DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA 1713]

Schedules of Controlled Substances: Placement of Cipepofol in Schedule IV

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Interim final rule; request for comments.

SUMMARY: On May 29, 2026, the United States Food and Drug Administration (FDA) approved a new drug application for Cypsedo (cipepofol) for induction of general anesthesia in adults undergoing surgery. The Department of Health and Human Services provided the Drug Enforcement Administration (DEA) with a scheduling recommendation to place cipepofol, chemically known as 2-[(1*R*)-1-cyclopropylethyl]-6-isopropylphenol, in schedule IV of the Controlled Substances Act (CSA). In accordance with the CSA, as amended by the Improving Regulatory Transparency for New Medical Therapies Act, DEA is hereby issuing an interim final rule placing cipepofol in schedule IV of the CSA.

DATES: This rule is effective August 27, 2026. Comments must be submitted electronically or postmarked on or before September 28, 2026. The electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing, together with a written statement of position on the matters of fact and law asserted in the hearing, must be received on or before September 28, 2026.

ADDRESSES: Interested persons may file written comments on this rulemaking in accordance with 21 U.S.C. 811(j)(3) and 21 CFR 1308.43(g). To ensure proper handling of comments, please reference ''Docket No. DEA1713'' on all correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration (DEA) encourages commenters to submit comments electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the web page or attach a file for lengthier comments. Please go to *https://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. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.
- *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 an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrissette Drive, Springfield, VA 22152.
- *Hearing requests:* All requests for hearing and waivers of participation, together with a written statement of position on the matters of fact and law asserted in the hearing, must be filed with the DEA Administrator, who will make the determination of whether a hearing will be needed to address such matters of fact and law in the rulemaking. Such requests must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. For informational purposes, a courtesy copy of requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/OALJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrissette Drive, Springfield, Virginia 22152.
- *Paperwork Reduction Act Comments:* All comments concerning collections of information under the Paperwork Reduction Act must be submitted to the Office of Information and Regulatory Affairs, OMB, Attention: Desk Officer for DOJ, Washington, DC 20503. Please state that your comment refers to Docket No. DEA1713.

FOR FURTHER INFORMATION CONTACT: Dr. Terrence L. Boos, Drug & Chemical Evaluation Section, Diversion Control Division, Drug Enforcement Administration; Telephone: (571) 362–3249.

SUPPLEMENTARY INFORMATION: In this interim final rule (IFR), Drug Enforcement Administration (DEA) is adding cipepofol to schedule IV of the Controlled Substances Act (CSA).

Posting of Public Comments

All comments received in response to this docket are considered part of the public record. DEA will make comments available for public inspection online at *https://www.regulations.gov,* unless reasonable cause is given. Such information includes personal or business identifying information (such as name, address, State or Federal identifiers, etc.) voluntarily submitted by the commenter.

Commenters submitting comments which include personal identifying information (PII), 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. DEA 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. DEA will post only the redacted comment on *https://www.regulations.gov* for public inspection. DEA generally will not redact additional information contained in the comment marked ''TO BE PUBLICLY POSTED.'' The Freedom of Information Act applies to all comments received.

For easy reference, an electronic copy of this document and supplemental information to this IFR are available at *http://www.regulations.gov.*

Request for Hearing or Appearance; Waiver

Pursuant to 21 U.S.C. 811(j)(3), an interested person may ''request a hearing.'' Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551–559.[1] 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

[1] 21 CFR 1308.41–1308.45; 21 CFR part 1316, subpart D.

(3) state briefly the position of the person with regard to the objections or issues.

Any interested person may file a waiver of an 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.[2]

All requests for hearings and waivers of 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 a hearing will be needed to address such matters of fact and law in the rulemaking will be made by the Administrator. If a hearing is needed, DEA will publish a notice of hearing on the interim final rule in the **Federal Register**.[3] Further, once the Administrator determines a hearing is needed to address such matters of fact and law in rulemaking, he 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.

In accordance with 21 U.S.C. 811 and 812, the purpose of a hearing would be to determine whether cipepofol meets the statutory criteria for placement in schedule IV.

Legal Authority

Under the CSA, as amended in 2015 by the Improving Regulatory Transparency for New Medical Therapies Act (section 2(b) of Pub. Law 114–89), DEA is required to commence an expedited scheduling action with respect to certain new drugs approved by the Food and Drug Administration (FDA). As provided in 21 U.S.C. 811(j), this expedited scheduling is required where both of the following conditions apply: (1) The Secretary of the Department of Health and Human Services (HHS) has advised DEA that a New Drug Application (NDA) has been submitted for a drug that has a stimulant, depressant, or hallucinogenic effect on the central nervous system (CNS), and that it appears that such drug has an abuse potential; and (2) the Secretary of HHS recommends that DEA control the drug in schedule II, III, IV, or V pursuant to 21 U.S.C. 811(a) and (b). In these circumstances, DEA is required to issue an IFR controlling the drug within 90 days.

Subsection 811(j)(2) states that the 90-day timeframe starts the later of (1) the date DEA receives HHS's scientific and medical evaluation/scheduling recommendation, or (2) the date DEA receives notice of the NDA approval by HHS. Subsection 811(j)(3) specifies that the rulemaking shall become immediately effective as an IFR without requiring DEA to demonstrate good cause therefore. Thus, the purpose of subsection 811(j) is to speed the process by which DEA schedules newly approved drugs that are currently either in schedule I or not controlled (but which have sufficient abuse potential to warrant control) so that such drugs may be marketed without undue delay following FDA approval.[4]

Subsection 811(j)(3) further provides that the IFR shall give interested persons the opportunity to comment and to request a hearing. After the conclusion of such proceedings, DEA must issue a final rule in accordance with the scheduling criteria of 21 U.S.C. 811(b) through (d), and 812(b).

Background

Cipepofol is a new molecular entity with CNS activity, acting as a positive allosteric modulator and agonist at the gamma-aminobutyric acid A ($GABA_A$) receptor, inducing chloride ion influx and reversing action potential generation in neuronal tissue. The chemical structure and mechanism of action of cipepofol are similar to those of the FDA-approved drugs propofol and fospropofol. Also, the mechanism of action of cipepofol is similar to certain FDA-approved neuroactive steroid products, which are controlled in schedule IV (*i.e.,* alfaxalone, brexanolone, and zuranolone) or schedule V (*i.e.,* ganaxolone).

Determination To Schedule Cipepofol

On May 6, 2026, DEA received from HHS a scientific and medical evaluation entitled ''Basis for the Recommendation to Control Cipepofol in Schedule IV of the Controlled Substances Act'' and a scheduling recommendation. Pursuant to 21 U.S.C. 811(b) and (c), this document contained an eight-factor analysis of the abuse potential, legitimate medical use, and dependence liability of cipepofol, along with HHS's recommendation to control cipepofol under schedule IV of the CSA.

In response, DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by HHS, along with all other relevant data, and completed its own eight-factor review pursuant to 21 U.S.C. 811(c). DEA concluded that cipepofol meets the 21 U.S.C. 812(b)(4) criteria for placement in schedule IV of the CSA.

Pursuant to subsection 811(j), and based on HHS's scheduling recommendation, the approval of the NDA by HHS/FDA, and DEA's determination, DEA is issuing this IFR to schedule cipepofol as a schedule IV controlled substance under the CSA.

Included below is a brief summary of each factor as analyzed by HHS and DEA, and as considered by DEA in its scheduling action. Please note that both DEA and HHS analyses are available in their entirety under ''Supporting Documents'' in the public docket for this IFR at *https://www.regulations.gov,* under Docket Number ''DEA1713.'' Full analysis of, and citations to, the information referenced in the summary may also be found in the supporting and related material.

1. Its Actual or Relative Potential for Abuse

Cipepofol is currently legally marketed in China, where data shows zero abuse or misuse cases. According to HHS, because cipepofol has not been legally marketed in the United States, the legitimate drug channels for cipepofol are limited to the research conducted with the drug, and to manufacturing facilities and the supply chain to produce cipepofol for legitimate drug research. HHS further notes because cipepofol has not been legally marketed in the United States, abuse of cipepofol in the United States would be limited to incidents following diversion of supplies from research or manufacturing activities of cipepofol. Both DEA and FDA are not aware of any such incidents of diversion or abuse related to cipepofol. Accordingly, DEA's National Forensic Laboratory Information System (NFLIS)-Drug[5] data confirms there is no report of law enforcement encounters of cipepofol in the United States. Cipepofol targets $GABA_A$ receptors and shares a similar mechanism of action with both propofol (which has proposed schedule IV status due to its potential for abuse and

[2] 21 CFR 1316.49.

[3] 21 CFR 1308.44(b), 1316.53.

[4] Given the parameters of subsection 811(j), in DEA's view, it would not apply to a reformulation of a drug containing a substance currently in schedules II through V for which an NDA has recently been approved.

[5] NFLIS-Drug represents an important resource in monitoring illicit drug trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. NFLIS-Drug is a national forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by Federal, State and local forensic laboratories in the United States. While NFLIS-Drug data is not direct evidence of abuse, it can lead to an inference that a drug has been diverted and abused. *See Schedules of Controlled Substances: Placement of Carisoprodol Into Schedule IV,* 76 FR 77330, 77332 (Dec. 12, 2011). NFLIS-Drug data was queried on May 11, 2026.

dependence liability) and its prodrug, fospropofol (a schedule IV substance that can induce euphoria). It also shares a similar mechanism of action with certain controlled neuroactive steroids, including alfaxalone, brexanolone, and zuranolone (schedule IV), and ganaxolone (schedule V). Accordingly, both FDA and DEA concluded that cipepofol poses safety hazards and has an abuse potential similar to schedule IV substances.

2. Scientific Evidence of Its Pharmacological Effects, if Known

Based on *in vitro* binding and functional reports, HHS noted that cipepofol acts as a selective $GABA_A$ receptor positive modulator and agonist that induces chloride ion influx to cause neuronal hyperpolarization and thus achieve CNS depression.

Preclinical Behavioral Studies

Functional Studies: Single intravenous doses of cipepofol (up to 6 mg/kg) in rats produced dose-dependent increase in duration and level of anesthesia with effect declining within 45 minutes. Neurobehavioral tests at 2 and 24 hours post-dose showed no residual treatment-related effects.[6]

Conditioned Place Preference (CPP): A 6-day CPP study in rats compared cipepofol (1, 2, or 4 mg/kg) against vehicle and propofol. Data from the study showed that neither propofol nor cipepofol produced environmental preference or evidence of CPP. However, because literature shows propofol can induce CPP under different parameters, this negative result does not completely rule out the reward potential of cipepofol. HHS concluded these findings must be interpreted alongside broader abuse liability data.

Self-Administration: In rats trained to self-administer propofol (1.7 mg/kg/injection), substituting cipepofol (0.2, 0.4, and 0.8 mg/kg/injection) successfully maintained lever-pressing behavior. Higher doses caused a decrease in injection frequency but an increase in total drug intake. Response rates also likely fell due to the drug's sedative effects. HHS concluded that these data confirm cipepofol has rewarding and reinforcing properties.

Physical Dependence and Withdrawal: A 30-day study evaluated dependence in rats using titrated doses of cipepofol, propofol, morphine, or vehicle, followed by a 14-day abrupt withdrawal phase. The high dose of cipepofol (5.4 mg/kg/day) replicated human therapeutic exposure levels. Higher doses were omitted because profound sedation would impair the animals. Abruptly stopping cipepofol caused mild, intermittent withdrawal symptoms like temporary chewing and body shakes, mirroring the mild withdrawal profile of propofol. These findings indicate that cipepofol carries a low risk for physical dependence at therapeutic doses.

Pharmacological and Behavioral Studies in Human

Human Abuse Potential (HAP) studies assess a drug's abuse liability by comparing a test drug to active controls and placebos. As described in HHS's scientific and medical evaluation, an intravenous HAP study was conducted by the drug sponsor to assess the abuse potential of cipepofol in participants who were non-dependent, recreational drug users. High scores on specific visual analog scales (VAS), such as ''Drug Liking'' and ''High,'' indicate abuse potential. Propofol served as the active control because both drugs share a similar mechanism of action. The dose selection phase (part 1) used 43 subjects to select safe doses, establishing cipepofol doses at 0.175 mg/kg and 0.2 mg/kg, and propofol at 0.725 mg/kg. The main study was a randomized, double-blind- and active-controlled, four-way crossover trial (part 2) with 42 participants, though 2 were excluded from the final analysis due to oversedation and invariant responses. Ultimately, 40 participants completed the entire trial.

Regarding the pharmacodynamic (PD) results, cipepofol showed an abuse potential similar to propofol. Both active drugs scored significantly higher than the placebo, but participants liked both active drugs equally. These comparable liking scores demonstrate a similar liability for misuse. Cipepofol demonstrated a statistically significant increase in drug-liking over placebo, establishing its abuse potential, though it did not surpass that of propofol. Its psychological profile mirrors the standard anesthetic control. Regarding the pharmacokinetic (PK) results, cipepofol plasma levels peaked rapidly at 2 minutes, reaching 226 ng/mL for the 0.175 mg/kg dose and 257 ng/mL for the 0.2 mg/kg dose. The drug clearance was rapid, with levels falling below the 5 ng/mL lower limit of quantification by 8 hours post-dose. Total drug exposure was similar between both doses. Half-life and peak times showed no meaningful differences, matching the drug's rapid-onset and short-duration profile.

For safety and adverse events (AEs), abuse-related side effects were rare. In Part 1 of the clinical trial, propofol users reported euphoria and sleepiness, while cipepofol users reported one instance of depressed mood. The Part 2 qualification phase saw one instance of euphoria from propofol. During the Part 2 treatment phase, one oversedation event occurred from cipepofol, but no other abuse-related adverse events were observed.

The analysis of pooled Phase 1 data across 13 healthy volunteer studies highlights the value of subtherapeutic dosing for evaluating abuse potential, as therapeutic doses induce too much sedation. Out of 322 cipepofol recipients, 69 received subtherapeutic doses (<0.4 mg/kg) and 253 received therapeutic doses (≥0.4 mg/kg), while 46 received propofol. Dizziness was the top CNS adverse event, hitting 15% of the propofol group but only 4% of the therapeutic cipepofol group. Restlessness and disorientation occurred at 2% or less, solely in the therapeutic cipepofol cohort.

An HHS safety review of pooled Phase 2 and 3 studies showed minimal abuse-related adverse events, with comparable safety profiles between cipepofol and propofol across multiple clinical settings. Across open-label sedation trials (219 patients), procedural sedation and non-endotracheal surgical procedures (848 patients), and general anesthesia induction trials (1,365 patients), dizziness was consistently the most common central nervous system event, occurring at nearly identical rates between the two drugs (4% to 6% for cipepofol vs. 6% to 7% for propofol). Other abuse-related adverse events including excessive talking, somnolence, anxiety, restlessness, agitation, confusion, disorientation, and emotional disorder were rarely observed, affecting 1% or less of participants in both cohorts.

Another HHS review of United States and European Union Phase 3 data covering 723 cipepofol and 357 propofol recipients found dizziness was the most common CNS event. Other abuse-related events—specifically anxiety, restlessness, agitation, confusion, disorientation, and somnolence—occurred at low rates (≤1%) in both groups, with further details on physical dependence assessments found in Factor 7.

In summary, HHS concluded that no adverse events involving actual abuse, misuse, diversion, intentional overdose, or physical dependence occurred during the cipepofol clinical trials. Abuse-related events were rare and balanced between the cipepofol and propofol groups. Frequent reports of dizziness in both cohorts were distinct from

[6] HHS eight-factor analysis document. Page 6. 2026.

euphoria-related symptoms like elevated mood or feeling drunk, with the only instance of euphoric mood linked to cipepofol being a single report (verbatim term ''agitated'') during procedural sedation. Based on this comprehensive review, intravenous cipepofol demonstrates reinforcing effects similar to propofol, indicative of its abuse potential.

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

Cipepofol, chemically known as 2-[(1*R*)-1-cyclopropylethyl]-6-isopropylphenol, is a new molecular entity. The final cipepofol product is distributed as a 2.5 mg/mL oil-in-water emulsion for injection, provided in 20 mL single-use vials. An HHS review indicates intravenous cipepofol distributes rapidly, peaking within 1 to 2 minutes. Cipepofol exhibits extensive tissue distribution and is 99% protein-bound in serum. The major metabolite of cipepofol was identified as M4 metabolite, which was found to be pharmacologically inactive and thus poses a negligible abuse risk. At a 0.4 mg/kg dose, plasma half-life of cipepofol is 1 to 5 hours. Kidneys clear 85% of the dose of cipepofol, mainly as metabolites M4 and M5–1. As discussed in the background section, cipepofol has an accepted medical use in treatment in the United States.

4. Its History and Current Pattern of Abuse

Because cipepofol is not marketed in the United States, domestic abuse data remains unavailable. Based on available postmarket data from China provided in the NDA submission, it is estimated that 14.5 million patients in China have received the drug and postmarket adverse event surveillance data shows no reports of abuse or misuse. Spontaneous reports in the Drug Adverse Event Reporting System (DAERS) noted side effects like dizziness, agitation, and hallucinations, but some published literature show no evidence of misuse. Furthermore, HHS noted that recent epidemiological data shows no documented instances of abuse. Population-level analyses from America's Poison Centers National Poison Data System (NPDS) and the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance (NEISS–CADES) confirm this absence, suggesting that it is likely cipepofol currently shows no cases of abuse or misuse due to its lack of U.S. approval. Data from preclinical and clinical studies indicate that the abuse potential of cipepofol is similar to that of propofol. HHS notes that consistent with the recommendation made in 2010 to place propofol in schedule IV of the CSA, there continue to be reports of propofol abuse and misuse, primarily in healthcare professionals with occupational access to the drug. Although there is currently no available data on the abuse or misuse of cipepofol, the information on propofol, a closely related drug, may provide some evidence supporting the abuse potential of cipepofol.

In summary, pharmacological data on cipepofol shows that it produces abuse-related effects and has an abuse potential similar to that of propofol and other schedule IV CNS depressants.

5. The Scope, Duration, and Significance of Abuse

Cipepofol has been marketed exclusively in China since 2021 and remains unavailable in the United States, resulting in limited domestic abuse data. Current HHS reviews indicate no documented instances of abuse, misuse, or diversion, though this finding is restricted by the drug's brief clinical history. Consequently, potential extra-medical use is projected to remain confined to healthcare professionals with direct occupational exposure. Nonclinical and clinical data demonstrate an abuse potential comparable to propofol, a substance recommended for schedule IV designation. Furthermore, DEA's NFLIS-Drug database confirms that cipepofol is entirely absent from the illicit United States drug market. Because preclinical and clinical studies showed that cipepofol has an abuse potential that is similar to that of propofol, it is likely that upon its availability in the market, cipepofol may be abused.

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

A drug's abuse potential is a key indicator of its overall risk to public health risk. Thus, HHS started that because cipepofol possesses an abuse potential comparable to propofol, it is anticipated that cipepofol will exhibit a similar abuse profile and present a comparable public health risk to that of propofol.

To evaluate cipepofol's public health risk, HHS analyzed clinical trials and overdose data for cipepofol across diverse patient populations. In patients receiving cipepofol for general anesthesia induction, the most frequent common side effects included hypotension, nausea, and procedural pain, with dizziness being the top CNS effect. Furthermore, HHS noted that cipepofol overdose may lead to potentially fatal cardiovascular and respiratory depression if not promptly and adequately managed.

HHS recommends advising patients against driving or operating heavy machinery after receiving cipepofol, as its anesthetic effects, including drowsiness, and impair mental alertness. In summary, data from nonclinical and clinical studies indicate that cipepofol's abuse potential and public health risks are comparable to propofol, suggesting a risk profile consistent with schedule IV substances.

7. Its Psychic or Physiological Dependence Liability

Psychic (or psychological) dependence is a state similar to addiction and can be measured through animal self-administration studies, HAP studies, case reports, and epidemiological data. Rodent animal data shows that cipepofol is self-administered, providing evidence of cipepofol's reinforcing and rewarding properties. In propofol-trained rats, cipepofol maintained stable self-administration. Higher doses of cipepofol decreased injection counts but raised total drug intake. The response rate also decreased with higher doses of cipepofol, likely due to sedative effects. Similarly, HAP studies show cipepofol carries abuse potential that is comparable to propofol. Like propofol, cipepofol scored higher than placebo on the Drug Liking VAS E_{max} scale. In addition, sedative doses of cipepofol exhibit clear reinforcing effects in humans. The secondary endpoints (*i.e.,* VAS E_{max} for Overall Drug Liking and Take Drug Again) also support a risk for psychological dependence. Collectively, these findings show it is likely that cipepofol can produce psychological dependence.

Physical dependence develops from physiological adaptation to repeated drug use and manifests as withdrawal symptoms after abrupt drug discontinuation or reduction of a drug. HHS assessed the physical dependence liability of cipepofol in rats after repeated administration of cipepofol for 30 days followed by a 14-day abrupt discontinuation phase. In this study, cipepofol was compared to vehicle, morphine, and propofol. Morphine as the positive control was associated with a significant increase in withdrawal symptoms (*e.g.,* significant decrease in body weight, increased wet dog shakes, writhing, teeth chattering, chewing, and ptosis) following abrupt discontinuation of morphine. Abrupt cipepofol discontinuation was associated with limited, intermittent behavioral changes including withdrawal symptoms like

weight loss and teeth chattering. Likewise, propofol discontinuation after 30 days of repeated administration showed a similar minimal withdrawal profile.

HHS noted that clinical trials did not systematically evaluate cipepofol's physical dependence. However, a limited subset of participants in some clinical trials were assessed for discontinuation-emergent adverse events (DEAEs). DEAEs occurred more than four hours after stopping cipepofol. Reported DEAEs included nausea, vomiting, insomnia, and palpitations, but these events occurred with low frequency.

Published literature notes withdrawal syndromes following continuous propofol infusions. Because cipepofol shares a similar chemical structure, mechanism, and abuse potential with propofol, it is anticipated that cipepofol, like propofol, may also experience physical dependence. Therefore, the overall data suggests that chronic administration of cipepofol may result in physiologic dependence.

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

Cipepofol is not an immediate precursor of any controlled substance, as defined by 21 U.S.C. 802(23).

Conclusion: After considering the scientific and medical evaluation and scheduling recommendation provided by HHS, and its own eight-factor analysis, DEA has determined that these facts and all relevant data constitute substantial evidence of potential for abuse of cipepofol. As such, DEA hereby schedules cipepofol as a controlled substance under the CSA.

Determination of Appropriate Schedule

The CSA lists the findings required to place a drug or other substance in any particular schedule (I, II, III, IV, or V).[7] After consideration of the analysis and recommendation of the Assistant Secretary for Health of HHS and review of all available data, the Administrator of DEA, pursuant to 21 U.S.C. 812(b)(4), finds that:

(1) Cipepofol has a low potential for abuse relative to the drugs or other substances in schedule III.

Cipepofol is an intravenous anesthetic for adults that modulates GABAA receptors to inhibit neurons. The drug produces dose-dependent anesthesia and shows reinforcing properties by maintaining self-administration in propofol-trained rats. In human abuse potential studies, subtherapeutic doses mimicked propofol's positive subjective effects. However, clinical trials showed a low (< 2%) incidence of abuse-related adverse events, matching propofol rates except for higher dizziness. Consequently, due to its similarities to propofol (schedule IV), cipepofol has a low abuse potential relative to Schedule III substances under the CSA.

(2) Cipepofol has a currently accepted medical use in treatment in the United States.

Cipepofol was approved by FDA for the induction of general anesthesia in adults undergoing surgery. Thus, cipepofol has a currently accepted medical use in treatment in the United States.

(3) Abuse of cipepofol may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule III.

A rat study showed limited behavioral changes upon abrupt cipepofol discontinuation, while clinical trials found that most post-discontinuation events mirrored common treatment effects, with rare instances of insomnia or palpitations. Research indicated that cipepofol's reinforcing properties in animal models are comparable to propofol. Furthermore, human abuse potential studies at subtherapeutic doses showed that subjective responses to cipepofol were statistically indistinguishable from those of propofol. Consequently, cipepofol is associated with a low risk of physical or psychological dependence relative to schedule III substances.

Based on these findings, the Administrator concludes that cipepofol warrants control in schedule IV of the CSA.[8]

Requirements for Handling Cipepofol

Cipepofol is subject to the CSA's schedule IV regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distributing, dispensing, importing, exporting, research, and conduct of instructional activities, including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, dispenses, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses) cipepofol must be registered with DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312. These registration requirements, however, are not applicable to patients (end users) who possess cipepofol pursuant to a lawful prescription.

2. *Disposal of Stocks.* Any person unwilling or unable to obtain a DEA registration must surrender all quantities of currently held cipepofol, or may transfer all quantities of currently held cipepofol to a person registered with DEA. Cipepofol is required to be disposed of in accordance with 21 CFR part 1317, in addition to all other applicable federal, state, local, and tribal laws.

3. *Security.* Cipepofol is subject to schedule III–V security requirements for DEA registrants and must be handled and stored in accordance with 21 CFR 1301.71–1301.77, pursuant to 21 U.S.C. 821, 823, and 871(b). Non-practitioners handling cipepofol must also comply with the employee screening requirements of 21 CFR 1301.90–1301.93. These requirements, however, are not applicable to patients (end users) who possess cipepofol pursuant to a lawful prescription.

4. *Labeling and Packaging.* All labels and packaging for commercial containers of cipepofol must comply with 21 U.S.C. 825 and 958(e) and be in accordance with 21 CFR part 1302.

5. *Inventory.* Every DEA registrant who possesses any quantity of cipepofol must have an initial inventory of all stocks of controlled substances (including cipepofol) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to 21 U.S.C. 827, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

Any person who registers with DEA to handle cipepofol must take an initial inventory of all stocks of controlled substances (including cipepofol) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11(a) and (b).

After the initial inventory, every DEA registrant must take inventory of all controlled substances (including cipepofol) on hand every two years, pursuant to 21 U.S.C. 827, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11. These requirements, however, are not applicable to patients (end users) who possess Cipepofol pursuant to a lawful prescription.

6. *Records and Reports.* DEA registrants must maintain records and submit reports for cipepofol, pursuant to 21 U.S.C. 827, 832(a), and 958(e), and in accordance with 21 CFR 1301.74(b) and (c) and parts 1304, 1312, and in

[7] 21 U.S.C. 812(b).

[8] 21 U.S.C. 812(b)(4).

accordance with 21 CFR 1301.74(b) and (c) and parts 1304, 1312, and 1317.

7. *Prescriptions.* All prescriptions for cipepofol, or products containing cipepofol, must comply with 21 U.S.C. 829, and be issued in accordance with 21 CFR parts 1306 and 1311, subpart C.

8. *Manufacturing and Distributing.* In addition to the general requirements of the CSA and DEA regulations that are applicable to manufacturers and distributors of schedule IV controlled substances, such registrants should be advised that (consistent with the foregoing considerations) any manufacturing or distribution of cipepofol may only be for the legitimate purposes consistent with the drug's labeling, or for research activities authorized by the Federal Food, Drug, and Cosmetic Act, as applicable, and the CSA.

9. *Importation and Exportation.* All importation and exportation of cipepofol must be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

10. *Liability.* Any activity involving cipepofol not authorized by, or in violation of, the CSA or its implementing regulations, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Administrative Procedure Act

The APA (5 U.S.C. 553) generally requires notice and comment for rulemakings. However, 21 U.S.C. 811(j) provides that in cases where a certain new drug is (1) approved by HHS, under section 505(c) of the FDCA, and (2) HHS recommends control in CSA schedule II–V, DEA shall issue an IFR scheduling the drug within 90 days. As stated in the legal authority section, the 90-day time frame is the later of: (1) the date DEA receives HHS's scientific and medical evaluation/scheduling recommendation, or (2) the date DEA receives notice of the NDA approval by HHS. Additionally, subsection 811(j) specifies that the rulemaking shall become immediately effective as an IFR without requiring DEA to demonstrate good cause.

Executive Orders 12866, 14192, and 14294

This rule has been determined to be not significant for purposes of E.O. 12866 and accordingly has received a waiver under E.O. 14192.

DEA scheduling actions are not subject to E.O. 14294, Fighting Overcriminalization in Federal Regulations.

Executive Order 12988, Civil Justice Reform

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

Executive Order 13132, Federalism

This rulemaking does not have federalism implications warranting the application of E.O. 13132. The proposed rule does 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.

Executive Order 13175, Consultation and Coordination With Indian Tribal Governments

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

Paperwork Reduction Act

This rule would require compliance with the following existing OMB collections: 1117–0003, 1117–0004, 1117–0006, 1117–0008, 1117–0009, 1117–0010, 1117–0012, 1117–0014, 1117–0021, and 1117–0056. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Regulatory Flexibility Act

The Regulatory Flexibility Act (RFA), 5 U.S.C. 601–612, applies to rules that are subject to the notice-and-comment requirements the APA at 5 U.S.C. 553. The RFA's requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, DEA is not required by the APA or any other law to publish a general notice of proposed rulemaking. As noted in the above discussion regarding the applicability of the APA, DEA is not required to publish a general notice of proposed rulemaking. Consequently, the RFA does not apply to this IFR.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 *et seq.,* DEA has determined and certifies that this proposed 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 . . . .'' Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Congressional Review Act

This rule is not a major rule as defined by the Congressional Review Act (CRA), 5 U.S.C. 804. However, pursuant to the CRA, DEA is submitting a copy of this IFR to both Houses of Congress and to the Comptroller General.

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, DEA amends 21 CFR part 1308 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. In § 1308.14:

■ a. Redesignate paragraphs (c)(11) through (60) as paragraphs (c)(12) through (61);

■ b. Add a new paragraph (c)(11) to read as follows:

§ 1308.14 Schedule IV.

* * * * *

(c) * * *

*	*	*	*	*	
(11) Cipepofol					2139
*	*	*	*	*	

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Signing Authority

This document of the Drug Enforcement Administration was signed on August 25, 2026, by DEA Administrator Terrance C. Cole. That document with the original signature and date is maintained by DEA. For administrative purposes only, and in compliance with requirements of the Office of the Federal Register, the undersigned DEA Federal Register Liaison Officer has been authorized to sign and submit the document in electronic format for publication, as an official document of DEA. This administrative process in no way alters

the legal effect of this document upon publication in the **Federal Register**.

Heather Achbach,

Federal Register Liaison Officer, Drug Enforcement Administration.

[FR Doc. 2026–17536 Filed 8–25–26; 4:15 pm]

BILLING CODE 4410–09–P

DEPARTMENT OF THE TREASURY

Office of Foreign Assets Control

31 CFR Chapter V

Publication of Iran-Related Web General Licenses AA and BB

AGENCY: Office of Foreign Assets Control, Treasury.

ACTION: Publication of web general licenses.

SUMMARY: The Department of the Treasury's Office of Foreign Assets Control (OFAC) is publishing two Iran-related general licenses (GLs): GLs AA and BB, which were previously made available on OFAC's website upon issuance.

DATES: GLs AA and BB were issued on August 24, 2026. See **SUPPLEMENTARY INFORMATION** for additional relevant dates.

FOR FURTHER INFORMATION CONTACT: OFAC: Assistant Director for Regulatory Affairs, 202–622–4855; or *https://ofac.treasury.gov/contact-ofac.*

SUPPLEMENTARY INFORMATION:

Electronic Availability

This document and additional information concerning OFAC are available on OFAC's website: *https://ofac.treasury.gov/.*

Background

On August 24, 2026, OFAC issued GL AA to authorize certain transactions otherwise prohibited by Executive Order (E.O.) 13902 of January 10, 2020, ''Imposing Sanctions With Respect to Additional Sectors of Iran'' (85 FR 2003, January 14, 2020) that are ordinarily incident and necessary to the wind down of transactions, or maintenance of operations, involving certain entities through 12:01 a.m. eastern daylight time, October 23, 2026. OFAC also issued GL BB to authorize, through 12:01 a.m. eastern daylight time, September 8, 2026, certain transactions otherwise prohibited by the Iranian Transactions and Sanctions Regulations (ITSR), 31 CFR part 560, that are ordinarily incident and necessary to the wind down of transactions that were previously authorized by the general licenses listed in GL BB. These GLs were made available on OFAC's website (*https://ofac.treasury.gov*) when they were issued. The text of these GLs is provided below.

OFFICE OF FOREIGN ASSETS CONTROL

Executive Order 13902 of January 10, 2020

(''Imposing Sanctions With Respect to Additional Sectors of Iran'')

GENERAL LICENSE AA

Authorizing Certain Activities Involving La Nivernaise De Raffinage SAS

(a) Except as provided in paragraph (b) of this general license, all transactions prohibited by Executive Order (E.O.) 13902 that are ordinarily incident and necessary to the wind down of any transaction, or the maintenance of operations, contracts, or other agreements in effect as of August 24, 2026, involving La Nivernaise De Raffinage SAS (''LNR''), or any entity in which LNR owns, directly or indirectly, a 50 percent or greater interest, are authorized through 12:01 a.m. eastern daylight time, October 23, 2026.

(b) This general license does not authorize any transactions otherwise prohibited by E.O. 13902, including transactions involving any person blocked pursuant to E.O. 13902 other than the blocked persons described in paragraph (a) of this general license, unless separately authorized.

Bradley T. Smith,

Director, Office of Foreign Assets Control.

Dated: August 24, 2026.

OFFICE OF FOREIGN ASSETS CONTROL

Iranian Transactions and Sanctions Regulations

31 CFR Part 560

GENERAL LICENSE BB

Authorizing the Wind Down of Certain Transactions Previously Authorized Under the Iranian Transactions and Sanctions Regulations

(a) Except as provided in paragraph (b), all transactions prohibited by the Iranian Transactions and Sanctions Regulations, 31 CFR part 560 (the ITSR), that are ordinarily incident and necessary to the wind down of any transaction previously authorized by one or more of the following general licenses are authorized through 12:01 a.m. eastern daylight time, September 8, 2026, provided that any payment to a blocked person is made into a blocked interest-bearing account located in the United States in accordance with the ITSR:

(1) 31 CFR 560.544 (''Certain educational activities by U.S. persons in third countries authorized'');

(2) 31 CFR 560.550 (''Certain noncommercial, personal remittances to or from Iran authorized'');

(3) 31 CFR 560.554 (''Importation and exportation of services related to conferences in the United States or third countries authorized'');

(4) Iran General License F (''Authorizing certain services in support of professional and amateur sports activities and exchanges involving the United States and Iran''); or

(5) Iran General License G (''Certain academic exchanges and the exportation or importation of certain educational services authorized'').

(b) This general license does not authorize any other transactions or activities prohibited by the ITSR, any other Executive order, or any other part of 31 CFR chapter V, unless separately authorized.

Bradley T. Smith,

Director, Office of Foreign Assets Control.

Dated: August 24, 2026.

Bradley T. Smith,

Director, Office of Foreign Assets Control.

[FR Doc. 2026–17491 Filed 8–26–26; 8:45 am]

BILLING CODE 4810–AL–P

DEPARTMENT OF THE TREASURY

Office of Foreign Assets Control

31 CFR Chapter V

Publication of a Determination Issued Pursuant to Executive Order 13902.

AGENCY: Office of Foreign Assets Control, Treasury.

ACTION: Publication of a determination.

SUMMARY: The Department of the Treasury's Office of Foreign Assets Control (OFAC) is publishing a sector determination pursuant to a January 10, 2020 Executive Order. The determination was previously issued on OFAC's website.

DATES: The determination was issued on August 24, 2026. See **SUPPLEMENTARY INFORMATION** for additional relevant dates.

FOR FURTHER INFORMATION CONTACT: OFAC: Assistant Director for Regulatory Affairs, 202–622–4855; or *https://ofac.treasury.gov/contact-ofac.*

SUPPLEMENTARY INFORMATION: