DEA has found that the control of mitragynine and 7-hydroxymitragynine in schedule I on a temporary basis is necessary to avoid an imminent hazard to public safety under the CSA, and no approved new drug applications or investigational new drug applications for mitragynine or 7-hydroxymitragynine exist, 21 U.S.C. 355. The Assistant Secretary also stated that the HHS has no objection to the temporary scheduling of mitragynine and 7-hydroxymitragynine. The Assistant Secretary responded to this notice by letter dated May 6, 2016. The Assistant Secretary by letter dated May 18, 2016, and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for mitragynine and 7-hydroxymitragynine. The Administrator transmitted notice of his intent to place mitragynine and 7-hydroxymitragynine into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of these opioids into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. Any final order will impose the administrative, civil, and criminal sanctions and regulatory controls applicable to schedule I controlled substances under the Controlled Substances Act on the manufacture, distribution, possession, importation, and exportation of, and research and conduct of instructional activities of these opioids.

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-442]

Schedules of Controlled Substances: Temporary Placement of Mitragynine and 7-Hydroxymitragynine Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of intent.

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this notice of intent to temporarily schedule the opioids mitragynine and 7-hydroxymitragynine, which are the main active constituents of the plant kratom, into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of these opioids into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to public safety. Any final order will impose the administrative, civil, and criminal sanctions and regulatory controls applicable to schedule I controlled substances under the Controlled Substances Act on the manufacture, distribution, possession, importation, and exportation of, and research and conduct of instructional activities of these opioids.

DATES: August 31, 2016.

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

SUPPLEMENTARY INFORMATION: Any final order will be published in the Federal Register and may not be effective prior to September 30, 2016.

Legal Authority

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

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

Section 201 of the CSA, 21 U.S.C. 811, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid an imminent hazard to public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, 21 U.S.C. 812, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. 21 U.S.C. 811(h)(1). The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into schedule I of the CSA. The Administrator transmitted notice of his intention to place mitragynine and 7-hydroxymitragynine in schedule I on a temporary basis to the Assistant Secretary by letter dated May 6, 2016. The Assistant Secretary responded to this notice by letter dated May 18, 2016, and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for mitragynine and 7-hydroxymitragynine. The Assistant Secretary also stated that the HHS has no objection to the temporary placement of mitragynine and 7-hydroxymitragynine into schedule I of the CSA. Neither mitragynine nor 7-hydroxymitragynine is currently listed in any schedule under the CSA, and no approved new drug applications or investigational new drug applications for mitragynine or 7-hydroxymitragynine exist. 21 U.S.C. 355. The DEA has found that the control of mitragynine and 7-hydroxymitragynine in schedule I on a temporary basis is necessary to avoid an imminent hazard to public safety.
Kratom preparations, which contain the main active alkaloids mitragynine and 7-hydroxymitragynine, are easily obtained from smoke shops and over the Internet. In the United States, kratom, also known in Southeast Asia as thang, thom, krathom, kakuam, ketum, and biak. In recent years, the presence of the psychoactive plant kratom has increased dramatically on the recreational market in the United States due to its opioid-like effects. Numerous vendors selling kratom have appeared in the past few years, primarily on the Internet. The Internet is the most utilized source for the purchase of kratom products, making kratom just “a click” away for users. In the United States, law enforcement has markedly increasing its availability.

As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the Department of Health and Human Services (HHS) in carrying out the Secretary’s scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA, 21 U.S.C. 811(h)(1). Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. 21 U.S.C. 812(b)(1).

Mitragynine and 7-hydroxymitragynine, the Main Active Constituents of the Plant Kratom

Kratom, which contains the main active alkaloids mitragynine and 7-hydroxymitragynine, has a long history of use in Southeast Asia as an opium substitute. Kratom is also known in Southeast Asia as thang, thom, kratom, kakuam, ketum, and biak. In recent years, the presence of the psychoactive plant kratom has increased dramatically on the recreational market in the United States due to its opioid-like effects. Numerous vendors selling kratom have appeared in the past few years, markedly increasing its availability.

Kratom preparations, which contain the main active alkaloids mitragynine and 7-hydroxymitragynine, are easily obtained from smoke shops and over the Internet. The Internet is the most utilized source for the purchase of kratom products, making kratom just “a click” away for users. In the United States, law enforcement has seized kratom/mitragynine products in the following forms: powder/plant, powder, plant or vegetable material, capsules, tablets, liquids, gum/resin, and drug patch.
Since abusers obtain kratom, which contains the main active alkaloids mitragynine and 7-hydroxymitragynine, through unknown sources, the identity, purity, and quality of these substances are uncertain and inconsistent. Several studies have analyzed the concentrations of mitragynine and/or 7-hydroxymitragynine in different kratom products. The studies showed that there were inconsistencies in the levels of the opioid mitragynine present in similar kratom products, and some products contained other psychoactive substances (see 3-factor analysis). Based on the variability of the mitragynine concentration in each product, users may experience differing effects when consuming similar amounts of different products.

\[ Mitragynine is the most abundant alkaloid in kratom and constitutes about 66 percent of the total alkaloid content of the plant. The alkaloid content of mitragynine was 45 percent of all alkaloids detected during analyses performed. Such large relative differences in proportions of plant alkaloids (66%-45%) are common among plant species and will lead to variations in potency and the risk of overdose. \]

\[ 7-Hydroxymitragynine is a more potent agonist against mitragynine although it only comprises about 1.6 percent of the total alkaloid content of the plant. The alkaloid content of 7-hydroxymitragynine was 4 percent of all alkaloids detected in analyses performed. Such large relative differences in proportions of plant alkaloids (4.0%-1.6%) are common among plant species and will lead to variations in potency and the risk of overdose. \]

Evidence suggests that kratom, which contains the main active alkaloids mitragynine and 7-hydroxymitragynine, is abused individually, and with other psychoactive substances. In a 2016 publication, the Centers for Disease Control (CDC) characterized kratom exposures reported to poison centers and uploaded to the National Poison Data System (NPDS) \[^{10}\] from January 2010 through December 2015. During the stated timeframe, U.S. poison centers received 660 calls related to kratom exposure. Of the calls reported, 487 (73.8%) reported intentional exposure to kratom, and 595 (90.2%) reported ingestion of the drug. In addition to reports of isolated exposures to kratom (428 (64.8%)), reports of kratom being used with other substances (ethanol, benzodiazepines, narcotics, acetaminophen, and other botanicals) were also recorded. Additionally, forensic laboratory analyses of drug evidence have identified kratom/mitragynine, along with synthetic cannabinoids and synthetic opioids during the analyses of products seized on the illicit market. The consumption of kratom individually, or in conjunction with alcohol or other drugs, is of serious concern as it can lead to severe adverse effects and death.

\[^{5}\] The National Poison Data System (NPDS) is a national database of information logged by the country’s regional poison centers serving all 50 United States, Puerto Rico and the District of Columbia. The NPDS is maintained by the American Association of Poison Control Centers. NPDS case records are the result of call reports made by users (i.e., self-reports), friends and family members, and health care providers.

Kratom does not have an approved medical use in the United States and has not been studied as a treatment agent in the United States. Kratom has a history of being used as an opium substitute in Southeast Asia. Kratom has also been used to self-treat chronic pain and withdrawal symptoms from opioid use. Especially concerning, reports note users have turned to kratom as a replacement for other opioids, such as heroin. In the United States, kratom is misused to self-treat chronic pain and opioid withdrawal symptoms, with users reporting its effects to be comparable to prescription opioids. Users have also reported dose-dependent psychoactive effects to include euphoria, simultaneous stimulation and relaxation, analgesia, vivid dreams, and sedation (at higher doses). As noted in the actions by the United States Food and Drug Administration, kratom products have been encountered with false claims, an extremely concerning issue for public health and safety. These products are marketed as safe for self-medication, but have not been approved by the Food and Drug Administration (FDA) for any medical uses.


Information from the published literature, poison control centers data, and medical examiner data, suggests that kratom, which contains the main active alkaloids mitragynine and 7-hydroxymitragynine, is abused by a diverse population to include recreational opioid users, young adults, and adults. The most commonly described route of administration of kratom, which contains the main active alkaloids mitragynine and 7-hydroxymitragynine, is oral. The leaves are typically brewed and ingested as a tea; however, smoking, chewing the raw leaves (done traditionally), and ingestion of kratom capsules or resin extracts have also been reported.

**Factor 5. Scope, Duration and Significance of Abuse**

The abuse of kratom, containing the main active alkaloids mitragynine and 7-hydroxymitragynine, is increasing in the United States and remains extremely concerning for law enforcement and public health. As the abuse of the plant increases, as demonstrated by the increasing availability per border encounters, it has been noted that physicians should be aware of the kratom’s adverse health effects, toxicity, dependence, and withdrawal.


Reports from law enforcement indicate that kratom is being imported for widespread distribution to the public within the United States. Between February 2014 and July 2016, over 55,000 kilograms (kg) of kratom material were encountered by law enforcement at various ports of entry within the United States. Additionally, over 57,000 kg of kratom material offered for import at numerous ports of entry, between 2014 and 2016, are awaiting an FDA admissibility decision. The amount of kratom currently seized or awaiting an admissibility decision by law enforcement, between 2014 and 2016, is enough to produce over 12 million doses of kratom. Such alarming quantities create an imminent public health and safety threat.

According to press announcements released in 2014 and 2016, the FDA requested the seizure, by US Marshals, of more than 25,000 pounds of raw kratom material, nearly 90,000 bottles of dietary supplements labeled as containing kratom, and over 100 cases of products labeled as kratom, respectively. The FDA stated that kratom products "pose a risk to the public health and have the potential for abuse" and the seizure of certain kratom products was necessary "to safeguard the public from a dangerous product". The FDA has also warned the public not to use any products labeled as containing kratom due to serious concerns about toxicity and potential health impacts. To further protect the public health and safety from the large influx of kratom materials, the FDA issued and updated two import alerts related to numerous kratom and kratom-containing products. These import alerts allow for detention without physical examination of dietary supplements and bulk ingredients that are or contain kratom, and detention without physical examination of unapproved new drugs promoted in the United States, which includes kratom products that make false health claims. Since 2014, 121 firms have been added to these import alerts for importing kratom products.
In a 2016 publication, the CDC characterized kratom exposures reported to poison centers and uploaded to the NPDS from January 2010 through December 2015. These substances produce opioid-like effects, making their abuse a serious public health concern. Information from published literature, public health officials, and poison centers suggests that kratom poses an imminent hazard to public safety. The use of kratom and associated products, which contain the main active alkaloids mitragynine and 7-hydroxymitragine, pose an imminent hazard to public safety. The use of kratom and associated products, which contain the main active alkaloids mitragynine and 7-hydroxymitragine, pose an imminent hazard to public safety.

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

The use of kratom and associated products, which contain the main active alkaloids mitragynine and 7-hydroxymitragine, pose an imminent hazard to public safety. These substances produce opioid-like effects, making their abuse a serious public health concern. Information from published literature, public health officials, and poison control center data demonstrate that the use of kratom, which contains the main active alkaloids mitragynine and 7-hydroxymitragine, has caused numerous adverse effects on users. In a 2016 publication, the CDC characterized kratom exposures reported to poison centers and uploaded to the NPDS from January 2010 through December 2015.
These exposures resulted in medical outcomes that varied in severity, ranging from minor (having minimal signs or symptoms that resolved rapidly with no residual disability), moderate (having non-life-threatening and no residual disability, but requiring some form of treatment), major (having life-threatening signs or symptoms with some residual disability), and death. Additionally, several adverse effects related to kratom exposure were reported, which include agitation or irritability, tachycardia, nausea, drowsiness, and hypertension. The severity of the reported outcomes, health effects, and increased use of kratom suggests an emerging public health threat.

\[\text{Page 59933}\]

Information from the scientific literature also demonstrates the health risks associated with kratom use. Reports of hepatotoxicity, psychosis, seizure, weight loss, insomnia, tachycardia, vomiting, poor concentration, hallucinations, and death associated with kratom use have been documented. Additionally, published case reports describe events where individuals sought medical care for the purported use of kratom. Some examples of the reported adverse events involving kratom exposure are described in the 3-factor analysis.

Numerous deaths associated with kratom, which contains the main active constituents mitragynine and 7-hydroxymitragynine, have been reported indicating that this substance is a serious public health threat. In 2016, DEA has received correspondences from state officials which indicate that there were a significant number of overdoses and traffic fatalities directly, or indirectly, involving kratom. Deaths related to kratom exposure have been reported in the scientific literature, and sixteen other deaths related to kratom exposure, have been confirmed by autopsy/medical examiner reports (mitragynine and 7-hydroxymitragynine were identified in biological samples). Of these deaths, 15 occurred between 2014 and 2016. This information demonstrates the severe risks associated with kratom misuse and the increasing occurrence of fatal outcomes related to kratom exposure. Details of some of these events are summarized in the 3-factor analysis.

Finding of Necessity of Schedule I Placement To Avoid Imminent Hazard to Public Safety

In accordance with 21 U.S.C. 811(h)(3), based on the available data and information, summarized above, the continued uncontrolled manufacture, distribution, reverse distribution, importation, exportation, conduct of research and chemical analysis, and abuse of mitragynine and 7-hydroxymitragynine pose an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for these substances in the United States. A substance meeting the statutory requirements for temporary scheduling, 21 U.S.C. 811(h)(1), may only be placed in schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for mitragynine and 7-hydroxymitragynine indicate that these substances have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision.

Conclusion

This notice of intent initiates an expedited temporary scheduling action and provides the 30-day notice pursuant to section 201(h) of the CSA. In accordance with the provisions of section 201(h) of the CSA, the Administrator considered available data and information, herein set forth the grounds for his determination that it is necessary to temporarily schedule mitragynine and 7-hydroxymitragynine in schedule I of the CSA, and finds that placement of these opioid substances into schedule I of the CSA is necessary in order to avoid an imminent hazard to the public safety.

Because the Administrator hereby finds that it is necessary to temporarily place these opioids into schedule I to avoid an imminent hazard to the public safety, any subsequent order to temporarily scheduling these substances will be effective on the date of publication in the Federal Register, and will be in effect for a period of two years, with a possible extension of one additional year, pending completion of the regular scheduling process. The Administrator to issue such a final order as soon as possible after the expiration of 30 days from the date of publication of this notice. Mitragynine and 7-hydroxymitragynine will then be subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, importation, exportation, research, conduct of instructional activities and chemical analysis, and possession of a schedule I controlled substance.

The CSA sets forth specific criteria for scheduling a drug or other substance. Regular scheduling actions in accordance with 21 U.S.C. 811(a) are subject to formal rulemaking procedures done “on the record after opportunity for a hearing” conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The regular scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the regular scheduling process of formal rulemaking are subject to judicial review. 21 U.S.C. 877.

Regulatory Matters

Section 201(h) of the CSA, 21 U.S.C. 811, provides for an expedited temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary of HHS. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, the DEA believes that the notice and comment requirements of section 553 of the Administrative Procedure Act (APA), 5 U.S.C. 553, do not apply to this notice of intent. In the alternative, even assuming that this notice of intent might be subject to section 553 of the APA, the Administrator finds that there is good cause to forgo the notice and comment requirements of section 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Although the DEA believes this notice of intent to issue a temporary scheduling order is not subject to the notice and comment requirements of section 553 of the APA, the DEA notes that in accordance with 21 U.S.C. 811(h)(4), the Administrator will take into consideration any comments submitted by the Assistant Secretary with regard to the proposed temporary scheduling order.

Further, the DEA believes that this temporary scheduling action is not a “rule” as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of
the Regulatory Flexibility Act (RFA). The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable here, as here, the DEA is not required by section 553 of the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been reviewed by the Office of Management and Budget (OMB).

This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

\[\text{[Page 59934]}\]

**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, the DEA proposes to amend 21 CFR part 1308 as follows:

**PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES**

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

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

2. In Sec. 1308.11, add paragraphs (h)(28) and (29) to read as follows:

   **Sec. 1308.11 Schedule I**

      * * * *

      (h) * * *

      (28) Mitragynine (to include synthetic equivalents as well as mitragynine naturally contained in the plant of the genus and species name: Mitragyna speciosa Korth, also known as kratom) its isomers, esters, ethers, salts and salts of isomers, esters and ethers—(9823)

      (29) 7-Hydroxymitragynine (to include synthetic equivalents as well as 7-hydroxymitragynine naturally contained in the plant of the genus and species name: Mitragyna speciosa Korth, also known as kratom) its isomers, esters, ethers, salts and salts of isomers, esters and ethers—(9838)


Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-20803 Filed 8-30-16; 8:45 am]

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