sanctioned drug channels in the United States, and there is a lack of data indicating diversion occurring from these entities or activities.

However, there are significant additional sources of marijuana in the United States, including from illicit cultivation and production, illicit importation from other countries, and from State programs that permit dispensing of marijuana for medical use and, in some States, recreational adult use. HHS Basis for Rec. at 8.

Given this unique landscape, DEA believes that the lack of data indicating diversion of marijuana from federally sanctioned drug channels to the illicit market is not indicative of a lack of potential for abuse of the drug. DEA anticipates that additional data on diversion from State programs and DEA-registered manufacturers may aid in a determination of whether diversion is taking place.

C. Whether individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of their professional practice.

As HHS notes, the Food and Drug Administration (“FDA”) has not approved a New Drug Application (“NDA”) for a drug product containing botanical marijuana for any therapeutic indication. Thus, the only way an individual can use marijuana on the basis of medical advice through legitimate channels under Federal law is by participating in research under an IND. However, 38 States and the District of Columbia have enacted laws allowing individuals to use marijuana under certain circumstances for medical purposes. Outside of the Federal- and State-sanctioned medical use of marijuana, individuals are using marijuana on their own initiative for medical, as well as nonmedical, purposes. Epidemiological data related to nonmedical use of marijuana is detailed in HHS’s analysis of Factor 4. HHS Basis for Rec. at 8.

DEA notes that data is not available to determine the number of individuals using marijuana under State law. According to 2022 National Survey on Drug Use and Health (“NSDUH”) data on people who are 12 and older in the United States, 61.9 million people reported using marijuana in the past year, and marijuana was the illicit drug used with the greatest frequency.¹³ Specifically, 42.3 million people reported use in the past month, including 14.7 million people who vaped marijuana in that same period, representing 5.2 percent of the study’s target population.¹⁴ Furthermore, as reported by NSDUH in 2022, 3.7 million people initiated marijuana use in the past year, with more than half (53 percent or 2.0 million people) initiating marijuana use before the age of 21.¹⁵ DEA also notes that HHS concluded that, outside of the Federal- and State-sanctioned medical use of marijuana, individuals are using marijuana on their own initiative for medical as well as nonmedical purposes. HHS Basis for Rec. at 8. In 2016, DEA reached a similar conclusion.¹⁶ In addition to the data considered in the HHS Basis for Recommendation, and by HHS and DEA in their earlier eight-factor analyses, DEA anticipates that updated epidemiological survey data since 2022 may be appropriate for consideration.

D. Whether the drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that it will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or

¹³ Substance Abuse & Mental Health Servs. Admin., *Key Substance Use and Mental Health Indicators in the United States: Results from the 2022 National Survey on Drug Use and Health* 14 (Nov. 2023), <https://www.samhsa.gov/data/sites/default/files/reports/rpt42731/2022-nsduh-nnr.pdf>.

¹⁴ *Id.* at 13.

¹⁵ *Id.* at 27.

¹⁶ 81 FR at 53691 (“Based on the large number of individuals reporting current use of marijuana and the lack of an FDA-approved drug product in the United States, one can assume that it is likely that the majority of individuals using marijuana do so on their own initiative rather than on the basis of medical advice from a licensed practitioner.”).

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.

Marijuana has been a schedule I substance since the CSA was enacted in 1970. *See* Pub. L. 91-513, tit. II, sec. 202(c), 84 Stat. 1236, 1249 (1970); 21 U.S.C. 812(c); *see also* 21 CFR 1308.11(d)(23). The primary compound in marijuana that is responsible for its abuse potential is Δ 9-THC (also known as dronabinol, when specifically referring to the (-)-*trans*- Δ 9-THC stereoisomer), which has agonist activity at cannabinoid CB₁ receptors. HHS found that there are extensive nonclinical and clinical studies establishing that marijuana, due to the CB₁ agonist activity of its main cannabinoid constituent Δ 9-THC, produces rewarding effects that would be consistent with observed long-term patterns of nonmedical use and abuse, both before and in the years since enactment of the CSA. HHS Basis for Rec. at 9. For further discussion of these effects, *see* HHS Basis for Rec. at 9–18 (Factor 2), 28–37 (Factor 4).

Additionally, FDA has approved two drug products containing dronabinol: Marinol (in 1985; schedule III) and Syndros (in 2016; schedule II). HHS Basis for Rec. at 9. Marinol was approved by FDA in 1985 for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who did not respond to conventional anti-emetic treatments. FDA approved Marinol in 1992 for the treatment of anorexia associated with weight loss in patients with acquired immunodeficiency syndrome (“AIDS”). After the first FDA approval, Marinol was transferred from schedule I to schedule II and was later rescheduled to schedule III. Syndros, a drug product also containing dronabinol but formulated in an oral solution, was approved by FDA in 2016 for the treatment of anorexia associated with weight loss in patients with AIDS, as well as nausea and vomiting associated with cancer chemotherapy in patients who failed to respond adequately to conventional anti-emetic treatments. In 2017, DEA rescheduled

“FDA-approved products containing dronabinol in an oral solution” from schedule I into schedule II. HHS Basis for Rec. at 4.

When Marinol and Syndros were being developed, they underwent a systematic evaluation of their abuse potential based on animal and human behavioral studies, which showed that dronabinol has abuse potential. The abuse-related studies confirmed the abuse potential of $\Delta 9$ -THC. HHS has concluded that these findings suggest that marijuana will continue to be used nonmedically, diverted from legitimate channels, and trafficked in illicit channels as a potential source for continued nonmedical use in the United States. HHS Basis for Rec. at 9; *see also* HHS Basis for Rec. at 37–45 (Factor 5).

HHS Conclusion With Respect to Factor 1

HHS determined that epidemiological data indicate that marijuana has the potential for creating hazards to the health of the user and to the safety of the community. However, as a relative finding on abuse liability, when comparing marijuana to heroin, oxycodone, hydrocodone, fentanyl, cocaine, ketamine, benzodiazepines, zolpidem, tramadol, and alcohol in various epidemiological databases that allow for some or all of these comparisons, marijuana is not typically among the substances producing the most frequent incidence of adverse outcomes or severity of substance use disorder. HHS Basis for Rec. at 9; *see also* HHS Basis for Rec. at 28–57 (Factors 4, 5, and 6). But as noted above, there are limitations in comparing descriptive data on adverse outcomes across drugs, although descriptive analyses of epidemiologic data are an established practice in previous eight-factor analyses. HHS Basis for Rec. at 9.

In 2016, DEA found that “[m]arijuana has a high potential for abuse. Preclinical and clinical data show that it has reinforcing effects characteristic of drugs of abuse. . . . Data on marijuana seizures show widespread availability and trafficking.” 81 FR at 53739. DEA

believes that additional data in this area may be appropriate for consideration in assessing marijuana's actual or relative potential for abuse.

2. Scientific Evidence of Marijuana's Pharmacological Effects, If Known

The second factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is the scientific evidence of marijuana's pharmacological effects, if known. In making its recommendation, HHS considered the scientific evidence of the pharmacological effects of marijuana based on the effects of Δ 9-THC. HHS conducted a scientific evaluation of the neurochemistry, receptor pharmacology, animal abuse-related behavioral effects, and human behavioral and physiological effects of marijuana. HHS Basis for Rec. at 9.

A. Neurochemistry and Receptor Pharmacology of Marijuana

Cannabis is the genus of a plant that contains numerous natural constituents, including cannabinoids. See HHS Basis for Rec. at 18–21 (discussing Factor 3). Because cultivated chemovars may vary in their composition and concentration of various chemical constituents, including with respect to whether they contain significant amounts of Δ 9-THC or other cannabinoids, marijuana products from different strains will have differing biological and pharmacological profiles. HHS Basis for Rec. at 10.

Marijuana contains at least 560 identified natural constituents, including 125 compounds classified as cannabinoids. Most major cannabinoid compounds occurring naturally in cannabis have been identified chemically, but new and minor compounds are continuously being characterized. HHS Basis for Rec. at 10.

The two most abundant cannabinoids present in marijuana are Δ 9-THC and CBD. Δ 9-THC is the major psychoactive intoxicating cannabinoid in marijuana and is the component of marijuana that is primarily responsible for its abuse potential. In contrast, CBD has negligible

abuse potential, as assessed by FDA during the NDA review for Epidiolex, an FDA-approved drug product containing plant derived, highly purified CBD. HHS Basis for Rec. at 10.

There are two cannabinoid receptors: CB₁ and CB₂. CB₁ and CB₂ receptors belong to the family of G-protein-coupled receptors and present a typical seven transmembrane-spanning domain structure. Cannabinoid receptors primarily link to an inhibitory G protein (G_{i/o}), such that adenylate cyclase activity is inhibited when a cannabinoid ligand binds to the receptor. This, in turn, prevents the conversion of adenosine triphosphate to the second messenger, cyclic AMP (“cAMP”), which decreases cAMP levels. As HHS’s analysis described, G proteins also contain beta/gamma G protein units that are also liberated following ligand binding, which then bind to and alter ion channel function, including inhibition of voltage-gated ion channels and activation of potassium channels. Ligand binding can also activate some subforms of phospholipase C as well as beta-arrestin protein. All of these second messenger routes amplify the neural signal following cannabinoid binding at the CB₁ and CB₂ receptors. HHS Basis for Rec. at 10.

CB₁ receptors are found primarily in the central nervous system (“CNS”), but are also present in peripheral tissues, such as the liver, heart, and lungs. In the brain, CB₁ receptors are expressed with highest density in the cortical regions, hippocampus, basal ganglia, and cerebellum and with lowest density in brainstem and hypothalamic areas. The localization of these receptors may explain cannabinoid effects on movement coordination, memory, and cognition. Additionally, CB₁ receptors are found in glial cells as well as in the immune system. However, the concentration of CB₁ receptors is considerably lower in peripheral tissues than in the CNS. CB₂ receptors are found primarily in the immune system, including in numerous leukocyte cell types, as well as in activated CNS microglia. Additionally, there is some evidence that CB₂ receptors are localized in the brain, primarily in the cerebellum and hippocampus. The

distribution of CB₂ receptors throughout the body is less extensive than the distribution of CB₁ receptors. HHS Basis for Rec. at 10–11.

There are two endogenous cannabinoid receptor agonists: anandamide and arachidonyl glycerol (“2-AG”). At CB₁ receptors, anandamide is a partial agonist with low intrinsic efficacy while 2-AG is a full agonist with high intrinsic efficacy. These endogenous cannabinoid ligands are present in central as well as peripheral tissues. A combination of uptake and hydrolysis terminates the action of anandamide and 2-AG. The endogenous cannabinoid system is a locally active signaling system activated on demand in response to changes to the local conditions to help restore homeostasis. The endogenous cannabinoid system, including the endogenous cannabinoids and the cannabinoid receptors, demonstrates substantial plasticity in response to several physiological and pathological stimuli. This plasticity is particularly evident in the CNS. HHS Basis for Rec. at 11.

Δ9-THC and CBD have varying affinity and effects at the cannabinoid receptors. HHS determined that Δ9-THC is a partial agonist at both CB₁ (K_i = 18–218 nM) and CB₂ receptors (K_i = 36–309 nM). However, CB₁ receptors are the main pharmacological site of action for Δ9-THC, making CB₁ receptors the site that is responsible for the abuse potential of marijuana. The other CNS site where Δ9-THC may have activity is the 5HT₃ receptor, where it functions as an antagonist. In contrast, CBD has low affinity for both CB₁ and CB₂ receptors and may act as a negative allosteric modulator or weak antagonist at these sites. CBD has additional CNS effects as a serotonin 5HT_{1A} agonist and a serotonin 5HT_{2A} weak partial agonist, as well as a serotonin 5HT_{3A} antagonist. HHS Basis for Rec. at 11.

In the past 30 years, the potency of marijuana with regard to Δ9-THC has increased dramatically. HHS described one study finding that the concentration of Δ9-THC in marijuana

samples in the United States increased from 3 percent in 1991 to 17.1 percent in 2017. These increases are likely due to an increase in the number of high potency samples (*i.e.*, sinsemilla) in the overall samples tested. Based on an evaluation of marijuana seized by DEA, the majority of samples contained high concentrations of Δ 9-THC and low concentrations of CBD. HHS Basis for Rec. at 11–12.

B. Animal Abuse-Related Behavioral Effects

Self-Administration

Self-administration is a method that assesses the ability of a drug to produce rewarding effects. The presence of rewarding effects increases the likelihood that individuals will try to obtain additional quantities of a drug. Animal self-administration of a drug is often useful in suggesting whether humans will experience a particular substance as having rewarding effects, which is indicative of abuse potential. For example, the tendency of rhesus monkeys to self-administer a drug is correlated with humans' propensity to abuse it. HHS Basis for Rec. at 12.

Since self-administration is a methodology in which the test drug is typically administered intravenously to rats, it is not possible to evaluate botanical marijuana through self-administration. However, given that Δ 9-THC is the primary substance that confers abuse potential to marijuana, its ability to induce self-administration can serve as an indicator of the abuse potential of marijuana. HHS Basis for Rec. at 12.

HHS concluded, after weighing the relevant scientific evidence, that Δ 9-THC produces rewarding effects that lead an animal to repeatedly seek out the substance. HHS Basis for Rec. at 12. Specifically, some studies have demonstrated successful animal self-administration of Δ 9-THC following intravenous administration, administration of inhaled vapor, oral administration, and intracerebroventricular administration. Other recent animal studies have not been able to

produce Δ 9-THC self-administration following intravenous administration and oral administration, but HHS concluded that these results were due to the specific methodology of those respective studies, rather than valid evidence of the rewarding effects of Δ 9-THC, and thus do not negate HHS's reliance on studies in which Δ 9-THC was actively self-administered by animals. HHS Basis for Rec. at 12–13.

Furthermore, a comprehensive deconstruction of which animal methodology is optimal for producing preclinical self-administration of Δ 9-THC is not necessary for an evaluation of the abuse potential of marijuana in humans because it is already clear that humans utilize marijuana for its rewarding properties. HHS Basis for Rec. at 13. Animal self-administration is used primarily to predict whether a novel substance is likely to be used by humans for its rewarding properties as an indication of its abuse potential. However, epidemiological data already amply demonstrates that humans self-administer substances that contain Δ 9-THC, including botanical marijuana, for their ability to produce positive subjective responses, including euphoria. HHS Basis for Rec. at 13; *see also* sections VI.4–6 of this preamble (discussing Factors 4–6).

Conditioned Place Preference

A conditioned place preference (“CPP”) study is another method for determining whether drugs have rewarding properties; a CPP study relies on an animal's decision to spend time in a location associated with receiving a drug. The studies in which Δ 9-THC successfully produced CPP occurred under very specific experimental conditions, similar to the Δ 9-THC self-administration studies in animals. Experimental manipulations in CPP studies with Δ 9-THC have included varying the animal species, sex, dose, or route of administration; introducing flavors to obscure unpleasant taste; and varying the drug history of the animals tested. However, as with animal self-administration, the purpose of CPP studies is typically to determine if a new

drug produces rewarding sensations, which would suggest that a drug has abuse potential in humans. Since it is clear that humans self-administer substances that contain Δ 9-THC, including botanical marijuana, HHS determined that it was not necessary to determine which CPP methods are optimal for demonstrating that Δ 9-THC has rewarding properties in animals. HHS Basis for Rec. at 13.

Drug Discrimination Studies

Drug discrimination is a method in which animals indicate whether a test drug produces sensations similar to those produced by a training drug with a known pharmacological mechanism of action. Drug discrimination is considered to be an abuse-related study only when the training drug is a known drug of abuse that is scheduled under the CSA and the test drug may have abusable effects similar to the training drug based on having a similar mechanism of action to the training drug. Because animal drug discrimination studies often use Δ 9-THC as the standard for establishing if new drugs have classic marijuana-like pharmacological activity, HHS did not examine whether this method should be applied when evaluating the abuse potential of Δ 9-THC. HHS Basis for Rec. at 14.

C. Human Behavioral and Physiological Effects

Subjective Effects of Δ 9-THC

The psychological, behavioral, and subjective responses to marijuana in humans have been known and characterized since antiquity. In the modern period, data on the psychological, behavioral, and subjective responses to marijuana are available from the drug labels of FDA-approved drug products, from prospective human abuse potential (“HAP”) studies, from accounts published in the scientific and medical literature, and from an evaluation published in

2017 by the National Academies of Science, Engineering, and Medicine (“NASEM”). HHS Basis for Rec. at 14.

FDA-Approved Drug Products Containing Δ 9-THC

Clinical scientific studies investigated the effects of Δ 9-THC on humans during the development of the FDA-approved drug product Marinol, which contains 2.5, 5, and 10 mg dronabinol ((-)-*trans*- Δ 9-THC of synthetic origin in sesame seed oil). During controlled clinical trials (as reported in section 6.1 of the drug labels for Marinol and Syndros (which relied on the safety data from Marinol during drug development)), various adverse events (“AEs”) were observed, including amnesia, anxiety/nervousness, ataxia, confusion, depersonalization, hallucination, asthenia, palpitations, tachycardia, vasodilation/flush, euphoria, paranoid reaction, somnolence, abnormal thinking, dizziness, abdominal pain, nausea, and vomiting. HHS Basis for Rec. at 14–15.

HAP Studies

HAP studies evaluate whether a test drug produces positive subjective responses compared to a placebo and a known drug of abuse that is scheduled under the CSA and serves as the positive control. If the test drug produces rewarding effects that are statistically significantly greater than the placebo, and beyond the acceptable placebo range of response, it is an indication that the drug may have abuse potential. The relative abuse potential is suggested by the responses from the positive control on these measures in comparison to the test drug. HHS Basis for Rec. at 15.

After analyzing a number of HAP studies of marijuana and Δ 9-THC, which varied in the in dose of Δ 9-THC, the route of administration, or whether the Δ 9-THC was provided in the form of marijuana or isolated compound, HHS identified a number of commonalities. First,

following administration of the study drug (*i.e.*, marijuana or $\Delta 9$ -THC), there were increases in positive subjective responses. Second, the studies demonstrated increases on the Addiction Research Center Inventory scales for the morphine benzedrine group (euphoria), marijuana, and amphetamine. HHS concluded that these data consistently demonstrated that $\Delta 9$ -THC, in the form of marijuana or as an isolated compound, produces rewarding effects that are indicative of abuse potential when it is administered under controlled experimental conditions. Third, and in contrast to the prior findings, the data also demonstrated that the administration of marijuana or $\Delta 9$ -THC may result in negative subjective responses reflecting negative drug effects and sedation; these are often delayed in onset from when the positive subjective effects begin. HHS noted that the positive and negative subjective responses following administration of marijuana or $\Delta 9$ -THC were often dose-dependent. It also noted that there were typically few differences between responses to marijuana and $\Delta 9$ -THC, or between responses based on route of administration of the study drug. HHS Basis for Rec. at 15.

Common Responses to Marijuana in Humans Published in Scientific and Medical Literature

HHS concluded that the responses to dronabinol reported during development of Marinol and the responses to marijuana and $\Delta 9$ -THC reported in HAP studies paralleled the common responses to marijuana that have been described by other medical scientists. These responses include positive subjective responses (such as euphoria or happiness), sedative responses (such as drowsiness or changes in sleep), anxiety and negative responses (such as panic attacks, agitation, and paranoia), perceptual changes (such as hallucinations and changes in perception), psychiatric, social, and cognitive changes (such as drug abuse, delusions, memory and concentration impairment, and impaired judgment), and physiological responses (such as nausea, tachycardia, facial flushing, dry mouth, tremor, dizziness, ataxia, and hyperemesis). The

literature reviewed by HHS also concluded that the positive changes that occur following use of marijuana are pleasurable to many humans and are associated with drug-seeking and drug-taking; and that these effects are typically dose-dependent, with higher doses and routes of administration that produce faster onset producing more intense responses and the likelihood of more negative subjective effects. HHS Basis for Rec. at 16–17.

National Academies of Science, Engineering, and Medicine (NASEM)

HHS also reviewed a book-length evaluation of marijuana by NASEM entitled *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*.¹⁷ According to HHS, in this evaluation, NASEM provided a brief summary of the clinical features of marijuana intoxication and found that (1) during acute cannabis intoxication, the user's sociability and sensitivity to certain stimuli (*e.g.*, colors, music) may be enhanced, the perception of time is altered, and the appetite for sweet and fatty foods is heightened; (2) some users report feeling relaxed or experiencing a pleasurable rush or buzz after smoking cannabis; (3) these subjective effects were often associated with decreased short-term memory, dry mouth, and impaired perception and motor skills; and (4) when very high blood levels of $\Delta 9$ -THC were attained, persons might experience panic attacks, paranoid thoughts, and hallucinations. HHS Basis for Rec. at 17–18.

HHS Conclusion With Respect to Factor 2

Based on its analysis of the studies discussed above, HHS concluded that $\Delta 9$ -THC, the substance largely responsible for the abuse potential of marijuana, is a partial agonist at the cannabinoid CB₁ receptor. When $\Delta 9$ -THC is administered to animals, it produces rewarding

¹⁷ National Academies of Science, Engineering, & Medicine, *The Health Effects of Cannabis & Cannabinoids: The Current State of Evidence & Recommendations for Research* (2017), <https://nap.nationalacademies.org/read/24625/chapter/1>.

responses, as evidenced by its ability to induce self-administration and CPP. This is consistent with the data from human studies and from clinical observations, where administration of Δ^9 -THC or use of marijuana produces euphoria and other pleasurable responses, as well as sedation and anxiety responses. Psychiatric, social, and cognitive responses, which are often experienced as negative, are also reported, as are physiological responses such as dry mouth, ataxia, and increased hunger. As described in HHS's analysis of Factor 4, *see* HHS Basis for Rec. at 32–37, the rewarding responses observed in humans are consistent with the prevalence of nonmedical use of marijuana, which includes abuse of the substance. Abuse of marijuana by individuals can lead to other negative consequences, including addiction and the need to seek medical attention through calls to poison centers or visits to an ED, as described in Factor 5, *see* HHS Basis for Rec. at 38–39, 42. HHS Basis for Rec. at 18.

DEA believes that additional data on marijuana's pharmacological effects may be appropriate for consideration in assessing this factor.

3. The State of Current Scientific Knowledge Regarding Marijuana

The third factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is the state of current scientific knowledge regarding marijuana. In considering this factor and making its recommendation, HHS examined the chemistry of marijuana and the human pharmacokinetics of marijuana. HHS Basis for Rec. at 18–24.

Chemistry

Cannabis is a genus of annual flowering plant with digitate leaves in the family *Cannabaceae* Martinov that likely originated in Central or Southeast Asia over 10,000 years ago and was first cultivated in China for fiber and seed production. Cultivation eventually spread across Asia, Africa, and Europe and then to the Americas. A longstanding and significant historical debate by botanists and taxonomists continues today regarding the number of species

in the *Cannabis* genus, but it is generally treated as a single, highly polymorphic species known as *Cannabis sativa* L., with the other two previously reported species listed as *Cannabis indica* Lam. and *Cannabis ruderalis* Janisch. Plants previously believed to be part of the latter two species are generally recognized as varieties (or subspecies) of *Cannabis sativa* L., which are commonly referred to as *sativa* var. *indica* and *sativa* var. *ruderalis*. *Cannabis sativa* and *sativa* var. *indica* plants are widely cultivated for their size, branching, and cannabinoid content, while *sativa* var. *ruderalis* is rarely cultivated alone because it is shorter, is often unbranched, and has very low cannabinoid content. Worldwide *Cannabis* varieties are separated into hundreds of different cultivars and strains. Plants selected for cultivation are known as cultivated varieties or cultivars, whereas plants reproduced asexually from a cultivar through clonal propagation are known as strains. These practices have resulted in significantly different chemical profiles for *Cannabis* cultivars, and the classification term to account for these chemical profile differences has evolved. The term “chemovar” accounts for the plant’s chemical profile and is a more meaningful classification for clinical researchers studying the plant’s potential drug effects. Marijuana products developed from diverse chemovars will have different safety, biological, pharmacological, and toxicological profiles. HHS Basis for Rec. at 18–19.

Cannabis is a dioecious plant, meaning female and male flowers occur on separate plants, and rarely occurs as a monoecious plant (*i.e.*, single plant containing male and female flowers). The glandular trichomes found on the female plant’s unfertilized flower heads and bracts contain the highest concentrations of cannabinoids. For this reason, unfertilized female chemovars are favored to harvest large inflorescences (*i.e.*, complete flower head) for their rich cannabinoid and terpene content. HHS Basis for Rec. at 19.

The *Cannabis sativa* L. plant naturally contains many different compounds, and more than 550 have been identified, such as cannabinoids, terpenoids, flavonoids, stilbenoids, steroids,

polysaccharides, benzoquinone, phenanthrenes, spiroindans, lignans, fatty acids, sugars, hydrocarbons, amino acids, and proteins. Cannabinoids are mainly found in living *Cannabis sativa* L. plants in their non-psychoactive carboxylated forms (*i.e.*, acid form), which require drying, heating, combustion, or aging to decarboxylate to their neutral forms, and are primarily composed of C₂₁ terpenophenolic compounds. The most abundant neutral form cannabinoids are Δ9-THC and CBD, but nearly 200 have been identified in the plant and are divided into subclasses: cannabigerols, cannabichromenes, CBDs, Δ9-THCs, (-)-Δ8-*trans*-tetrahydrocannabinols (“Δ8-THCs”), cannabicyclols, cannabielsoins, cannabinols, cannabinodiols, cannabitriols, and the miscellaneous cannabinoids. HHS Basis for Rec. at 19.

Like any other botanical substance, marijuana plants are heterogeneous in nature and contain a complex chemical profile. Moreover, variable organic plant material, as well as manufactured preparations, result in a variety of product forms that dictate different routes of administration, associated risks, and differences in quality of the product used, which may also influence risk for users. Among other things, these differences can result from differences in harvest location, growing conditions, the season in which the marijuana is harvested, and the manner in which the marijuana is processed, handled, transported, and tested. The potential for high variability of marijuana and marijuana-derived products, both in product composition and impurity profile, is a major consideration for the potential variability of drug effects and safety. HHS Basis for Rec. at 19–20.

Processing of marijuana and its use in further manufacturing can lead to a range of forms that individuals may use or consume, including crude mixtures and highly purified substances of botanical origin, many of which may be cannabinoid compounds. Among known cannabinoids in the *Cannabis* plant, both Δ9-THC and Δ8-THC produce marijuana’s psychoactive effects. Because Δ9-THC is significantly more abundant than Δ8-THC, marijuana’s intoxicating effects

are largely attributed to the former. Only small quantities of Δ^8 -THC acid and Δ^8 -THC have been identified in plants. HHS Basis for Rec. at 20.

As noted above, the 2018 amendments to the CSA removed hemp from the definition of marijuana. However, the term “cannabis” is still often broadly used to refer to a wide variety of products manufactured from the *Cannabis sativa* L. plant, regardless of their control status. As a result of the 2018 amendments to the CSA, a large hemp marketplace exists, containing a wide variety of products. In addition, the public has access to cannabis products within the CSA definition of marijuana through State-authorized adult-use (*i.e.*, nonmedical use) and medical-use programs, as well as via the illicit marketplace. *See* HHS Basis for Rec. at 28–37 (Factor 4). Because of these diverse sources of marijuana, there is a lack of unified controls on cultivation and manufacturing, which raises concerns related to the safety, quality, and consistency of botanical substances (*e.g.*, botanical raw materials, extracts, and intermediates) and final product formulations that are currently accessed for medical and nonmedical use. Products sourced from State-authorized adult-use and medical-use programs are subject to a patchwork of inconsistent product standards and safety requirements. Although some State programs have a set of standards (for example, on manufacturing, testing, labeling, and packaging), each program’s controls are different, leading to a wide variation of products across State-authorized programs. And the illicit marketplace is not subject to any standards or oversight. As a result, the range of products within the CSA’s definition of marijuana encompasses a large degree of variation in forms for consumption, composition of biologically relevant constituents, potency, and contaminants. HHS Basis for Rec. at 21.

In short, marijuana has hundreds of chemovars containing variable concentrations of Δ^9 -THC, cannabinoids, and other compounds. As a result, in evaluating whether to recommend that marijuana be rescheduled, HHS focused to the greatest extent possible on wide-ranging

substances derived from cannabis plants that are vehicles for the self-administration of $\Delta 9$ -THC as the key biologically active substance on which the CSA's current definition of marijuana is based. HHS Basis for Rec. at 21.

Human Pharmacokinetics of $\Delta 9$ -THC

HHS reported that the pharmacokinetics of $\Delta 9$ -THC in humans—*i.e.*, the study of how the body interacts with $\Delta 9$ -THC—have been evaluated following inhaled administration of marijuana and oral administration of marijuana. These are the most frequently used routes of administration for marijuana or isolated $\Delta 9$ -THC. HHS Basis for Rec. at 21.

Marijuana is commonly administered by humans via inhalation through smoking and, more recently, through vaping (*e.g.*, heating and inhalation of botanical matter or other volatile substances containing $\Delta 9$ -THC). Generally, inhalation of a drug is the route that produces the fastest rate of drug absorption. Once marijuana is inhaled, $\Delta 9$ -THC is absorbed through the lungs in the form of an aerosol within seconds. Peak plasma levels of $\Delta 9$ -THC following inhalation occur very quickly, within 6 to 10 minutes. Psychoactive effects begin immediately following absorption, although peak subjective effects do not coincide with peak plasma $\Delta 9$ -THC levels and are often delayed. Following administration of marijuana through inhalation, the bioavailability of $\Delta 9$ -THC is 10 percent to 35 percent. That bioavailability is relatively low and varies widely due to several factors. An individual's experience and technique with smoking marijuana also determines the dose absorbed. HHS Basis for Rec. at 22.

When marijuana or $\Delta 9$ -THC is administered orally (such as by eating marijuana-infused foods), the effects start within 30 to 90 minutes, reach their peak at 1.5 to 3 hours, and remain measurable for 4 to 12 hours. Oral bioavailability of $\Delta 9$ -THC, following ingestion of an edible containing marijuana or isolated $\Delta 9$ -THC, ranges from 5 to 20 percent. The low and variable

bioavailability of $\Delta 9$ -THC from oral ingestion is a consequence of its first-pass hepatic elimination from blood and erratic absorption from stomach and bowel. Ingestion of brownies containing marijuana also results in lower $\Delta 9$ -THC plasma levels relative to inhalation of marijuana. HHS Basis for Rec. at 22–23.

Although there are differences in absorption of $\Delta 9$ -THC depending on route of administration, the distribution, metabolism, and excretion of $\Delta 9$ -THC is similar regardless of how the drug is administered. Plasma concentrations of $\Delta 9$ -THC decrease quickly after absorption through rapid distribution into tissues and through liver metabolism. Because $\Delta 9$ -THC has high lipophilicity, the apparent volume of distribution of $\Delta 9$ -THC is high (10 L/kg) as it is distributed initially into organs such as lung, heart, brain, and liver that are highly perfused. Over time with regular exposure to marijuana, $\Delta 9$ -THC will concentrate and be retained in fat. HHS Basis for Rec. at 23.

Metabolism of $\Delta 9$ -THC occurs primarily via cytochrome P450 isozymes (CYP2C9, CYP2C19, and CYP3A4) via microsomal hydroxylation to both active and inactive metabolites. The primary active metabolite of $\Delta 9$ -THC is 11-hydroxy- $\Delta 9$ -THC. $\Delta 9$ -THC clears from the blood relatively rapidly, largely because it is redistributed to other tissues in the body. Metabolism of $\Delta 9$ -THC in most tissues is relatively slow or absent. The majority of the absorbed $\Delta 9$ -THC dose is eliminated in feces, and about 33 percent in urine. HHS Basis for Rec. at 23.

HHS Conclusion With Respect to Factor 3

In conclusion, HHS found that the pharmacokinetic profile of marijuana varies greatly depending on route of administration. Inhalation of marijuana produces a rapid increase in plasma levels of $\Delta 9$ -THC and an immediate onset of psychological effects. In comparison, oral

administration of marijuana produces a much slower increase in plasma levels of Δ 9-THC and onset of psychological effects. Once Δ 9-THC has been absorbed, however, the metabolism and excretion of Δ 9-THC follows a standard path. HHS Basis for Rec. at 24.

DEA likewise notes that there is considerable variability in the cannabinoid concentrations and chemical constituency among marijuana samples and that the interpretation of clinical data related to marijuana is complicated. A primary issue is the lack of consistent concentrations of Δ 9-THC and other substances in marijuana, which complicates the interpretation of the effects of different marijuana constituents. Additionally, the non-cannabinoid components in marijuana may potentially modify the overall pharmacological and toxicological properties of various marijuana strains and products. DEA anticipates that additional data on other marijuana constituents, routes of administration of marijuana, and the impact on Δ 9-THC potency may be appropriate for consideration.

4. Marijuana's History and Current Pattern of Abuse

The fourth factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is marijuana's history and current pattern of abuse, which can include its abuse relative to relevant comparator substances that are abused. *See* HHS Basis for Rec. at 28–37. HHS concluded that it is appropriate to consider the Federal- and State-level history of marijuana control, marijuana sources for nonmedical and medical use, marijuana use in the United States since passage of the CSA, and current patterns of use and abuse of marijuana. HHS Basis for Rec. at 28.

Federal History of Marijuana Control

According to HHS, marijuana was described in the United States Pharmacopoeia¹⁸ as early as 1850. Around the time that Congress passed the Pure Food and Drug Act of 1906, Pub. L. 59-384, 34 Stat. 768, drugs such as marijuana, alcohol, heroin, morphine, and cocaine began to be characterized by the Federal Government as addictive and dangerous. These drugs were frequently included in patent medicines, often without the consumer's knowledge. The 1906 law required accurate drug labeling with respect to ingredients and dosage. But it did not prohibit the sale or possession of drugs characterized as addictive and dangerous drugs, including marijuana. As nonmedical use of marijuana and opioids became more popular in the United States, Congress provided funding in 1929 for two "narcotic farms" in Lexington, Kentucky, and Fort Worth, Texas, which were medical treatment centers run by the Public Health Service for federal prisoners who were "habitual users of narcotics," including marijuana-derived products. HHS Basis for Rec. at 28–29.

In the first half of the twentieth century, marijuana use was curbed by several Federal laws. In 1931, the importation of marijuana into the United States began to be restricted under regulations under the Pure Food and Drug Act, except for medicinal purposes. The Marihuana Tax Act of 1937, Pub. L. 75-238, 50 Stat. 551, imposed taxes that effectively prohibited marijuana use for medical, nonmedical, scientific, or industrial purposes. Five years later, in 1942, marijuana was removed from the United States Pharmacopoeia. Through the imposition of mandatory minimums, the Boggs Act of 1951, Pub. L. 82-255, 65 Stat. 767, lengthened the average sentence for first time marijuana offenders to 2 to 5 years, similar to that for opioid

¹⁸ The United States Pharmacopoeia was formed as an "independent, scientific, non-profit organization dedicated to public health" that published "a national, uniform set of guidelines for the best understood medicinal substances and preparations of the day." *Building Trust for Over 200 Years: A Timeline of USP*, U.S. Pharmacopoeia, <https://www.usp.org/200-anniversary/usp-timeline> (last visited May 11, 2024).

offenses, regardless of whether the individual was a nonmedical user or a trafficker. The Narcotic Control Act of 1956, Pub. L. 84-728, 70 Stat. 567, increased the minimum sentence for a first offender for marijuana to 2 to 10 years. HHS Basis for Rec. at 29.

Despite the legal consequences, nonmedical marijuana use increased dramatically in the 1960s, especially among youth. Congress passed the CSA in 1970. The CSA effectively repealed all previous Federal drug laws, including the Marihuana Tax Act, and provided a unified framework for control of drugs with abuse potential. When the CSA was enacted, marijuana was placed into schedule I, which prohibited use of marijuana for medicinal or nonmedical purposes other than legitimate scientific research and analysis. This placement was consistent with the criteria established by the CSA under 21 U.S.C. 812. HHS Basis for Rec. at 29–30.

Marijuana Control at the State Level

According to HHS, changes in State-level marijuana laws in the United States in the modern era began in 1996 with the approval of Proposition 215, the Compassionate Use Act, by voters in California. This law legalized the use, possession, and cultivation of marijuana for treatment of patients with cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis, migraine, or any other illness for which marijuana provides relief, when recommended by a physician. Under the law, marijuana could also be cultivated by patient caregivers. HHS Basis for Rec. at 30.

As of August 2023, when HHS submitted its Basis for Recommendation to DEA, State-level laws allowing medicinal use of marijuana had been passed in a total of 38 States, plus the District of Columbia: Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Hawaii, Illinois, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nevada, New

Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Dakota, Utah, Vermont, Virginia, Washington, and West Virginia. Medical use of marijuana was legalized through the action of 20 State legislatures and by 18 ballot measures.¹⁹ HHS Basis for Rec. at 30.

In 2012, Colorado and Washington became the first States to legalize the nonmedical use of marijuana. As of August 2023, State-level legalization of the nonmedical use of marijuana has occurred in a total of 23 States and the District of Columbia: Alaska, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Illinois, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nevada, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, Virginia, and Washington. Nonmedical use of marijuana was legalized by ballot initiatives in 13 States and by State legislatures in 9 States. HHS Basis for Rec. at 30.

Marijuana Use in the United States Since Passage of the CSA

Marijuana use has varied since the CSA was passed in 1970. Gallup Poll data from 1969 to 2013 show a steady increase over time in affirmative responses to whether the respondent had personally tried marijuana, with only 4 percent of people saying they had tried marijuana in 1969 compared to 38 percent in 2013. As HHS observed, the 2017 NASEM report stated that the prevalence of marijuana use peaked in the late 1970s, declined through the 1980s, and then increased again in the mid-1990s. From 2007 to 2017, there were steady year-over-year increases in the share of the general population that used marijuana in the past month, although

¹⁹ Data on the number of patients who participate in State-sanctioned medical cannabis use is available here: *Medical Cannabis Patient Numbers*, Marijuana Pol’y Project, <https://www.mpp.org/issues/medical-marijuana/state-by-state-medical-marijuana-laws/medical-marijuana-patient-numbers> (last visited May 13, 2024).

there is no clear explanation for the post-2007 increase in use rates. HHS Basis for Rec. at 31–32.

Current Patterns of Use and Abuse of Marijuana

In considering current patterns of use and abuse of marijuana and marijuana-derived products, HHS analyzed epidemiological databases from 2015 to the most recent years of available data (which vary among data sources). A wide variety of epidemiological databases provide necessary data for HHS’s analyses. These include the NSDUH; Behavioral Risk Factor Surveillance System (“BRFSS”); Research Abuse, Diversion and Addiction-Related Surveillance (“RADARS”); Nonmedical Use of Prescription Drugs (“NMURx”); Monitoring the Future (“MTF”); Youth Risk Behavioral Surveillance System (“YRBSS”); and International Cannabis Policy Study (“ICPS”). HHS Basis for Rec. at 32.

National Survey on Drug Use and Health

Based on NSDUH data, HHS concluded that from 2015 to 2019 the past-year use of marijuana for any reason (nonmedical and medical) among people ages 12 years and older increased from 14 percent to 18 percent. By contrast, past-year (nonmedical and medical) use of comparator drugs that have FDA-approved therapeutic indications declined or remained relatively stable over the same timeframe, including hydrocodone (22 percent to 16 percent), benzodiazepines (12 percent to 11 percent, 2017 to 2019 only), oxycodone (11 percent to 9 percent), tramadol (7 percent to 6 percent), zolpidem (4 percent to 3 percent), and ketamine (less than 1 percent). Although there were trend breaks for the years 2020 and 2021,²⁰ marijuana past-year use continued to increase during these two years. HHS Basis for Rec. at 32–33.

²⁰ HHS noted that NSDUH data collection was disrupted in 2020 and 2021 due to the COVID-19 pandemic, leading to trend breaks in these years. HHS Basis for Rec. at 32.

Based on NSDUH data, HHS concluded that from 2015 to 2019, the prevalence of past-year nonmedical use of marijuana (*i.e.*, use without a health care provider (“HCP” recommendation) among people ages 12 years and older also increased. HHS’s finding was based on an increase in the prevalence of overall nonmedical use of marijuana from 12 percent to 15 percent and on an increase in nonmedical use of marijuana only, without nonmedical use of other drugs that are abused, from 8 percent to 11 percent during this period. There was a slight decrease in both categories in 2020, but the prevalence of both kinds of uses increased again in 2021 (to 16 percent and 11 percent, respectively) to levels that were higher than those reported in 2019. In contrast, the prevalence of past-year nonmedical use of comparator drugs was less than 3 percent for heroin, cocaine, oxycodone, hydrocodone, tramadol, benzodiazepines, and zolpidem, which is much less than that for marijuana, either alone or with other drugs. Over the 2015 to 2021 reporting period, the overall use of these comparator drugs declined slightly or remained fairly stable. Notably, the majority of individuals who reported nonmedical use of marijuana did not report nonmedical use of the comparator drugs. And over the same reporting period of 2015 to 2021, the prevalence of past-year use of alcohol ranged from 62 percent to 65 percent for individuals ages 12 years and older, far exceeding the prevalence for marijuana or other comparator drugs. These data demonstrate that alcohol has the highest prevalence of past-year-only use, followed by nonmedical use of marijuana. The prevalence of the other comparators is far below that of alcohol and marijuana. HHS Basis for Rec. at 33.

HHS also concluded that the NSDUH data show that most individuals who used marijuana in the past year did not do so based on a recommendation from an HCP, but marijuana use was more frequent among users with an HCP recommendation. The yearly percentage of individuals who used marijuana but did not have an HCP recommendation ranged between 84 and 89 percent between 2015 and 2021; by comparison, exclusive medical use of marijuana that

was recommended by an HCP ranged between 7 and 10 percent of marijuana users in the same period. According to HHS, approximately 50 percent of those individuals without an HCP recommendation used marijuana for 60 or fewer days in the year, while 29 percent used marijuana for more than 241 days in the year. In contrast, for those individuals whose use of marijuana was sometimes or always recommended by an HCP, 51 percent and 55 percent (respectively) used marijuana at least 241 days in the year. HHS Basis for Rec. at 33–34.

The NSDUH data from 2021 showed that among individuals who used any marijuana in the past year, 69 percent used marijuana in the prior month. For comparator drugs, the percentage of individuals with past-year use who used each substance nonmedically in the past month was 76 percent for alcohol, 49 percent for heroin, 38 percent for cocaine, and 28 percent for ketamine. HHS Basis for Rec. at 34.

Behavioral Risk Factor Surveillance System

BRFSS is a national, State-based, cross-sectional telephone survey conducted by the Centers for Disease Control and Prevention (“CDC”). The participants in the 2021 BRFSS module for marijuana included approximately 68 million individuals 18 years and older, residing in 24 States and Territories: Alaska, Connecticut, Delaware, Hawaii, Idaho, Illinois, Indiana, Kentucky, Maine, Maryland, Minnesota, Montana, Nebraska, Nevada, New Hampshire, New York, North Dakota, Ohio, Oklahoma, Rhode Island, Utah, Vermont, Wyoming, and Guam. HHS Basis for Rec. at 34.

For the 2021 survey year, the estimated prevalence of past-month marijuana use for any reason in the BRFSS survey was 12 percent, with 88 percent reporting no marijuana use. Among those with past-month marijuana use, the mean frequency of use was 17 days per month, with half of respondents reporting that they used marijuana 20 to 30 days per month. This pattern was consistent across all age and sex categories. HHS Basis for Rec. at 34.

When the reason for use was evaluated, the percentage of individuals who reported use for both medical and nonmedical reasons was 39 percent, compared to 36 percent for those who reported use for nonmedical reasons only, and 25 percent for those who reported use for medical reasons only. Those individuals who reported past-month use of marijuana for medical reasons were more likely to be adults 55 years and older, while individuals who reported past-month marijuana use for nonmedical reasons only were more likely to be younger adults aged 18 to 24 years. HHS Basis for Rec. at 34.

Individuals who reported using marijuana in the past 30 days for both nonmedical and medical reasons were more likely (62 percent) to report marijuana use near daily (20 to 30 days per month) than individuals who reported marijuana use for nonmedical reasons only (34 percent). Similarly, individuals who used marijuana for medical reasons only were also more likely (57 percent) to report near daily use than those who used it for nonmedical reasons only. HHS Basis for Rec. at 34.

Researched Abuse, Diversion and Addiction-Related Surveillance System Survey of Nonmedical Use of Prescription Drugs

The RADARS System conducts the NMURx Program, a serial, cross-sectional, online survey of the general adult population (18 years and older) to elicit information on the nonmedical use of drugs (prescription, nonprescription, unapproved, and illicit). The NMURx Program estimates represent measures of past-year drug use in an enriched sample of United States adults with higher-than-average nonmedical use of prescription pain relievers and illicit drugs. NMURx program data demonstrated that past-year use of marijuana was reported by 21 percent of individuals, while past-year use of comparator substances was substantially lower: benzodiazepines (4 percent), hydrocodone, oxycodone, tramadol (2 percent), cocaine or crack (less than 2 percent), and illicit fentanyl, heroin, and ketamine (less than 1 percent). This pattern

of much greater marijuana use compared to other drugs is consistent with the patterns reported in NSDUH and BRFSS. HHS Basis for Rec. at 35.

Monitoring the Future

MTF collects information on the use of selected prescription and illicit drugs and alcohol by conducting an annual, nationally representative, cross-sectional survey of 8th, 10th, and 12th graders in public and private schools.²¹ MTF data showed that during the years 2012 to 2022, the illicit drug most frequently used by 12th-grade students who reported past-year drug use was marijuana/hashish (approximately 35 percent per year from 2012 to 2020, with a reduction to 30 percent per year in 2021 and 2022). In contrast, in 2022, alcohol was used by 52 percent of 12th-grade students within the last 12 months, similar to percentages in 2019 and 2020 (52 percent and 55 percent, respectively), but higher than the 2021 level of 47 percent. All other comparator drugs (hydrocodone, heroin, tramadol, cocaine, ketamine, and zolpidem) were each used in the past year by fewer than 5 percent of 12th graders from 2012 to 2022. HHS Basis for Rec. at 35.

MTF data for past-month use showed a similar pattern. During the years 2012 to 2022, the illicit drug most frequently used by 12th-grade students who reported past-month drug use was marijuana/hashish (approximately 20 to 22 percent per year) compared to past-month use of cocaine (approximately 1 percent per year) or heroin (less than 0.5 percent per year). However, past-month alcohol use by 12th-grade students (28 percent) exceeded that of marijuana in 2022. For those who used marijuana in the past month, 6 to 7 percent used it daily. By comparison, for those who used cocaine and heroin in the last month, less than one percent used it daily. MTF

²¹ As a result of the COVID-19 pandemic, there is a potential trend break in the 2020 MTF data. HHS Basis for Rec. at 35.

does not provide past-month use data for hydrocodone, heroin, tramadol, ketamine, or zolpidem. HHS Basis for Rec. at 35.

Youth Risk Behavior Surveillance System

YRBSS was established by the CDC and conducts school-based surveys every 2 years, in partnership with State, local, Territorial, and Tribal governments, with a focus on youth health behavior in the United States. The YRBSS high school component, the Youth Risk Behavior Survey, includes a nationally representative survey of 9th- through 12th-grade students. YRBSS data showed that from 2009 to 2019, approximately 20 percent of students in 9th through 12th grade reported using marijuana at least once in the past month during each year evaluated. When students 17 years and older were asked how old they were when they first used marijuana, 43 percent reported they initiated use between the ages of 15 to 16 years, 25 percent initiated use between the ages of 13 to 14 years, and 13 percent initiated use at 12 years of age and younger. YRBSS data also showed, however, that past-month alcohol use by high school students (29 percent) in 2019 was greater than that of marijuana use, while past month prescription opioid misuse (including codeine, hydrocodone, or oxycodone) (7 percent) in 2019 was much lower than that of both alcohol and marijuana use. HHS Basis for Rec. at 36.

International Cannabis Policy Study

ICPS conducted serial, cross-sectional surveys from 2019 to 2021 of individuals ages 16 to 65 years living in the United States to understand the public health impact of marijuana legalization. HHS's evaluation of that survey data focused on respondents who reported at least some past-year marijuana nonmedical use (by indicating that they were not a medical marijuana user, defined as someone who uses marijuana only to treat a medical condition). HHS Basis for Rec. at 36.

According to HHS, ICPS data showed that the prevalence of past-year nonmedical use of marijuana ranged from 18 percent to 22 percent of individuals surveyed from 2019 to 2021, while the prevalence of past-month nonmedical use was lower, ranging from 12 percent to 14 percent of individuals surveyed. Individuals aged 26 to 34 years had the highest relative prevalence of nonmedical marijuana use, with 26 percent reporting past-year use and 18 percent reporting past-month use. When those individuals who reported past-year marijuana use in 2021 were asked why they used the drug, 33 percent reported use for medical reasons, while 61 percent were classified as using marijuana for nonmedical reasons only. (The other 6 percent did not respond.) HHS Basis for Rec. at 36.

When frequency of nonmedical use of marijuana was evaluated in ICPS for those individuals who used marijuana nonmedically at least once a year, individuals aged 16 to 17 years had the highest percentage of use less than once a month (approximately 40 percent, compared to approximately 25 to 31 percent for other age cohorts); while individuals aged 26 to 34 years had the highest percentage of daily use (approximately 43 percent, compared to approximately 34 to 37 percent for individuals in other adult cohorts and approximately 24 percent among individuals 16 and 17 years). Among individuals who used marijuana for nonmedical reasons in the past year, 49 percent reported never using alcohol and marijuana at the same time, while 35 percent sometimes used the two substances together, 9 percent often used them together, and 5 percent used alcohol every time they used marijuana. HHS Basis for Rec. at 36–37.

HHS Conclusion With Respect to Factor 4

In light of the evidence cited above, HHS determined that certain conclusions could be drawn about marijuana's current pattern of abuse. HHS concluded that the use of marijuana for medical and nonmedical purposes is extensive in the United States. HHS also concluded that the

prevalence of marijuana use is less than that of alcohol and significantly more than that of other drugs of abuse that are scheduled under the CSA. Specifically, HHS noted that NSDUH data from 2015 to 2019 showed that the prevalence of past-year use of alcohol was five to six times greater than that of nonmedical use of marijuana. In contrast, the prevalence of past-year nonmedical use of heroin, cocaine, oxycodone, hydrocodone, tramadol, benzodiazepines, and zolpidem was four to five times less than that of marijuana nonmedical use. Similar past-year comparative drug use data were reported in RADARS-NMURx, MTF, and ICPS. HHS Basis for Rec. at 37. In 2016, DEA found that marijuana continues to be the most widely used illicit drug. It noted that in 2014, there were 22.2 million current users; that there were also 2.6 million new users, most of whom were less than 18 years of age; and that marijuana was the most frequently identified drug identified in Federal, State, and local forensic laboratories. 81 FR at 53739. In addition to the data provided in the HHS Basis for Recommendation and the data considered by HHS and DEA in their 2015 eight-factor analyses, DEA anticipates that additional information arising from this rulemaking will further inform the findings that must be made to reschedule marijuana, including with respect to this factor. DEA also notes that, according to the World Health Organization, cannabis is globally the most commonly used psychoactive substance under international control.²² Accounting for half of all drug seizures worldwide, the global annual prevalence of cannabis consumption is 2.5 percent or about 147 million people.²³ In 2016, an estimated 28.6 million individuals age 12 or older were current (in the past month) illicit drug

²² World Health Org., *The Health and Social Effects of Nonmedical Cannabis Use*, at v (2016), <https://iris.who.int/bitstream/handle/10665/251056/9789241510240-eng.pdf>.

²³ Alcohol, Drugs & Addictive Behaviours Unit, *Cannabis*, World Health Org., <https://www.who.int/teams/mental-health-and-substance-use/alcohol-drugs-and-addictive-behaviours/drugs-psychoactive/cannabis> (last visited May 13, 2024).

users.²⁴ By 2020, approximately 59.3 million individuals age 12 or older reported using an illicit drug within the past year; 83.6 percent (49.6 million) of those past-year illicit drug users reported using marijuana.²⁵ In 2022, the Domestic Cannabis Eradication and Suppression Program was responsible for the eradication of 4,435,859 illegally cultivated outdoor cannabis plants and 1,245,980 illegally cultivated indoor plants for a total of 5,681,839 illegally cultivated marijuana plants.²⁶ DEA believes that additional data on marijuana’s pattern of abuse may be appropriate for consideration in assessing this factor.

5. The Scope, Duration, and Significance of Abuse

The fifth factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is the scope, duration, and significance of marijuana abuse. In conducting its analysis, HHS analyzed the consequences over time of marijuana abuse compared to the abuse of other substances based on data from the United States Poison Centers National Poison Data System (“NPDS”), NSDUH, TEDS, the National Addictions Vigilance Intervention and Prevention Program (“NAVIPPRO”), the National Emergency Department Sample (“NEDS”), the National Inpatient Sample (“NIS”), and the National Forensic Laboratory Information System (“NFLIS”). HHS Basis for Rec. at 37–45.

Epidemiological Data on Consequences of Marijuana Abuse

National Poison Data System

²⁴ Substance Abuse & Mental Health Servs. Admin., *Key Substance Use and Mental Health Indicators in the United States: Results from the 2016 National Survey on Drug Use and Health 1* (2017), <https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.pdf>.

²⁵ Substance Abuse & Mental Health Servs. Admin., *Key Substance Use and Mental Health Indicators in the United States: Results from the 2020 National Survey on Drug Use and Health 2* (2021), <https://www.samhsa.gov/data/sites/default/files/reports/rpt35325/NSDUHFFRPDFWHTMLFiles2020/2020NSDUHFFR1PDFW102121.pdf>.

²⁶ *Domestic Cannabis Suppression/Eradiation Program*, DEA, <https://www.dea.gov/operations/eradication-program> (last visited May 13, 2024).

Data from NPDS provide information on the scope of contacts with a poison center (“PC”) following marijuana abuse relative to abuse of selected comparators. HHS Basis for Rec. at 38.

The number of PC abuse cases for a substance (either alone or in combination with another substance) for the period of 2015 to 2021 showed that the highest number of PC abuse cases was for alcohol, followed by heroin and then benzodiazepines. The fourth highest number of PC abuse cases was for marijuana, with all other comparators showing fewer PC abuse cases. When the PC abuse cases for 2015 to 2021 were analyzed for cases involving a single substance only, the rank order of PC abuse cases by number was the same as the order from all PC abuse cases for substances used alone or in combination with another substance, meaning that marijuana accounted for the fourth highest number of PC abuse cases for a single substance. HHS Basis for Rec. at 38.

HHS’s analysis of the data from 2015 to 2021 showed cases resulting from abuse (as opposed to those resulting from other causes, such as accidental ingestion) made up the largest proportion of PC cases for illicit fentanyl (72 percent), heroin (65 percent), cocaine (41 percent) and ketamine (40 percent). The fifth highest percentage was for cases involving marijuana (36 percent), followed by alcohol (15 percent), oxycodone (13 percent), benzodiazepines (8 percent), hydrocodone (5 percent), tramadol (4 percent), and zolpidem (3 percent). A similar analysis for single-substance-only abuse for the same period showed that the three substances most likely to lead to a PC call following abuse were heroin (65 percent), oxycodone (47 percent), and tramadol (47 percent). The fourth highest percentage was for marijuana and ketamine (46 percent), followed by alcohol (43 percent), zolpidem (40 percent), hydrocodone (37 percent), illicit fentanyl (34 percent), benzodiazepines (32 percent), and cocaine (28 percent). HHS Basis for Rec. at 38.

Annual utilization-adjusted abuse case rates were calculated by dividing the number of PC abuse case counts by the prevalence of past-year use based on NSDUH estimates from people aged 12 years and older, for the period 2015 to 2019, for both (1) any past-year use of the substance and (2) past-year nonmedical use of the substance. These utilization-adjusted rates convey the likelihood that use of a drug will result in PC abuse cases when considering how many people use the drug for either (1) any reason or (2) nonmedical reasons. The utilization-adjusted abuse rates for any past-year use of a substance showed the highest rate for heroin (increasing from 4,038 to 7,201 cases per one million people). The next highest rates were for ketamine, cocaine, and benzodiazepines; all these rates were considerably lower than the rate for heroin. The rates for marijuana (relatively stable at 75 to 70 cases per one million people) and oxycodone were similar, as were the rates for alcohol, zolpidem, tramadol, and hydrocodone; all these rates were considerably lower than the rates for ketamine, cocaine, and benzodiazepines. A similar pattern of utilization-adjusted abuse rates was seen among cases involving a single substance only during the same time period. HHS Basis for Rec. at 39.

An analysis of medical outcomes related to exposure based on severity, timing, and assessment of clinical effects for all single-substance PC abuse cases involving marijuana or comparator drugs showed that serious medical outcomes (moderate effect, major effect, or death) were greatest for illicit fentanyl (81 percent) and heroin (79 percent), followed by oxycodone (70 percent), ketamine (64 percent), tramadol (62 percent), cocaine (59 percent), hydrocodone (44 percent), marijuana (41 percent), benzodiazepines (32 percent), alcohol (31 percent), and zolpidem (27 percent). HHS noted that death rates are underreported in NPDS, but HHS observed that the highest death rate was for fentanyl (25 percent); cocaine, heroin, and alcohol had comparatively very low death rates (3 percent, 2 percent, and 2 percent, respectively), with all other comparators reporting death rates of less than 1 percent. HHS Basis for Rec. at 39–40.

National Survey on Drug Use and Health

Data from NSDUH provide nationally representative information on the prevalence of substance use disorder (“SUD”) in 2021 among individuals aged 12 years or older who reported nonmedical use of marijuana in past year in comparison to heroin, cocaine, or alcohol use in the past year. A diagnosis of SUD is made when an individual endorses at least 2 of the 11 criteria for SUD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (“DSM-V”). Individuals are classified with a mild SUD if they meet two to three of the criteria, a moderate SUD if they meet four to five of the criteria, and a severe SUD if they meet six or more of the criteria. HHS Basis for Rec. at 40.

NSDUH data showed that, among individuals with past-year heroin use in 2021, there was an 81 percent prevalence of meeting the criteria for a heroin SUD. In comparison, there was a 30 percent prevalence of meeting the criteria for marijuana SUD among individuals who used marijuana for nonmedical reasons only (17 percent mild, 8 percent moderate, and 5 percent severe). For individuals who used marijuana for nonmedical purposes and did not use other drugs illicitly, there was a slightly lower prevalence (24 percent) of meeting the criteria for SUD (15 percent mild, 6 percent moderate, and 3 percent severe). For cocaine, 30 percent of individuals who used cocaine in the past year met criteria for cocaine SUD (13 percent mild, 5 percent moderate, and 12 percent severe). For individuals who used alcohol in the past year, the prevalence of alcohol SUD was 17 percent (10 percent mild, 4 percent moderate, and 3 percent severe). HHS Basis for Rec. at 40.

Although the 2021 NSDUH data showed that the likelihood of meeting the criteria for a SUD was highest for heroin, followed by marijuana, cocaine, and alcohol, the absolute number of individuals who met the criteria had a different order. Alcohol had the highest number of such individuals (approximately 29,544,000), followed by marijuana (approximately 13,078,000

people with marijuana nonmedical-only use, and approximately 7,454,000 with nonmedical-only use and no nonmedical use of other drugs), cocaine (approximately 1,408,000), and heroin (approximately 894,000). HHS Basis for Rec. at 40.

Treatment Episode Data Set

TEDS is a database run by SAMHSA within HHS that presents information on the demographic and substance use characteristics of annual admissions for treatment for alcohol and drug abuse in State-approved facilities that are required by the States to provide TEDS client-level data. Because TEDS is based only on reports from these facilities, TEDS data do not represent the total national demand for substance abuse treatment or the prevalence of substance abuse in the general population. HHS Basis for Rec. at 40–41.

Out of 1.4 million admissions documented in the 2020 TEDS dataset, the most frequently reported primary drug of admission was alcohol (31 percent, or 442,014 admissions), followed by heroin (21 percent, or 292,126 admissions), marijuana (10 percent, or 139,481 admissions), and cocaine (5 percent, or 71,725 admissions). Other comparator drugs were each reported as the primary drug in less than 2 percent of admissions. Over the reporting period of 2015 to 2020, the proportion of admissions each year ranged from 30 to 33 percent for alcohol; from 21 to 26 percent for heroin; from 10 to 14 percent for marijuana; and from 5 to 6 percent for cocaine. The proportion of admissions with marijuana as the primary drug declined each year from 14 percent in 2015 to a low of 10 percent in 2020, while the proportion of admissions with cocaine as the primary drug increased slightly during this time from 5 percent in 2015 to 6 percent in 2019. During this reporting period, other comparator drugs were each reported as the primary drug in less than 2 percent of admissions each year. HHS Basis for Rec. at 41.

In 2020, marijuana and cocaine were most likely to be reported as the secondary drug at admission (25 percent and 24 percent, respectively), followed by alcohol (15 percent), heroin (8

percent), and benzodiazepines (6 percent), with all other comparators reported as less than 2 percent. For tertiary drugs at admission, marijuana (29 percent) was reported most frequently, followed by cocaine (18 percent), alcohol (16 percent), and heroin (5 percent), with all other comparators reported as less than 2 percent. HHS Basis for Rec. at 41.

National Addictions Vigilance Intervention and Prevention Program

NAVIPPRO is a surveillance system for substance use and nonmedical use of prescription medication in a convenience sample of adults seeking treatment or being assessed for SUD treatment at participating facilities across the United States. NAVIPPRO Addiction Severity Index-Multimedia Version (“ASI-MV”) is a clinical assessment tool that collects data on recent drug use behaviors for evaluation and treatment planning at intake. From 2020 through 2021, there were a total of 76,249 NAVIPPRO ASI-MV assessments in individuals entering or being assessed for SUD treatment at a center participating in the NAVIPPRO network. The drug most frequently endorsed for past-month use was marijuana (20,458 individuals, or 27 percent), followed by alcohol (5 or more alcoholic drinks per day, 16,388 individuals, or 22 percent), heroin (9,078 individuals, or 16 percent), fentanyl (6,186 individuals, or 8 percent), hydrocodone (3,448 individuals, or 5 percent), oxycodone (3,186 individuals, or 4 percent), cocaine or crack (5,417 individuals, or 7 percent), tramadol (543 individuals, or 1 percent), and ketamine (169 individuals, or less than 1 percent). HHS Basis for Rec. at 41.

Nationwide Emergency Department Sample

NEDS is the largest all-payer ED database in the United States, as developed for HHS’s Agency for Healthcare Research and Quality (“AHRQ”). NEDS is a sample of records from ED visits from the State Emergency Department Databases, which capture discharge information on all ED visits that do not result in hospital admission, and the State Inpatient Databases, which contain information on patients first seen in the ED and then admitted. The 2020 ED sample

covered 995 hospital EDs and 41 States; the unweighted 2020 sample contained data from over 28 million ED visits, which resulted in a weighted estimate of 123 million ED visits. HHS compared ED visits that noted an alcohol, marijuana, or cocaine-related disorder; this comparison included ED visits not directly due to a specific substance-related disorder, but in which the patient was recorded as having had an alcohol, marijuana, or cocaine-related disorder in the administrative claim associated with the visit. HHS Basis for Rec. at 42.

Based on NEDS data, from 2016 to 2020, the highest estimated number of annual ED visits was for an alcohol-related disorder, with between 4 million and 4.1 million visits each year, 3.2 million of which involved alcohol as a single substance. Over the same timeframe, estimated annual ED visits involving a marijuana-related disorder ranged from approximately 1.3 million to over 1.7 million, with the estimated annual ED visits for single-substance marijuana disorder ranging from 757,731 to 1.08 million. For cocaine, the estimated annual ED visits involving a related disorder were between 559,165 and 774,737, with annual visits for single-substance cocaine-related disorder ranging from 204,257 to 266,614. HHS Basis for Rec. at 42.

HHS calculated a utilization-adjusted rate of estimated ED visits, and the highest rate was for cocaine-related disorder, which ranged from 11,765 to 14,014 visits per 100,000 individuals, of which 4,011 to 4,952 were single-substance visits. Marijuana had the second-highest utilization-adjusted rate of estimated ED visits, ranging from 3,472 to 3,940 per 100,000 individuals 2,017 to 2,413 of which were single-substance visits. The utilization-adjusted rate of visits involving an alcohol disorder, the lowest of the three substances, ranged from 2,225 to 2,327 per 100,000 individuals, of which 1,775 to 1,843 were single-substance ED visits. HHS Basis for Rec. at 42–43.

National Inpatient Sample

NIS is the largest publicly available all-payer inpatient administrative health care database in the United States, and it is sponsored by AHRQ. It is a sample of discharges from participating community hospitals from 46 to 48 States and the District of Columbia each year, with approximately 7 million unweighted inpatient stays annually, accounting for weighted annual estimates of 35 million hospitalizations. HHS used NIS data to compare alcohol, marijuana, and cocaine. HHS Basis for Rec. at 43.

From 2016 to 2020, alcohol-related disorder had the highest estimated annual number of hospitalizations, at approximately 1.8 million each year, of which approximately 1.2 to 1.25 million involved single-substance alcohol-related disorder. Marijuana-related disorder had the second-highest estimated annual number of hospitalizations, increasing from 795,140 in 2016 to 914,810 in 2020, of which 373,160 to 452,985 were for single-substance marijuana-related disorder. Cocaine had the lowest estimated annual number of hospitalizations, ranging from 387,385 to 453,955, of which 94,695 to 112,725 were for single-substance cocaine-related disorder. HHS Basis for Rec. at 43.

HHS then calculated a utilization-adjusted rate of estimated hospitalizations, and the highest rate was for cocaine-related disorder, which ranged from 7,185 to 8,211 hospitalizations per 100,000 individuals with any past-year use, of which 1,796 to 2,039 were single-substance hospitalizations. Marijuana-related disorder had the second-highest rate of estimated hospitalizations, ranging from 1,850 to 2,117 per 100,000 individuals, of which 906 to 1,026 were single-substance hospitalizations. Alcohol had the lowest rate, ranging from 987 to 1,039 per 100,000 individuals, of which 675 to 715 were single-substance hospitalizations. HHS Basis for Rec. at 43.

National Forensic Laboratory Information System

NFLIS is a program of the Diversion Control Division of DEA. The NFLIS-Drug system is a component of the NFLIS that contains data that serve as a surveillance resource to monitor drug encounters by law enforcement across the United States, including data on drugs seized by law enforcement and submitted to Federal, State, and local forensic laboratories for analysis. In NFLIS, a law enforcement investigation (“case”) may result in one or more “reports” or “exhibits” of drug evidence, and each report or exhibit may contain one drug or multiple drugs. However, NFLIS-Drug data has limitations because not all drugs encountered by law enforcement are sent for analysis and not all drugs sent to reporting forensic laboratories are tested. To account for nonreporting laboratories, among other things, DEA publishes NFLIS-Drug national report estimates annually and semiannually. Analyzing national estimates data allows for a comparison of the number of reports by year and reporting trends. In calculating national and regional estimates, DEA uses all NFLIS-Drug reporting laboratories. HHS Basis for Rec. at 43–44.

In 2021, there were 1,326,205 drug reports from State and local forensic laboratories in the United States, an increase of 3 percent from 2020. Nationally, 61 percent of all drug reports in NFLIS were identified as involving methamphetamine (406,200 reports or 31 percent), cannabis/THC (167,669 reports or 13 percent), cocaine (165,162 reports or 12 percent), or heroin (72,315 reports or 5 percent). HHS Basis for Rec. at 44–45.

In 2021, there were 1,027,219 drug-specific cases submitted to and analyzed by State and local laboratories, a 2 percent increase from 2020. Although the total NFLIS-Drug number of drug reports increased in 2021 from 2020, the total number of cases and drugs reported continues to be noticeably lower than the numbers reported for the years before the COVID-19 pandemic. Nationally, in 2021, 45 percent of all drug cases contained one or more reports of methamphetamine, followed by cocaine (18 percent), cannabis/THC (17 percent), and heroin (8

percent). Nationally, the number of cannabis/THC reports as well as the number of cases in which cannabis/THC was identified decreased from 2015 through 2021, including a decrease from 188,735 to 167,669 from 2020 to 2021. HHS noted that this could mean there was a decrease in the number of cannabis/THC encounters, but it could also mean that there was a decrease in the number of exhibits submitted by law enforcement for analysis or a decrease in the number of exhibits processed (analyzed) by forensic laboratories. HHS Basis for Rec. at 45.

HHS Conclusion With Respect to Factor 5

In HHS's view, the most notable conclusion from its evaluation of epidemiological databases related to the medical outcomes from drug abuse is that, for all evaluated measures from 2015 to 2020, the rank order of comparators in terms of greatest adverse consequences typically placed alcohol (unscheduled), heroin (schedule I), and cocaine (schedule II) in the first or immediately subsequent position, with marijuana in a lower position. This pattern also held for PC data for serious medical outcomes, including death, where marijuana was in the lowest ranking group. HHS determined that this demonstrated that there is consistency across databases, across substances, and over time, and that although abuse of marijuana produces clear evidence of harmful consequences, including SUD, the consequences are relatively less common and less harmful than some other comparator drugs. Additionally, HHS concluded, the number of law enforcement encounters with marijuana decreased from 2020 to 2021, at a time when law enforcement encounters were increasing for other scheduled drugs of abuse. However, as it noted with respect to Factor 1.A, HHS emphasized that there are limitations in comparing descriptive data on adverse outcomes across drugs, although descriptive analyses of epidemiologic data are an established practice in previous eight-factor analyses. HHS Basis for Rec. at 45.

In 2016, DEA found that abuse of marijuana is widespread and significant. 81 FR at 53739. In addition, DEA found in 2016 that a significant proportion of all admissions for substance abuse treatment are for marijuana/hashish as the primary drug of abuse. *Id.* DEA notes that national data demonstrate that marijuana is one of the most widely used federally illicit substances in the United States, consistent with findings from the HHS Basis for Recommendation. According to the NSDUH, in 2022, among people aged 12 or older in the United States, an estimated 61.9 million people (22 percent) had used marijuana in the past year, and 42.3 million (15.0 percent) had used it in the past month. DEA notes that, according to one National Institutes of Health-supported study, the prevalence of daily marijuana use reached its highest level reported in 2021, at 11 percent of Americans aged 12 or older, a 3 percent increase from 2017 and a 5 percent increase from 2012.²⁷ It also notes that the average percentage of Δ9-THC in seized marijuana has increased over time.²⁸ Also, TEDS data showed that, in 2020, marijuana was the primary drug of admission in approximately 10 percent of all admissions to substance abuse treatment among patients aged 12 and older. HHS Basis for Rec. at 41, 46. DEA also notes that TEDS data for 2021 reported that marijuana/hashish was the primary substance of abuse in 10.2 percent of all admissions to substance abuse treatment among patients aged 12 and older.²⁹ The 2021 TEDS data further reported that New York, California, Georgia, North Carolina, New Jersey, Texas, Minnesota, South Carolina, Florida, and Connecticut accounted for 55.9 percent of admissions to substance use treatments services where

²⁷ *Marijuana and hallucinogen use among young adults reached all time-high in 2021*, Nat'l Inst. on Drug Abuse (Aug. 22, 2022), <https://nida.nih.gov/news-events/news-releases/2022/08/marijuana-and-hallucinogen-use-among-young-adults-reached-all-time-high-in-2021>.

²⁸ *Cannabis Potency Data*, Nat'l Inst. on Drug Abuse (Nov. 23, 2022), <https://nida.nih.gov/research/research-data-measures-resources/cannabis-potency-data>.

²⁹ Substance Abuse & Mental Health Servs. Admin., *Treatment Episode Data Set (TEDS) 2021: Admissions to and Discharges from Substance Use Treatment Services Reported by Single State Agencies* 10 (2023), <https://www.samhsa.gov/data/sites/default/files/reports/rpt42794/2021-teds-annual-report.pdf> (Figure 3.A.9).

marijuana/hashish was listed as the primary substance.³⁰ DEA also believes that additional information regarding the scope, duration, and significance of marijuana abuse may be appropriate for consideration in assessing this factor.

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

The sixth factor that DOJ and HHS must consider under 21 U.S.C. 811(c) is the risk posed to the public health by marijuana. In analyzing this factor, HHS examined NSDUH data related to the demographics of U.S. individuals meeting criteria for marijuana use disorder, TEDS data related to the demographics of admission to treatment centers for marijuana use disorder, NEDS and NIS data on admissions to EDs and hospitals related to marijuana poisoning, ToxIC Core Registry data on intentional and unintentional exposure, and NPDS data describing the risks to youth of unintentional exposure to marijuana. HHS also assessed the risks to the public health through NSDUH data on driving under the influence of marijuana in adults and high school students. Finally, HHS reported data regarding the risk of serious AEs and death associated with nonmedical use/use of uncertain intent of marijuana as reported to the FDA Adverse Event Reporting System, Center for Food Safety and Applied Nutrition Adverse Event Reporting System, National Vital Statistics System-Mortality (“NVSS-M”), DAWN, FDA’s Sentinel Distributed Database System, and Centers for Medicare and Medicaid Services, and as reflected in the Drug-Involved Mortality data linking NVSS-M to death certificates. HHS Basis for Rec. at 46.

HHS Conclusion With Respect to Factor 6

HHS’s detailed analysis of the risks posed by marijuana to the public health can be found at pages 46–57 of the HHS Basis for Recommendation. In summary, HHS found that the risks to

³⁰ *Id.* at 29 (Figure 6.B.4).

the public health posed by marijuana are low compared to other drugs of abuse (*e.g.*, heroin (schedule I), cocaine (schedule II)), based on its evaluation of various epidemiological databases for ED visits, hospitalizations, unintentional exposures, and, most importantly, for overdose deaths. The rank order of comparator drugs in terms of greatest adverse consequences typically places heroin, benzodiazepines, or cocaine in the first or immediately subsequent positions, with marijuana in a lower place in the ranking, especially when comparing among individuals who reported using the respective drugs at least once in the prior year. For overdose deaths, marijuana is always ranked the lowest among comparator drugs. HHS interpreted these evaluations to demonstrate that there is consistent evidence across databases, across substances, and over time that, although the abuse of marijuana poses a risk to public health, the risk is relatively lower than that posed by most other comparator drugs. However, as HHS noted in its discussion of Factor 1, *see* HHS Basis for Rec. at 7–8, there are limitations in comparing descriptive data on adverse outcomes across drugs. HHS Basis for Rec. at 57.

In 2016, DEA found that, “[t]ogether with the health risks outlined in terms of pharmacological effects above, public health risks from acute use of marijuana include impaired psychomotor performance, impaired driving, and impaired performance on tests of learning and associative processes. Chronic use of marijuana poses a number of other risks to the public health including physical as well as psychological dependence.” 81 FR at 53739–40. In addition to the data provided in the HHS Basis for Recommendation and the data considered by HHS and DEA in their prior eight-factor analyses, DEA anticipates that additional data on public safety risks, risks from acute and chronic marijuana use via oral and inhaled administration routes, and the impact of Δ 9-THC potency may be appropriate for consideration.

As discussed in the HHS Basis for Recommendation, DEA notes that studies have examined the risk associated with marijuana use and driving. HHS Basis for Rec. at 50. The

Rocky Mountain High Intensity Drug Trafficking Area reported in a publication that traffic deaths in Colorado in which drivers tested positive for marijuana more than doubled from 55 in 2013 to 131 in 2020, although other evidence in the same report suggests that DUI citations involving marijuana have grown at a rate similar to the rate for citations involving other drugs.³¹ DEA also identified some evidence suggesting that, among drivers who test positive for at least one drug in a traffic stop, a growing share test positive for cannabis.³²

7. *Marijuana's Psychic or Physiological Dependence Liability*

The seventh factor that DOJ and HHS are required to consider under 21 U.S.C. 811(c) is the psychic or physiologic dependence liability of marijuana.

A. Psychic Dependence

The term “psychic or psychological dependence” has been used to refer to a state similar to addiction. For diagnosis purposes, the DSM-V has combined the diagnoses “abuse” and “drug dependence” (*i.e.*, addiction), which the DSM’s Fourth Edition specified separately, into a single “substance use disorder,” which may occur in a broad range of severity, from mild to severe.

HHS Basis for Rec. at 57.

The abuse potential of a drug can be assessed, in part, by evaluating the rewarding effects produced by that drug in humans and animals. As HHS described in its analysis of Factor 2, *see* HHS Basis for Rec. at 12–13, rodent behavioral studies show that Δ 9-THC produces both self-administration and CPP. HHS determined that these results demonstrate that Δ 9-THC has rewarding properties that are indicative of abuse potential. Further, as HHS described in its

³¹ See 8 Rocky Mountain High Intensity Drug Trafficking Area, *The Legalization of Marijuana in Colorado: The Impact* 8, 13 (2021), https://www.rmhidta.org/_files/ugd/4a67c3_b391ac360f974a8bbf868d2e3e25df3d.pdf. Note that the publication did not address the timing of marijuana use associated with fatal traffic accidents.

³² See Fernando A. Wilson et al., *Fatal Crashes from Drivers Testing Positive for Drugs, 1993–2010*, 129 Public Health Reports 342, 347–348 (2014).

analysis of Factor 4, *see* HHS Basis for Rec. at 32–37, there is ample epidemiological evidence that marijuana is self-administered by humans, which may result from its ability to produce rewarding psychological effects, such as euphoria, *see* HHS Basis for Rec. at 15. HHS Basis for Rec. at 58.

In some individuals, extensive use of marijuana can lead to SUD. HHS noted that, in general, SUDs listed in the DSM-V are defined by an inability to cease drug use despite harmful consequences; Cannabis Use Disorder (“CUD”) shares this and other diagnostic criteria common to SUDs for other drugs of abuse. Estimates of CUD in individuals who regularly use marijuana vary and range from about 10 to 20 percent. These estimates are similar to data from the United States National Comorbidity Study, which showed that 9 percent of lifetime cannabis users met the criteria for dependence outlined in the DSM’s revised Third Edition at some time in their life, compared to 32 percent of tobacco users, 23 percent of opiate users, and 15 percent of alcohol users. The National Epidemiologic Survey on Alcohol and Related Conditions also reported a nine percent lifetime cumulative probability of transitioning from marijuana use to dependence, with a higher risk of dependence in individuals with a history of psychiatric or other substance dependence comorbidity. In the United States, data from the 2020 NSDUH show that approximately 14 million individuals aged 12 or older who use marijuana or other cannabinoid preparations met criteria for CUD, representing 5.1 percent of all individuals aged 12 or older meeting the NSDUH survey inclusion criteria. HHS Basis for Rec. at 58.

Individuals who develop a SUD, including CUD, may seek treatment. From 2015 to 2020, TEDS documented approximately 10.8 million treatment episode admissions reported by individuals treated at publicly funded substance use treatment programs. Out of 1.4 million treatment admissions documented by TEDS in 2020, marijuana was reported as the primary substance of abuse in approximately 10 percent of admissions, making it the third most

frequently reported primary substance of abuse, after alcohol (31.2 percent) and heroin (20.6 percent). A similar pattern was seen from 2015 to 2019. HHS Basis for Rec. at 58.

HHS concluded that the animal behavioral data show that Δ 9-THC produces rewarding properties that underlie the abuse potential of marijuana. Epidemiological data demonstrate that some individuals who use marijuana for its rewarding properties go on to develop CUD, which shows that marijuana can produce psychological dependence. Among those individuals who seek admission for treatment for SUD associated with a drug of abuse, marijuana was the third most frequently reported primary substance of abuse. Thus, marijuana can produce psychic dependence in some individuals who use the drug. HHS Basis for Rec. at 58–59.

B. Physical Dependence

Physical dependence is a state of adaptation manifested by a drug-class specific withdrawal syndrome produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, or administration of an antagonist. Although physical dependence is often associated with addiction, it can be produced by repeated administration of drugs both with and without abuse potential. HHS Basis for Rec. at 59.

As HHS discussed in its analysis of Factor 2, *see* HHS Basis for Rec. at 11, Δ 9-THC is a partial agonist at CB₁ receptors. When marijuana (or isolated Δ 9-THC) is administered chronically, there is a down-regulation of CB₁ receptors, which leads to behavioral tolerance. The underlying mechanism for marijuana withdrawal appears to be the uncoupling or desensitization of CB₁ receptors that precedes receptor down-regulation. Abrupt discontinuation of marijuana after prolonged administration produces withdrawal symptoms in rats and in humans that are typically opposite to those that occur with activation of the CB₁ receptor. Precipitated withdrawal can also be induced with administration of CB₁ antagonists following

chronic administration, while administration of CB₁ agonists can attenuate some withdrawal symptoms associated with marijuana discontinuation. These data confirm the importance of the CB₁ receptor in marijuana physical dependence. HHS Basis for Rec. at 59.

HHS noted that research has not yet documented the occurrence of withdrawal symptoms in individuals who use marijuana only occasionally. However, in individuals who use marijuana heavily and chronically, drug discontinuation can lead to a withdrawal syndrome. Most marijuana withdrawal symptoms begin within 24 to 48 hours of drug discontinuation, peak within two to six days, and reduce over one to two weeks as Δ⁹-THC levels decline. HHS Basis for Rec. at 59.

The most commonly reported withdrawal symptoms from clinical investigations are sleep difficulties, decreased appetite and weight loss, craving, irritability, anger, anxiety or nervousness, and restlessness. Less commonly reported withdrawal symptoms include depressed mood, sweating, shakiness, physical discomfort, and chills. HHS described the symptoms of “cannabis withdrawal” listed in the DSM-V as being similar to those reported in the experimental studies, including nervousness or anxiety, irritability or aggression, insomnia or unpleasant dreams, depressed mood, decreased appetite or weight loss, restlessness, abdominal pain, shakiness or tremors, sweating, fever, chills, and headache. HHS Basis for Rec. at 59–60.

HHS reported that up to 40 to 50 percent of individuals who use marijuana on a regular basis may experience physical dependence. A meta-analysis of 23,518 individuals who frequently used marijuana showed that 47 percent of subjects reported symptoms of marijuana withdrawal. The prevalence of physical dependence was 54 percent in outpatient samples, 17 percent in community samples, and 87 percent among inpatients in drug abuse treatment centers. This is consistent with data showing that 90 percent of individuals who were diagnosed with CUD also reported physical dependence. Further, individuals diagnosed with CUD experience

more severe and longer lasting withdrawal symptoms when discontinuing marijuana than individuals who do not have a diagnosis of CUD. This may be because individuals with CUD have greater exposure to marijuana. HHS Basis for Rec. at 60.

Symptoms associated with marijuana withdrawal appear to be relatively mild compared to those associated with alcohol withdrawal, which can include agitation, paranoia, seizures, and even death. Multiple studies comparing the withdrawal symptoms associated with tobacco (not scheduled in the CSA) and marijuana demonstrate that the magnitude and time course of the two withdrawal syndromes are similar. Animal studies have shown that after short-term administration of equianalgesic doses of heroin and $\Delta 9$ -THC to monkeys, withdrawal signs were observed after heroin administration but not after $\Delta 9$ -THC administration, further demonstrating that withdrawal from marijuana is associated with less severe symptoms than withdrawal from other drug classes. HHS Basis for Rec. at 60.

HHS Conclusion With Respect to Factor 7

In conclusion, HHS found experimental and clinical evidence that chronic, but not acute, use of marijuana can produce both psychic and physical dependence in humans. Epidemiological data, discussed in greater detail in the sections describing Factors 4 and 5 in sections VI.4 and VI.5 of this preamble, provide additional evidence of psychic dependence. The symptoms associated with both kinds of dependence are relatively mild for most individuals, although their severity may be greater with increased exposure to marijuana. HHS Basis for Rec. at 61.

In 2016, DEA found that “[l]ong-term, heavy use of marijuana can lead to physical dependence and withdrawal following discontinuation, as well as psychic or psychological dependence.” 81 FR at 53740. DEA notes that some physicians have argued that CUD is

underdiagnosed and undertreated in the medical setting,³³ and that other medical professionals have noted that CUD needs to be better understood and characterized to better inform users and treatment professionals.³⁴ DEA anticipates that additional psychic or physiological dependence liability may be appropriate for consideration.

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

The eighth factor that DOJ and HHS are required to consider under 21 U.S.C. 811(c) is whether marijuana is an immediate precursor of a substance already controlled under the CSA. HHS concluded that marijuana is not an immediate precursor of another controlled substance. HHS Basis for Rec. at 61. This finding is consistent with DEA’s finding in 2016. 81 FR at 53740. DEA welcomes additional information on this factor.

VII. Determination of Appropriate Schedule for Marijuana

After conducting the eight-factor analysis in 2023, HHS has recommended three findings regarding the appropriate schedule in which to place marijuana. The three findings relate to: (1) a substance’s abuse potential; (2) whether the substance has a CAMU; and (3) the safety or dependence potential of the substance. 21 U.S.C. 812(b); HHS Basis for Rec. at 62–65.

1. Potential for Abuse

In 2016, HHS found that many factors indicated marijuana’s high abuse potential, “including the large number of individuals regularly using marijuana, marijuana’s widespread use, and the vast amount of marijuana available for illicit use.” 81 FR 53688 at 53706. As a result of its most recent evaluation, which incorporates post-2016 data into its analysis, HHS has

³³ See, e.g., Theresa A. Matson et al., *Association Between Cannabis Use Disorder Symptom Severity and Probability of Clinically-Documented Diagnosis and Treatment in a Primary Care Sample*, 251 *Drug & Alcohol Dependence*, no. 110946, 2023.

³⁴ See, e.g., Gwen T. Lapham et al., *Prevalence of Cannabis Use Disorder and Reasons for Use Among Adults in a U.S. State Where Recreational Cannabis Use is Legal*, 6 *JAMA Open* no. e2328934, 2023, at 7.

recommended a finding that marijuana has a potential for abuse less than the drugs or other substances in schedules I and II.

Marijuana contains $\Delta 9$ -THC (also known as dronabinol when specifically referring to (-)-*trans*- $\Delta 9$ -THC stereoisomer), the substance responsible for the abuse potential of marijuana. $\Delta 9$ -THC has agonist properties at CB₁ cannabinoid receptors and produces rewarding responses in animals, as evidenced by its ability to produce self-administration and CPP. When marijuana is administered to humans under experimental conditions, it produces a wide range of positive subjective responses in addition to certain negative subjective responses. Common responses to marijuana when it is used by individuals for nonmedical purposes include euphoria and other positive subjective responses, as well as perceptual changes, sedative responses, anxiety responses, psychiatric, social, and cognitive changes, and physiological changes. HHS Basis for Rec. at 62.

HHS noted that epidemiological data from NSDUH show that marijuana is the most frequently used federally illicit drug in the United States on a past-year and past-month basis among the illicit comparator drugs considered. Although 50 percent of respondents in NSDUH reported using marijuana nonmedically fewer than 5 days per month, another 30 percent reported using it nonmedically for 20 days or more per month. HHS Basis for Rec. at 62.

Despite the high prevalence of nonmedical use of marijuana, HHS observed that an overall evaluation of epidemiological indicators suggests that it does not produce serious outcomes compared to drugs in schedules I or II. HHS found this especially notable given the availability of marijuana and marijuana-derived products that contain extremely high levels of $\Delta 9$ -THC. Due to such availability, the epidemiological data described in HHS's evaluation inherently include the outcomes from individuals who use marijuana and marijuana-derived

products that have doses of Δ 9-THC that range from low to very high, and yet the data demonstrate that these products overall are producing fewer negative outcomes than drugs in schedules I or II. HHS Basis for Rec. at 62.

HHS compared the rank ordering of selected drugs that are abused for various epidemiological measures and observed that marijuana was among the drugs at the very lowest ranking for a number of measures, including PC abuse cases, likelihood that any use would lead to a PC call, accidental or unintentional poisoning, utilization-adjusted rates of unintentional exposure, utilization-adjusted and population-adjusted rates for ED visits and hospitalizations, likelihood of being diagnosed with a serious SUD, deaths reported to PCs, and overdose deaths when used with other drugs or as a single substance (as total numbers and when utilization-adjusted). In contrast, comparators such as heroin (schedule I), oxycodone (schedule II), and cocaine (schedule II) typically were in the highest rank ordering on these measures. HHS Basis for Rec. at 62.

For the various epidemiological measures evaluated above, HHS noted that marijuana was also compared to controlled substances in schedule III (ketamine) and schedule IV (benzodiazepines, zolpidem, and tramadol), as well as to other schedule II substances (fentanyl and hydrocodone). The analyses were conducted in this manner to provide a comprehensive assessment of the relative abuse potential of marijuana. However, the rank order of these substances regarding harms does not consistently align with the relative scheduling placement of these drugs in the CSA due to the pharmacological differences between various classes of drugs. HHS Basis for Rec. at 63.

There are a number of confounding factors that likely influence the adverse outcomes measured in various epidemiological databases and account for the rank ordering of the drugs evaluated on these measures. For example, a different population abuses each substance, and

each substance has a different prevalence of abuse and a different profile of severe adverse outcomes in a setting of nonmedical use and abuse. Thus, it is challenging to reconcile the ranking of relative harms associated with the comparators used in this evaluation when the rankings differ across various epidemiological databases and when these rankings often do not align with the scheduling placement of these comparators under the CSA. HHS Basis for Rec. at 63.

To address these challenges, HHS evaluated the totality of the available data and has concluded that it supports the placement of marijuana in schedule III. Overall, these data demonstrate that, although marijuana is associated with a high prevalence of abuse, the profile of and propensity for serious outcomes related to that abuse lead to a conclusion that marijuana is most appropriately controlled in schedule III under the CSA. HHS Basis for Rec. at 63.

The Attorney General has considered HHS's recommendations and conclusions and accords HHS's scientific and medical determinations binding weight at this stage of the scheduling process. *See* OLC Op. at *22 n.6 ("HHS's recommendations with respect to 'scientific and medical matters' are binding for all eight factors listed in section 811(c)."). The Attorney General concurs with HHS's recommendation, for purposes of initiation of these rulemaking proceedings, that marijuana has a potential for abuse less than the drugs or other substances in schedules I and II.

2. Currently Accepted Medical Use in Treatment in the United States

In 2016, HHS recommended a finding that marijuana had no CAMU due in part to a lack of adequate safety studies or evidence that qualified experts accepted marijuana for use in treating a specific, recognized disorder. 81 FR 53688 at 53707. As a result of its most recent evaluation, which incorporates post-2016 data into its analysis, HHS recommends a finding that marijuana has a CAMU.

In making that recommendation, HHS analyzed whether there is (1) widespread current experience with medical use of the substance in the United States by licensed health care practitioners operating in accordance with implemented State-authorized programs, where the medical use is recognized by entities that regulate the practice of medicine; and (2) some credible scientific support for a least one of those medical uses. Applying this test, HHS recommended a finding that marijuana has a currently accepted medical use in the United States, specifically for the treatment of anorexia related to a medical condition, nausea and vomiting (*e.g.*, chemotherapy-induced), and pain. According to HHS, its evaluation also supported a finding that there is accepted safety for the use of marijuana under medical supervision for the treatment of anorexia related to a medical condition, nausea and vomiting (*e.g.*, chemotherapy-induced), and pain. HHS Basis for Rec. at 63–64.

In the past, DEA has concluded that a substance has a CAMU under the CSA only if one of two tests is satisfied. First, DEA has determined that a substance has a CAMU if the substance has been approved by FDA for marketing under the FDCA, either through the NDA process or by meeting the criteria to be recognized as a “Generally Recognized As Safe and Effective” (“GRASE”) drug. 57 FR 10499, 10503 (March 26, 1992). Second, DEA has determined a substance has a CAMU if the substance satisfies a five-part test established by DEA in 1992 that was based on the “core FDCA standards for acceptance of drugs for medical use”:

1. There must be adequate safety studies;
2. The drug’s chemistry must be known and reproducible;
3. There must be adequate and well-controlled studies proving efficacy;
4. The drug must be accepted by qualified experts; and
5. The scientific evidence must be widely available.

57 FR 10499, 10503–06 (1992); *see also All. for Cannabis Therapeutics v. DEA*, 15 F.3d 1131, 1135 (D.C. Cir. 1994).

In its most recent evaluation, HHS informed DEA of its view that DEA’s previous approach to determining whether a drug has a CAMU does not adequately account for certain indicia of medical use that, where present, are relevant to determining whether a substance has a CAMU for purposes of scheduling under the CSA. Specifically, HHS observed that DEA’s tests left no room for an evaluation of (1) whether there is widespread medical use of a drug under the supervision of licensed health care practitioners under State-authorized programs and, (2) if so, whether there is credible scientific evidence supporting such medical use. HHS therefore developed an alternative test composed of those two inquiries as a third, independently sufficient approach for determining whether a substance has a CAMU under the CSA. HHS applied this two-part test to marijuana and recommended a finding that marijuana has a CAMU under the CSA. HHS Basis for Rec. at 24–28.

Upon receiving HHS’s recommendation, the Attorney General requested that OLC advise on whether HHS’s test, if satisfied, established a CAMU “even if the drug has not been approved by FDA and even if the drug does not satisfy DEA’s five-part test.” OLC Op. at *3. OLC determined that DEA’s current approach to determining whether a drug has a CAMU is impermissibly narrow, because it “ignor[es] widespread clinical experience with a drug that is sanctioned by state medical licensing regulators.” *Id.* at *13–14; *see also id.* at *12. OLC further opined that satisfying HHS’s two-part inquiry is sufficient to establish that a drug has a CAMU. *Id.* at *4, *16–20. And OLC concluded that, while HHS’s CAMU recommendation is not binding on DEA, the medical and scientific determinations that underlie its recommendation are binding until the initiation of formal rulemaking proceedings, and that DEA must accord those determinations “significant deference” throughout the rulemaking process. *Id.* at *4, *20–26.

Under Part 1 of the HHS CAMU test, the Office of the Assistant Secretary for Health (“OASH”) considered whether there is widespread current experience with medical use of marijuana in the United States by licensed HCPs operating in accordance with implemented State-authorized programs, where such medical use is recognized by entities that regulate the practice of medicine under these State jurisdictions. Part 2 of the CAMU test evaluated whether there exists some credible scientific support for at least one of the medical conditions for which the Part 1 test is satisfied. The evaluation in Part 2, undertaken by FDA, was not meant to be, nor is it, a determination of safety and efficacy under the Federal Food, Drug, and Cosmetic Act’s drug approval standard for new human or animal drugs. Rather, HHS’s two-part test is designed to evaluate whether a substance, in this case marijuana, has a CAMU for purposes of drug scheduling recommendations and placement in a drug schedule consistent with criteria set forth in 21 U.S.C. 812(b). HHS Basis for Rec. at 24.

In the evaluation and assessment under Part 1 of the CAMU test, OASH found that more than 30,000 HCPs are authorized to recommend the use of marijuana for more than six million registered patients, constituting widespread clinical experience associated with various medical conditions recognized by a substantial number of jurisdictions across the United States. For several jurisdictions, these programs have been in place for several years, and include features that actively monitor medical use and product quality characteristics of marijuana dispensed. HHS Basis for Rec. at 24.

Based on OASH’s findings in Part 1 of the CAMU test, the Assistant Secretary for Health concluded that an FDA assessment under Part 2 of the CAMU test was warranted to determine if credible scientific support exists for the use of marijuana to treat at least one of the medical conditions identified by OASH under Part 1. HHS Basis for Rec. at 24.

At this stage of initiating a rulemaking, the Attorney General agrees with OASH that there is widespread clinical experience with marijuana for at least one medical condition.

FDA conducted Part 2 of the CAMU test for seven indications, based in part on OASH's findings under Part 1 of the CAMU test³⁵ and in part on FDA's own analysis of the landscape in which marijuana is currently used medically, including information from State-authorized programs on how and to what extent marijuana is being utilized for medical purposes. The seven indications are: (1) anorexia;³⁶ (2) anxiety;³⁷ (3) epilepsy; (4) inflammatory bowel disease ("IBD"); (5) nausea and vomiting; (6) pain; and (7) post-traumatic stress disorder ("PTSD"). FDA's evaluation under Part 2 of the CAMU test was based on systematic reviews of studies investigating the safety and effectiveness of marijuana, relevant professional societies' position statements, data from State medical marijuana programs and United States national surveys, and the labeling of FDA-approved products relevant to the analysis. HHS Basis for Rec. at 25.

In evaluating whether there exists some credible scientific support under Part 2 of the CAMU test for a particular use, factors in favor of a positive finding included whether:

(1) favorable clinical studies of the medical use of marijuana, although not necessarily adequate and well-controlled clinical studies that would support approval of an NDA, have been published

³⁵ In Part 1 of the CAMU test, OASH identified at least 15 medical conditions for which there is widespread current experience with medical use of marijuana in the United States by licensed HCPs operating in accordance with implemented State-authorized programs, where the medical use is recognized by entities that regulate the practice of medicine. These conditions include amyotrophic lateral sclerosis (commonly known as ALS), autism, cachexia, cancer, chronic pain, Crohn's disease, epilepsy or condition causing seizures, glaucoma, HIV/AIDS, multiple sclerosis, Parkinson's disease, persistent/severe muscle spasm, persistent/severe nausea, PTSD, and spasticity. FDA conducted Part 2 of the analysis for the medical conditions identified by OASH that were likely to have the most robust evidence available for review; because the analysis concluded that the Part 2 test has been met for at least one of the conditions identified in Part 1, there was no need to analyze all of them. HHS Basis for Rec. at 25 n.9.

³⁶ The anorexia indication reflects anorexia due to a medical condition (*e.g.*, HIV/AIDS) and does not represent anorexia nervosa. HHS Basis for Rec. at 25 n.10.

³⁷ While anxiety was not one of the specific medical conditions identified by OASH, it is included herein because anxiety was identified by the FDA during the Part 2 review of State-level usage data. FDA considered the medical use of marijuana for the treatment of anxiety of importance to evaluate given the reported prevalence of marijuana use for the treatment of anxiety regardless of the legal status of such use in a given jurisdiction. HHS Basis for Rec. at 25 n.11.

in peer-reviewed journals or (2) qualified expert organizations (*e.g.*, academic groups, professional societies, or government agencies) have opined in favor of the medical use or provided guidance to HCPs on the medical use. Factors that weigh against a finding that Part 2 of the CAMU test is met included whether: (1) data or information indicate that medical use of the substance is associated with unacceptably high safety risks for the likely patient population, *e.g.*, due to toxicity concerns; (2) clinical studies with negative efficacy findings for the medical use of marijuana have been published in peer reviewed journals; or (3) qualified expert organizations (*e.g.*, academic or professional societies, government agencies) recommend against the medical use of marijuana based on the available data at the time of their position statement. HHS Basis for Rec. at 25.

FDA’s review of the available information identified mixed findings of effectiveness across indications, ranging from data showing inconclusive findings to considerable evidence in favor of effectiveness, depending on the source. The largest evidence base for effectiveness exists for marijuana use within the pain indication (in particular, neuropathic pain). Numerous systematic reviews concluded that there exists some level of evidence supporting the use of marijuana for chronic pain. The 2017 NASEM report concluded there was “substantial evidence”³⁸ supporting the use of cannabis products relevant to this review for pain, as have other reviews. The AHRQ living systematic review has concluded that there is some support for the use of marijuana-related products in the treatment of chronic pain, but overall concluded these effects were small and the increased risk of dizziness, nausea, and sedation may limit the benefit. A systematic review of scientific and medical literature was conducted in 2023 by the

³⁸ The term “substantial evidence” refers to language used within the 2017 NASEM report and is not meant to represent “substantial evidence” as defined in 21 U.S.C. 355(d). HHS Basis for Rec. at 26 n.12.

University of Florida (“UF”) under contract with FDA. UF epidemiologists identified some data supporting effectiveness of marijuana, including some within their own meta-analysis; however, they ultimately concluded the results are inconclusive or mixed. FDA also conducted a separate analysis of published scientific reviews, several of which drew conclusions similar to those of UF. HHS Basis for Rec. at 25–26.

UF evaluated other therapeutic conditions mentioned above, *i.e.*, anorexia, anxiety, epilepsy, IBD, nausea, and PTSD, employing a similar systematic review of scientific and medical literature. UF found that there is low- to moderate-quality evidence supporting the use of marijuana as medical treatment for outcomes in anorexia, nausea and vomiting, and PTSD. FDA’s review of systematic reviews showed mixed results for these indications. In particular, FDA found that the potential for psychiatric adverse events associated with treating PTSD with marijuana may be more substantial than any limited benefit in observational studies. Although UF did not conclude that there was evidence in support of the effectiveness of marijuana in IBD, both their review and other systematic reviews found some benefit with respect to subjective symptoms in this condition. With regard to epilepsy and anxiety, both UF’s review and FDA’s review of other systematic reviews did not find support for marijuana providing benefit in the treatment of these conditions. Where positive results on effectiveness outcome measures were found, the effects and the quality of evidence were generally in the low-to-moderate range. UF did not find high quality evidence supporting worsening of outcomes in any indication. HHS Basis for Rec. at 26.

FDA concluded that none of the evidence from the systematic reviews included in the CAMU test Part 2 analysis identified any safety concerns that would preclude the use of marijuana in the indications for which there exists some credible scientific support for its therapeutic benefit. FDA assessed the clinical safety data identified in the literature from

controlled trials as generally consistent between sources but limited in the rigor of safety reporting. FDA also explained that the vast majority of the observational studies evaluated in the context of medical use were excluded from the final synthesis of evidence due to concerns regarding their quality (*e.g.*, only one observational study for the anxiety indication and one for the PTSD indication were included). According to FDA, data on safety from both clinical trials and observational studies were generally scarce, but the literature shows that marijuana has more AEs when compared to a placebo or active control group, however, typically in the mild to moderate severity range. HHS Basis for Rec. at 26.

FDA also reviewed results from State reporting data from 37 States with medical marijuana programs and surveys of patients using marijuana in Maryland and Minnesota, which had data available for review. Surveys of patients using marijuana in these two States found most patients did not report any side effects and those that did report side effects mostly described them as mild. Neither State's databases included patients who chose to stop using marijuana, which FDA noted might result in an overestimation of positive experiences. HHS Basis for Rec. at 27.

As of August 2023, FDA reported that the real-world data sources available to FDA, in general, lack the necessary elements to identify the exposure (*i.e.*, to marijuana), to distinguish the reason for use (medical vs. recreational) and, if applicable, the condition that prompted its medical use, and to permit sound inferential analyses. Therefore, they were not included in HHS's review. HHS Basis for Rec. at 27.

According to FDA, data from United States national surveys, in general, lacked details on patient characteristics and factors that prompted the use of marijuana for medical purposes, and data collection for these surveys was impacted by the COVID-19 pandemic. FDA observed that, despite these limitations, the data suggested that medical use of marijuana increases as age

increases. Only data from one survey provided information on the intended indication for use, suggesting that individuals often use marijuana to improve or manage conditions such as depression, anxiety, PTSD, pain, headaches or migraines, sleep disorders, nausea and vomiting, lack of appetite, and muscle spasms, but only approximately half of them reportedly had ever asked a health care professional for a recommendation to use medical marijuana. HHS Basis for Rec. at 27.

Additionally, although the safety data obtained from use in a medical context are considered to be the most relevant for the CAMU analysis, FDA evaluated the safety of marijuana in the nonmedical setting to inform the potential for more severe outcomes. Specifically, FDA evaluated safety outcomes related to marijuana use in the setting of nonmedical use, use of uncertain intent, and unintentional exposure through a variety of epidemiological data sources and in relation to several comparator substances controlled under the CSA, including drugs in schedule I: heroin (an illicit opioid drug); schedule II: hydrocodone and oxycodone (approved opioid prescription drug products), cocaine and fentanyl (largely illicitly produced drugs in the nonmedical use setting, although there are approved prescription drugs); schedule III: ketamine (an approved prescription drug); and schedule IV: zolpidem, benzodiazepines, and tramadol (approved prescription drugs). According to FDA, the comparative data demonstrate that, even in the context of nonmedical use, marijuana has a less concerning overall safety profile relative to the comparators for a number of important outcomes (*e.g.*, single substance use overdose death, hospitalizations). However, FDA observed that in young children, population-adjusted rates of ED visits and hospitalizations involving marijuana poisoning were higher than heroin, cocaine, and benzodiazepines for the periods studied. Of note, some of the comparator substances are approved for use in conditions similar to the

indications for which marijuana was evaluated in the CAMU analysis (*e.g.*, opioids for pain, benzodiazepines for anxiety-related conditions). HHS Basis for Rec. at 27.

FDA also considered position statements from professional organizations relevant to the indications discussed. The vast majority of professional organizations did not recommend the use of marijuana in their respective specialties; however, none specifically recommended against it, with the exception of the American Psychiatric Association, which stated that marijuana is known to worsen certain psychiatric conditions. HHS Basis for Rec. at 27–28.

On balance, FDA found the available data indicated that there is some credible scientific support for the use of marijuana in the treatment of chronic pain, anorexia related to a medical condition, and nausea and vomiting, with varying degrees of support and consistency of findings. Additionally, no safety concerns were identified in FDA’s review that would indicate that medical use of marijuana poses unacceptably high safety risks for the indications where there is some credible scientific evidence supporting its therapeutic use. HHS Basis for Rec. at 28.

Based on the totality of the available data, FDA concluded that there exists some credible scientific support for the medical use of marijuana in at least one of the indications for which there is widespread current experience in the United States, as identified by OASH under Part 1 of the CAMU test. The indications evaluated were anorexia related to a medical condition, anxiety, epilepsy, IBD, nausea and vomiting (*e.g.*, chemotherapy-induced), pain, and PTSD. FDA clarified that the analysis and conclusions on the available data are not meant to imply that safety and effectiveness have been established for marijuana that would support FDA approval of a marijuana drug product for a particular indication. However, FDA determined that the available data do provide some level of support for the way marijuana is being recommended by health care practitioners in clinical practice. Thus, based on the widespread HCP experience and the extent of medical use evaluated by OASH under the Part 1 test, and FDA’s evaluation of

available credible scientific support described herein for at least some therapeutic uses identified in the Part 1 test, HHS recommended a finding that, for purposes of the drug scheduling criteria in 21 U.S.C. 812(b), marijuana has a CAMU for: anorexia related to a medical condition; nausea and vomiting (*e.g.*, chemotherapy-induced); and pain. HHS Basis for Rec. at 28.

The Attorney General has considered HHS's recommendations and conclusions and accords HHS's scientific and medical determinations binding weight until the initiation of the formal rulemaking process. *See* OLC Op. at *24. Applying HHS's two-part test, and in light of OLC's legal opinion that the HHS's test is sufficient under the CSA, the Attorney General concurs with HHS's conclusion, for purposes of the initiation of these rulemaking proceedings, that there is a CAMU for marijuana.

3. Level of Physical or Psychological Dependence

As a result of its most recent evaluation, which incorporates post-2016 data into its analysis, HHS has recommended a finding that abuse of marijuana may lead to moderate or low physical dependence or high psychological dependence. HHS Basis for Rec. at 65.

According to HHS, clinical studies have demonstrated that marijuana produces physical and psychological dependence. Regarding physical dependence, as evidenced by its associated withdrawal symptomology upon abrupt discontinuation of use, the most commonly reported marijuana withdrawal symptoms in clinical investigations are sleep difficulties, decreased appetite and weight loss, craving, irritability, anger, anxiety or nervousness, and restlessness. Marijuana withdrawal symptoms typically peak within two to six days and decline over one to two weeks as Δ 9-THC is eliminated. Similarly, the drug labels for the FDA-approved drug products Marinol and Syndros state that, following chronic administration of dronabinol, drug discontinuation leads to irritability, insomnia, and restlessness at 12 hours, and by 24 hours the

withdrawal symptoms can include hot flashes, sweating, rhinorrhea, diarrhea, and anorexia.

HHS Basis for Rec. at 64.

HHS observes that marijuana withdrawal syndrome has been reported in individuals with heavy, chronic marijuana use, but its occurrence in occasional users of marijuana has not been established. The marijuana withdrawal syndrome appears to be relatively mild compared to the withdrawal syndrome associated with alcohol, which can include more serious symptoms such as agitation, paranoia, seizures and even death. Multiple studies comparing the withdrawal symptoms associated with marijuana and tobacco demonstrate that the magnitude and time course of the two withdrawal syndromes are similar. HHS Basis for Rec. at 64.

HHS also notes that the ability of marijuana to produce psychic dependence is shown through its ability to produce rewarding effects that underlie its nonmedical use and epidemiological outcomes related to abuse, as detailed in the first finding on abuse potential. HHS Basis for Rec. at 64–65.

Based on the evidence, HHS determined that the abuse of marijuana may lead to moderate or low physical dependence, depending on frequency and degree of marijuana exposure. HHS further concluded that marijuana can produce psychic dependence in some individuals, but that the likelihood of serious outcomes is low, suggesting that high psychological dependence does not occur in most individuals who use marijuana. HHS Basis for Rec. at 65.

The Attorney General has considered HHS's recommendations and conclusions and accords HHS's scientific and medical determinations binding weight at this stage of the scheduling process. *See* OLC Op. at *22 n.6. For purposes of the initiation of these rulemaking proceedings, the Attorney General concurs with HHS's conclusion that the abuse of marijuana

may lead to moderate or low physical dependence, depending on frequency and degree of marijuana exposure.

Determination to Propose Rescheduling Marijuana to Schedule III

HHS has recommended a finding that marijuana has a CAMU. HHS Basis for Rec. at 63–64. After considering the foregoing facts and data and the recommendation of HHS, and after according binding weight to HHS’s scientific and medical determinations, the Attorney General concludes that there is, at present, substantial evidence that marijuana does not warrant control under schedule I of the CSA. Accordingly, the Attorney General is issuing this notice of proposed rulemaking to initiate rulemaking proceedings to reschedule marijuana. 21 U.S.C. 811(b).

HHS has recommended that marijuana be transferred from schedule I to schedule III rather than from schedule I to schedule II based on its evaluation that the drug has a relatively lower level of abuse compared to drugs currently scheduled in schedules I and II and its evaluation that marijuana may lead to moderate or low physical dependence and has a low likelihood of psychic dependence. Consistent with HHS’s analysis, the Attorney General has determined at this initial stage that marijuana does not appear to meet the elements of a schedule II drug, which include a high potential for abuse and a likelihood of severe physiological or physical dependence from such abuse. 21 U.S.C. 812(b)(3). Rather, marijuana’s profile as a drug with a lower degree of abuse potential than schedule I (*e.g.*, heroin) and schedule II (*e.g.*, fentanyl, cocaine) drugs and a moderate to low level of physical dependence militates in favor of rescheduling it in schedule III. Accordingly, in this notice of proposed rulemaking, the Attorney General is proposing to reschedule marijuana in schedule III and solicits comments on these preliminary findings.

Types of Marijuana to Be Rescheduled

This rescheduling of marijuana would apply to marijuana as listed in 21 CFR 1308.11(d)(23). The rescheduling also would apply to marijuana extracts as defined in 21 CFR 1308.11(d)(58) because they meet the statutory definition of marijuana and, prior to 2017, were included in 21 CFR 1308.11(d)(23). *See Establishment of a New Drug Code for Marijuana Extract*, 81 FR 90194 (Dec. 14, 2016). In addition, this proposal would apply to Δ 9-THC derived from the marijuana plant (other than the mature stalks and seeds) that falls outside the definition of hemp, because it meets the statutory definition of marijuana.

This proposal would not apply to synthetically derived THC, which is outside the CSA's definition of marijuana. Those tetrahydrocannabinols that can be derived only through a process of artificial synthesis (*e.g.*, delta-10-tetrahydrocannabinol) are excluded. HHS provided a recommendation only relating to "marijuana" as defined in the CSA. That definition is limited to the plant (other than the mature stalks and seeds) and derivatives of the plant. Therefore, synthetic THC will remain in schedule I. This rulemaking would not affect the status of hemp (as defined in 7 U.S.C. 1639o), because hemp is excluded from the definition of marijuana. This rulemaking is not proposing to reschedule any drug product containing marijuana or THC that previously has been rescheduled out of schedule I (*e.g.*, Marinol and Syndros). Nor does it impact the status of any previously scheduled synthetic cannabinoids.

VIII. International Treaty Obligations

In proposing an appropriate schedule for marijuana, the Attorney General must also consider compliance with the treaty obligations of the United States. As the CSA recognizes, the United States is a party to the Single Convention. 21 U.S.C. 801(7). Parties to the Single Convention are obligated to maintain various control provisions related to the drugs that are covered by the treaty. *See, e.g.*, Single Convention arts. 2, 4. Congress enacted many of the

CSA’s provisions for the specific purpose of ensuring U.S. compliance with the treaty. *See* OLC Op. at *27. Among these is a scheduling provision, 21 U.S.C. 811(d)(1). Section 811(d)(1) provides that, where a drug is subject to control under the Single Convention, the Attorney General must “issue an order controlling such drug under the schedule he deems most appropriate to carry out such [treaty] obligations, without regard to the findings required by [21 U.S.C. 811(a) or 812(b)] and without regard to the procedures prescribed by [21 U.S.C. 811(a) and (b)].”³⁹

Marijuana is a drug covered in the Single Convention under the term “cannabis.”⁴⁰ OLC initially advised in 1972 that controls under Article 21 of the Single Convention would not be satisfied if marijuana were listed in schedule III, IV, or V of the CSA. Memorandum for John E. Ingersoll, Director, Bureau of Narcotics and Dangerous Drugs, from Mary C. Lawton, Deputy Assistant Attorney General, Office of Legal Counsel, *Re: Petition to Decontrol Marijuana*; Interpretation of Section 201 of the Controlled Substances Act of 1970 at 12–13 (Aug. 21, 1972). However, OLC has reexamined the conclusion of its 1972 memorandum, taking into account statutory amendments since 1972 and a possibility it did not consider in 1972: placing marijuana into schedule III while issuing regulations that would enable the United States to comply with its

³⁹ As noted above, OLC and the D.C. Circuit do not understand the “without regard” clause in section 811(d)(1) as prohibiting the Attorney General from following the normal scheduling practices when international obligations are involved. Instead, they have interpreted it as requiring the Attorney General to identify which schedules would satisfy the international obligations of the United States with respect to a particular drug and, if more than one schedule would do so, to select among schedules using the procedures set forth in sections 811(a), 811(b), and 812(b). *See* OLC Op. at *29 n.8; *NORML II*, 559 F.2d at 747.

⁴⁰ Under the Single Convention, “[c]annabis plant” means any plant of the genus *Cannabis*.” Single Convention art. 1(1)(c). The Single Convention defines “cannabis” to mean “the flowering or fruiting tops of the cannabis plant (excluding the seeds and leaves when not accompanied by the tops) from which the resin has not been extracted, by whatever name they may be designated.” *Id.* art. 1(1)(b). This definition of “cannabis” under the Single Convention is slightly less inclusive in certain respects than the CSA definition of “marijuana,” which includes all parts of the cannabis plant except for the mature stalks, sterilized seeds, oil from the seeds, and certain derivatives thereof. *See* 21 U.S.C. 802(16). Cannabis and cannabis resin are included in the list of drugs in Schedule I of the Single Convention, and cannabis is subject to the same controls as Schedule I drugs as well as additional controls. *See* Single Convention art. 2(6); *id.* art. 28.

international obligations. OLC Op. at *4, 26–35. OLC has concluded that both the Single Convention and the CSA allow the Attorney General to satisfy the treaty obligations of the United States with respect to marijuana by supplementing scheduling decisions with additional controls under the CSA. *Id.*

If marijuana were listed in schedule III, most of the Single Convention’s obligations would continue to be met by CSA statutory authorities and associated regulations. *See* OLC Op. at *33–34. One potential gap concerns the quota on manufacturing cannabis required by Article 21 of the Convention, but that gap can be filled using the CSA’s regulatory authorities. *See id.* at *34; *see also, e.g.*, 21 U.S.C. 821 (authorizing the Attorney General to impose restrictions “relate[ed] to the . . . control of the manufacture” of a drug); *id.* 871(b) (authorizing the Attorney General to issue regulations “necessary and appropriate for the efficient execution of his functions under this subchapter”); *id.* 822(b) (allowing the Attorney General to regulate “the extent” of manufacture of a drug through registration); *id.* 823(e) (requiring the Attorney General to register an applicant to manufacture a schedule III drug “unless he determines that the issuance of such registration is inconsistent with the public interest”).

In addition, if marijuana is transferred into schedule III, DEA will continue to have authority to maintain its existing regulatory scheme, located at 21 CFR part 1318, governing the registration of manufacturers seeking to plant, grow, cultivate, or harvest marijuana, as required to comply with Articles 23 and 28 of the Single Convention. Authority for those regulations currently flows from 21 U.S.C. 823(a), which is applicable to drugs in schedules I and II. OLC has concluded, however, that 21 U.S.C. 823(e), which is applicable to drugs in schedules III, IV, and V, provides an alternative source of authority for complying with Articles 23 and 28 of the Single Convention. *See* OLC Op. at *34 n.9. The CSA also recognizes that the United States is also a party to the Convention on Psychotropic Substances, Feb. 21, 1971, 32 U.S.T. 543, 1019

U.N.T.S. 175 (“Convention on Psychotropic Substances”). *See also* 21 U.S.C. 801a(2). As with the Single Convention, parties to the Convention on Psychotropic Substances are obligated to take various control measures related to the drugs that are covered by the treaty. *Id.* Congress implemented the additional authority necessary to comply with the Convention on Psychotropic Substances through various amendments to the CSA. *Id.* 801a(2)–(3).

Δ9-THC is a substance covered by schedule II of the Convention on Psychotropic Substances. In this rule, DOJ proposes to reschedule Δ9-THC that falls within the CSA’s definition of marijuana into CSA schedule III. As is the case for marijuana under the Single Convention, the controls available under CSA schedule III are sufficient to comply with the requirements of the Convention on Psychotropic Substances with respect to Δ9-THC, although additional regulatory action may be necessary to implement certain Convention requirements, such as the export and import authorizations required by Article 12. *See, e.g., Schedules of Controlled Substances: Rescheduling of the Food and Drug Administration Approved Product Containing Synthetic Dronabinol [(-)-D⁹-(trans)-Tetrahydrocannabinol] in Sesame Oil and Encapsulated in Soft Gelatin Capsules From Schedule II to Schedule III*, 64 FR 35928, 35928 (July 2, 1999). *Compare, e.g.,* Convention on Psychotropic Substances art. 12(1) (requiring export and import authorizations for substances in Convention Schedule II), *with* 21 U.S.C. 952(b)(2) (authorizing import permits for CSA schedule III substances), *and id.* 953(e)(2) (authorizing export permits for CSA schedule III substances).

Accordingly, concurrent with this rulemaking, DEA will consider the marijuana-specific controls that would be necessary to meet U.S. obligations under the Single Convention and the Convention on Psychotropic Substances in the event that marijuana is rescheduled to schedule III, and, to the extent they are needed if marijuana is rescheduled, will seek to finalize any such regulations as soon as possible.

IX. Requirements for Handling Marijuana and Other Applicable Controls

If marijuana is transferred to schedule III, the regulatory controls applicable to schedule III controlled substances would apply, as appropriate, along with existing marijuana-specific requirements and any additional controls that might be implemented, including those that might be implemented to meet U.S. treaty obligations. The manufacture, distribution, dispensing, and possession of marijuana would also remain subject to applicable criminal prohibitions under the CSA. 21 U.S.C. 841–844.

In addition, marijuana would remain subject to applicable provisions of the FDCA. For example, under the FDCA, a drug containing a substance within the CSA’s definition of “marijuana” would need FDA approval to be lawfully “introduce[d] or deliver[ed] for introduction into interstate commerce,” unless an IND is in effect for that drug. *See* 21 U.S.C. 355(a), 355(i), 331(d). To date, although there have been INDs for drugs containing a substance within the CSA’s definition of “marijuana,” no such drugs have been approved by FDA.

DOJ is seeking comment on the practical consequences of rescheduling marijuana into schedule III under the relevant statutory frameworks.

Conclusion

Based on the legal opinion of OLC and consideration of the scientific and medical evaluation and accompanying recommendation of HHS, the Attorney General is initiating a

rulemaking that proposes the placement of marijuana in schedule III of the CSA. DOJ is soliciting comments on this proposal.

X. Regulatory Analyses

1. Executive Orders 12866 (Regulatory Planning and Review), 13563 (Improving Regulation and Regulatory Review) and 14094 (Modernizing Regulatory Review)

In accordance with 21 U.S.C. 811(a), this scheduling action is subject to formal rulemaking procedures done “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 criteria for removing a drug or other substance from the list of controlled substances. Such actions are exempt from review by the Office of Management and Budget pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563 and 14094.

While this scheduling action is exempt from review under Executive Order 12866, DOJ recognizes this action may have unique economic impacts. As stated above, marijuana is subject to a number of State laws that have allowed a multibillion dollar industry to develop. DOJ acknowledges that there may be large impacts related to Federal taxes and research and development investment for the pharmaceutical industry, among other things. DOJ is specifically soliciting comments on the economic impact of this proposed rule. DOJ will revise this section at the final rule stage if warranted after consideration of any comments received.

2. Executive Order 12988 (Civil Justice Reform)

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

3. *Executive Order 13132 (Federalism)*

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

4. *Executive Order 13175 (Consultation and Coordination With Indian Tribal Governments)*

This proposed rule does not have Tribal implications warranting the application of Executive Order 13175. This rule 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.

5. *Regulatory Flexibility Act*

DOJ has concluded that this action may have a significant economic impact on a substantial number of small entities under the Regulatory Flexibility Act, 5 U.S.C. 601 *et seq.* For example, section 280E of the Internal Revenue Code bars businesses from claiming tax deductions for otherwise allowable expenses where the business “consists of trafficking in controlled substances (within the meaning of schedule I and II of the Controlled Substances Act).” 26 U.S.C. 280E. If marijuana is ultimately transferred to schedule III, section 280E would no longer serve as a statutory bar to claiming deductions for those expenses. In addition, small entities engaged in research on marijuana may be subject to different research protocols set by DEA if the research is conducted on a schedule III substance rather than a schedule I substance.⁴¹ However, DOJ is currently not in a position to estimate the number of small entities

⁴¹ See Drug Enforcement Admin., *Researcher’s Manual* 18–21 (2022), [https://www.deadiversion.usdoj.gov/GDP/\(DEA-DC-057\)\(EO-DEA217\)_Researchers_Manual_Final_signed.pdf](https://www.deadiversion.usdoj.gov/GDP/(DEA-DC-057)(EO-DEA217)_Researchers_Manual_Final_signed.pdf).

affected by these or other potential effects of this action. DOJ seeks comment and additional information to inform its analysis.

6. Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act of 1995 (“UMRA”), 2 U.S.C. 1501 *et seq.*, DOJ has determined 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 annually for inflation) in any 1 year.” *See* 2 U.S.C. 1532(a). Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA.

7. Paperwork Reduction Act of 1995

This action does not impose any new or revised “collection[s] of information” as defined by the Paperwork Reduction Act of 1995, 44 U.S.C. 3502(3).

XI. Proposed Regulatory Text

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 as follows:

PART 1308— SCHEDULES OF 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), 956(b), unless otherwise noted.

2. Amend § 1308.11 by removing paragraph (d)(23) and paragraph (d)(58) and redesignating paragraphs (d)(24) through (d)(104) as (d)(23) through (d)(102), respectively.

3. Amend § 1308.11 by revising the renumbered paragraph (d)(30) to read as follows:

(d) * * *

(30) Tetrahydrocannabinols - 7370

(i) Meaning tetrahydrocannabinols, except as in paragraphs (d)(30)(ii) and (iii) of this section, naturally contained in a plant of the genus Cannabis (cannabis plant), as well as synthetic equivalents of the substances contained in the cannabis plant, or in the resinous extracts of such plant, or synthetic substances, derivatives, and their isomers with similar chemical structure and pharmacological activity to those substances contained in the plant.

(ii) Tetrahydrocannabinols does not include any material, compound, mixture, or preparation that falls within the definition of hemp set forth in 7 U.S.C. 1639o.

(iii) Tetrahydrocannabinols does not include any substance that falls within the definition of marijuana set forth in 21 U.S.C. 802(16).

4. Amend § 1308.13 by adding new paragraphs (h), (i), and (j) to read as follows:

§ 1308.13 Schedule III.

* * * * *

(h) Marijuana, as defined in 21 U.S.C. 802(16).

(i) Marijuana Extract, meaning an extract containing one or more cannabinoids that has been derived from any plant of the genus Cannabis, containing greater than 0.3 percent delta-9-tetrahydrocannabinol on a dry weight basis, other than the separated resin (whether crude or purified) obtained from the plant.

(j) Naturally Derived Delta-9-Tetrahydrocannabinols.

(i) Meaning those delta-9-tetrahydrocannabinols, except as in paragraphs (j)(ii) and (j)(iii) of this section, that are naturally contained in a plant of the genus Cannabis (cannabis plant).

(ii) Naturally derived delta-9-tetrahydrocannabinols do not include any material, compound, mixture, or preparation that falls within the definition of hemp set forth in 7 U.S.C. 1639o.

(iii) Naturally derived delta-9-tetrahydrocannabinols do not include any delta-9-tetrahydrocannabinols contained in substances excluded from the definition of marijuana as set forth in 21 U.S.C. 802(16)(B)(ii).

* * * * *

May 16, 2024
Date



Merrick B. Garland
Attorney General