

approval of a new drug application (NDA).

Section 505(j)(7) of the FD&C Act requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the “Approved Drug Products With Therapeutic Equivalence Evaluations,” which is known generally as the “Orange Book.” Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug’s NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

PRALIDOXIME CHLORIDE (AUTOINJECTOR) (pralidoxime chloride) solution, 600 mg/2 mL (300 mg/mL), is the subject of NDA 018986, held by Meridian Medical Technologies, Inc., and initially approved on April 26, 1983. **PRALIDOXIME CHLORIDE (AUTOINJECTOR)** is indicated for intramuscular use as an adjunct to atropine in the treatment of poisoning by nerve agents having anticholinesterase activity.

PRALIDOXIME CHLORIDE (AUTOINJECTOR) (pralidoxime chloride) solution, 600 mg/2 mL (300 mg/mL), is currently listed in the “Discontinued Drug Product List” section of the Orange Book.

Premier Research International, LLC, submitted a citizen petition dated March 25, 2026 (Docket No. FDA–2026–P–3632), under 21 CFR 10.30, requesting that the Agency determine whether **PRALIDOXIME CHLORIDE (AUTOINJECTOR)** (pralidoxime chloride) solution, 600 mg/2 mL (300 mg/mL), has been voluntarily withdrawn for reasons of safety or effectiveness.

After considering the citizen petition and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that **PRALIDOXIME CHLORIDE (AUTOINJECTOR)** (pralidoxime chloride) solution, 600 mg/2 mL (300 mg/mL), was not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information

suggesting that **PRALIDOXIME CHLORIDE (AUTOINJECTOR)** (pralidoxime chloride) solution, 600 mg/2 mL (300 mg/mL), was withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of **PRALIDOXIME CHLORIDE (AUTOINJECTOR)** (pralidoxime chloride) solution, 600 mg/2 mL (300 mg/mL), from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have found no information that would indicate that this drug product was withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list **PRALIDOXIME CHLORIDE (AUTOINJECTOR)** (pralidoxime chloride) solution, 600 mg/2 mL (300 mg/mL), in the “Discontinued Drug Product List” section of the Orange Book. The “Discontinued Drug Product List” delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to this drug product may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2026–N–10429]

Design and Safety Considerations for Clinical Trials Involving Ibogaine Drug Products; Request for Information

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for information; establishment of a public docket.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is describing the approaches it is considering for the design of early-phase clinical trials of ibogaine drug products and is opening a public docket to receive comments. The Department of

Health and Human Services (HHS) is funding clinical development of ibogaine, and the first federally supported trials are expected to study ibogaine in adults with opioid use disorder (OUD) and adults with post-traumatic stress disorder (PTSD). FDA is building on the guidance for industry entitled “Psychedelic Drugs: Considerations for Clinical Investigations” by seeking comments, data, and information from the public on protocol elements relevant to ibogaine development—including dose selection and escalation, care setting, safety monitoring, eligibility criteria, stopping rules, and safety oversight, in part, because the Federal Government is funding work in this area. FDA will consider all information provided in response to this Request for Information (RFI) to inform whether and how these specific elements should be considered in its review of Investigational New Drug Applications (INDs) involving ibogaine.

DATES: Submit either electronic or written comments, data, or information by November 20, 2026.

ADDRESSES: You may submit comments, data, and information as follows. Please note that late, untimely filed comments will not be considered. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of November 20, 2026. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- **Federal eRulemaking Portal:** <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else’s Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you

do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see “Written/Paper Submissions” and “Instructions”).

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2026-N-10429 for “Design and Safety Considerations for Clinical Trials Involving Ibogaine Drug Products; Request for Information.” Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- *Confidential Submissions*—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access

the information at: <https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

FOR FURTHER INFORMATION CONTACT: Bernard Fischer, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 4208, Silver Spring, MD 20993-0002, 855-543-3784, IbogaineRFI@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is responsible under the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 301 *et seq.*) and the Public Health Service Act for protecting and promoting the public health through the regulation of human drugs, biological products, medical devices, foods, and other products. FDA’s oversight of drug products—including ibogaine drug products and other psychedelic drugs—spans preclinical investigation through the full lifecycle of an approved product. FDA remains committed to innovation and recognizes the potential of psychedelic drugs to treat substance use disorders and certain psychiatric and neurologic conditions, while upholding its public health mission to ensure that drugs are safe, effective, and of high quality.

Consistent with this commitment, FDA has taken significant steps to support implementation of Executive Order 14401 of April 18, 2026, “Accelerating Medical Treatments for Serious Mental Illness” (91 FR 21709, April 22, 2026). Executive Order 14401 establishes a policy of accelerating innovative research models and appropriate drug approvals to help increase access to psychedelic drugs for serious mental illness, and it specifically notes that ibogaine compounds show potential in clinical studies to address serious mental illnesses for patients whose conditions persist after completing standard therapy.

On July 14, 2026, FDA issued the final guidance for industry entitled “Psychedelic Drugs: Considerations for Clinical Investigations” (Psychedelics Guidance) (91 FR 43101). The guidance provides general considerations for

sponsors developing psychedelic drugs for the treatment of certain medical conditions and discusses recommendations for clinical investigations using psychedelic drugs. The Agency has also allowed an early-phase clinical study of noribogaine hydrochloride, a derivative of ibogaine, to proceed under an IND as a potential treatment for alcohol use disorder. Consistent with Executive Order 14401, FDA is coordinating with other components of HHS to support the development of ibogaine drug products under appropriate safeguards, including gathering data that bears on the considerations described below.

Federal Support for Ibogaine Clinical Development

HHS, through the Advanced Research Projects Agency for Health (ARPA-H), is funding a program to collect safety and efficacy data through early-phase clinical trials. HHS, through the National Institute on Drug Abuse (NIDA), is also funding research on ibogaine for the potential treatment of OUD. Data collected through these federally funded programs, which will be made available publicly to investigators and sponsors, may support future later-stage studies to develop ibogaine under an IND.

FDA has identified serious safety risks with ibogaine drug products that have the potential for exposing human subjects to an unreasonable and significant risk of illness or injury (see 21 CFR 312.42(b)(1)(i)), including prolongation of the heart rate-corrected QT (QTc) interval and the associated risk of life-threatening arrhythmia, neurotoxicity in nonclinical studies, and uncertainty regarding an appropriate starting dose for humans. The approaches under consideration in section II are intended to address these risks to the extent possible. To accelerate development of ibogaine drug products across development programs, FDA is describing the approaches it is considering and seeking comment on each before taking any additional action, such as issuing guidance. The elements described below provide further detail of one possible approach and are consistent with the recommendations in Psychedelics Guidance. The Agency asks clinicians, researchers, prospective sponsors, patients, and the public to provide feedback.

In determining whether a proposed investigation would expose participants to an unreasonable and significant risk of illness or injury, FDA considers the seriousness of the condition, the adequacy of available therapy, and the safeguards built into the trial. FDA’s

review of any IND, including an IND supported by federal funds, remains governed by the FD&C Act and FDA's regulations, and nothing in this RFI predetermines FDA's action on any submission.

Research on Ibogaine Drug Products

While published reports suggest potential benefits of ibogaine for treatment of substance use disorders and certain psychiatric and neurologic conditions—including mood disorders, PTSD, and traumatic brain injury—ibogaine also has serious known risks. Clinical data have shown that ibogaine has serious cardiovascular risks and commonly causes substantial QTc interval prolongation, which has been associated with life-threatening ventricular arrhythmias and death. Commonly reported non-cardiac adverse events include changes in perception, impaired cognition, and impaired coordination and balance (ataxia). Published nonclinical toxicology studies in rodent and non-rodent species have reported dose-dependent neurotoxicity, ranging from tremors and ataxia at lower doses to neuronal degeneration, neuroinflammation, convulsions, and death at higher doses.

The published literature on ibogaine also has significant limitations, particularly the detail needed to characterize the investigational drug product adequately (e.g., dose, quality, purity, and potency). Most studies also lack participant-level data and reliable summary-level safety, efficacy, and pharmacokinetic data.

Uncertainty about the benefit-risk profile of ibogaine drug products and evidence limitations of studies involving ibogaine is not new. In 1993, FDA convened the Drug Abuse Advisory Committee to discuss an ibogaine IND for potential treatment of cocaine dependence, focusing specifically on whether sufficient safety data existed to allow testing of ibogaine in human volunteers (58 FR 38773, July 20, 1993). The discussion centered on the challenge of establishing a meaningful therapeutic window between efficacious and toxic doses. Committee members highlighted data on neurotoxicity, difficulties in appropriately characterizing risks to enable informed consent, the need for additional preclinical data, as well as the significant unmet need for treatments for cocaine use disorder.

The questions raised at that Advisory Committee meeting remain relevant today. However, ibogaine's association with QTc interval prolongation and torsades de pointes (TdP) was identified

after the Advisory Committee met in 1993, so the Committee did not address strategies to mitigate this particular life-threatening risk. FDA also recognizes, notwithstanding the various known risks, the seriousness of the health conditions at issue and the severity of unmet need that patients seeking ibogaine treatments face. Given this reality, FDA seeks information that might inform selection of populations and use cases for clinical research with ibogaine drug products under an IND where the potential risks may be acceptable. Through its current research funding, and based on available data supporting potential for a favorable benefit-risk assessment, HHS is prioritizing two initial populations, adults with OUD and adults with PTSD, in which the seriousness of the condition and the limits of available therapy may justify the known risks of ibogaine in a closely monitored early-phase trial conducted under an IND.

How FDA Evaluates Drugs That Prolong the QTc Interval

Some drugs delay cardiac repolarization, which manifests on the surface electrocardiogram as prolongation of the QTc interval. QTc prolongation increases the risk of TdP, a life-threatening ventricular arrhythmia. After several drugs were withdrawn from the market because of TdP between 1991 and 2003, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidance “E14 Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs” (ICH E14 guidance) (October 2005) was developed to address this critical safety risk. The ICH E14 guidance is applicable to chronically administered, single-dose, and episodically administered drugs. Potent QTc-prolonging drugs (e.g., sotalol, dofetilide) are initiated in the hospital setting and discontinued if the QTc interval exceeds 500 milliseconds (ms), the threshold above which the overwhelming majority of drug-induced TdP cases occur. Similarly, the 500 ms threshold (marked QTc prolongation) is used as a stopping criterion in drug development. This threshold for drug discontinuation is primarily intended to prevent further drug exposure outside the hospital setting and is therefore most applicable to chronically administered drugs. Ibogaine, however, is typically administered as a single dosage regimen or occasional intermittent dosing. Because TdP occurs in a minority of patients with a QTc-interval >500 msec and can be

terminated (drug infusions, direct current cardioversion, temporary transvenous pacing, etc.), it is conceivable that the benefit-risk balance of repeat ibogaine exposure could still be favorable if administered in an intensively monitored setting. Accordingly, the FDA seeks input on what data could potentially allow for repeated dosing despite known risks of TdP and corresponding established precedent for drug discontinuation among patients. FDA's preliminary thinking is that an initial trial could administer a single dose in an intensively monitored inpatient setting, as described in section II, and that data from such a trial could inform whether, and under what conditions, repeat dosing could be studied.

Experience with FDA-approved drugs may inform cardiac safety monitoring for ibogaine drug products. For example, ibutilide is an approved antiarrhythmic drug given by brief intravenous infusion to convert atrial fibrillation or atrial flutter to sinus rhythm, and it causes TdP in about 1.7 percent of patients. It should be administered by personnel trained to treat acute ventricular arrhythmias and requires continuous electrocardiographic monitoring for at least 4-hours (based on its short half-life) until the QTc-interval normalizes. Thus, while ibogaine has an active metabolite and likely would require more prolonged monitoring, the general safety monitoring approach for administration of ibutilide could be informative.

Under section 505(d) of the FD&C Act (21 U.S.C. 355(d)), for a new drug to be approved for marketing in the United States, FDA must determine that the drug is safe and effective for use under the conditions prescribed, recommended, or suggested in the product's labeling. Demonstrating effectiveness under this standard requires substantial evidence that the drug will have the effect it purports or is represented to have (see section 505(d) of the FD&C Act). Because all drugs can have adverse effects, the demonstration of safety requires a showing that the benefits of the drug outweigh its risks. Risks, such as substantial QTc prolongation, can be a basis for not approving a drug, or for placing an investigation on clinical hold, where the risk cannot feasibly be managed or outweighs the benefit, especially where the drug offers no clear advantage over available therapy and the available therapy appears to meet the needs of most patients. The benefit-risk assessment may take into consideration how serious the untreated

condition is and what benefit the drug has shown compared with existing options. Whether the risk can realistically be managed through labeling or other mechanisms is also a factor. Thus, FDA seeks input on considerations for patient safety that could help inform the Agency's evaluation of the overall benefit-risk profile of ibogaine drug products.

Other Safety Considerations for Ibogaine Drug Products

As described above, published studies in animals have reported that ibogaine can cause injury to the brain, including to the cerebellum. The 1993 Advisory Committee focused on whether a dose exists that is high enough to help patients, but low enough to avoid that injury. That question remains unresolved, and its answer depends on several issues that the published studies leave uncertain.

The most critical challenge is defining a threshold at which brain injury would be predicted to occur in humans based upon nonclinical data. If brain injury occurs only when drug exposure rises above a certain threshold, the goal would be to identify a therapeutic dose that keeps exposure below that threshold. Because neurotoxicity has been reported in several animal species, it is critical to gather nonclinical data on the blood concentrations that not only do not produce brain injury but also show no adverse effects. Comparing studies by dose alone can be misleading, because the same milligram (mg)-per-kilogram (kg) dose can result in very different blood levels depending on the animal species and how the drug is administered. FDA encourages the use of new approach methodologies in place of animal testing where appropriate.

Transient neurologic effects, particularly ataxia, are common after ibogaine administration; in one prospective study of patients with OUD who received a single 10 mg/kg dose, all participants experienced severe transient ataxia (Knuijver 2022). Whether ibogaine causes persistent neurologic or cognitive injury in humans at clinically used doses, however, has not been systematically studied, and the available reports generally lack the product characterization, exposure data, and structured follow-up needed to answer that question.

II. FDA's Initial Considerations on Trial Design for Ibogaine Drug Products

FDA welcomes INDs for ibogaine drug products and encourages sponsors to request a pre-IND meeting to discuss a specific proposed design. FDA has made

no final determination as to the characteristics that would allow a trial of an ibogaine drug product to proceed, and it must evaluate whether each IND is supported by adequate scientific justification. However, based on a thorough review of available information, FDA has developed preliminary thinking¹ on a design for an initial, open-label trial in which small groups of participants each receive a single dose of ibogaine, with the dose increasing from one group to the next. This section describes that thinking and requests comments, data, and information from interested parties to facilitate the initiation of clinical trials for ibogaine drug products. This RFI does not establish legally enforceable requirements or regulatory expectations, nor does it represent FDA's final views.

Several of the elements described below apply existing requirements and recommendations to ibogaine drug products, including the informed consent requirements of 21 CFR part 50, the QTc evaluation principles in the ICH E14 guidance and FDA's guidance entitled "E14 and S7B Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential—Questions and Answers" (E14/S7B Q&A guidance) (August 2022), the dose-selection principles in FDA's guidance on estimating the maximum safe starting dose, and the monitoring recommendations in the Psychedelics Guidance. Other elements are not derived from existing guidance and are described here for public comment. FDA will evaluate INDs on an individual basis and consider the applicability of these (and other) elements in the context of each sponsor's unique development plan. FDA will consider the comments submitted in response to this RFI and may issue new guidance or update existing guidance in accordance with 21 CFR 10.115, or take another action, as appropriate.

A. Trial Design and Dose

An initial trial could assess whether ibogaine can be given safely under close monitoring and test whether the monitoring plan works. The main goals could be to measure how the body processes ibogaine and its active metabolite, noribogaine, in terms of both pharmacokinetics (PK) and

pharmacodynamics (PD), how both ibogaine and noribogaine affect the heart, and how well participants tolerate ibogaine and noribogaine.

In initial trials, participants could be enrolled in sequential dose ascending groups, starting with an initial dose justified by the published literature and not exceeding 10 mg/kg. Within each group, participants could be dosed one at a time. A potential increase in dose for the next group could be considered after appropriate review, which may be conducted by a safety review committee (SRC), a data and safety monitoring board (DSMB), and the FDA.

CYP2D6 is the main enzyme that converts ibogaine to noribogaine, so participants could be genotyped for it, with only fast and intermediate metabolizers included, and doses adjusted if needed. Sponsors could also study whether pretreatment, such as with intravenous magnesium, reduces the magnitude of QTc-interval prolongation. The ibogaine used must be well characterized, with a certificate of analysis and the chemistry, manufacturing, and controls information required under 21 CFR 312.23(a)(7).

B. Care Setting and Monitoring

In study designs FDA is contemplating, the care setting should be an inpatient unit equipped to manage a life-threatening arrhythmia, which would likely include continuous heart rhythm monitoring, a physician-led team trained in advanced cardiac life support, a defibrillator at the bedside, drugs to treat TdP, emergency cardiac pacing, and ventilator support.

A recording before dosing (e.g., 24-hour recording) should be considered to establish each participant's baseline heart rhythm. Continuous monitoring should begin at dosing, ending when there are no abnormal rhythms and the QTc interval has returned to near its pre-dose value, which could be as long as 36 hours.

More broadly, at least two staff members should monitor each participant during the drug's acute effects, including one that is a licensed mental health professional (Psychedelics Guidance). Participants should be assessed for potential adverse events, which may include ataxia, seizures, suicidal thoughts, psychosis, and other psychiatric symptoms. Cognitive testing at baseline and repeated at intervals through 12 months after dosing may help distinguish short-term effects on cognition from lasting ones.

¹ This includes review of published literature on ibogaine, regulatory experience with drugs presenting similar safety profiles, review of information regarding ibogaine administration in settings outside the United States and other information available to the Agency, and consultation with other components of the Department.

C. Medications

Before dosing, participants should stop medications that prolong the QTc-interval, slow the heart rate, interact with CYP2D6, or raise serotonin levels. These include but are not limited to opioid agonist medications (e.g., methadone and buprenorphine), antipsychotics, antiemetics, and selective serotonin reuptake inhibitors (e.g., paroxetine, sertraline). Any medications used to treat side effects during the trial, such as antiemetics and sleep aids, should not prolong the QTc interval.

D. Study Stopping Rules

In the scenario FDA is considering, dosing should be paused for appropriate review, which may be conducted by an SRC, a DSMB, and the FDA, if any of the following occurs:

- a participant has a sustained ventricular arrhythmia or a seizure;
- a participant's QTc prolongation above 500 ms persists more than two days;
- a participant develops new suicidal thoughts or behavior after the acute effects wear off, or lasting perceptual disturbances;
- a death or serious adverse event possibly related to ibogaine occurs; or
- two or more participants in a group have severe adverse events.

E. Safety Oversight

In the trial FDA is envisioning, the SRC should include a cardiologist. The trial should also be overseen by an independent DSMB that includes a cardiologist, a neurologist, a psychiatrist, and a biostatistician. For trials enrolling participants with OUD, both bodies should include an addiction medicine physician. FDA could also request to review the trial data in certain circumstances, which may include the occurrence of an adverse event meeting the study stopping rules or prior to allowing dose escalation in a trial cohort.

F. Discharge and Follow-Up

FDA is also envisioning that the trial would have participants stay in the telemetry monitored unit for an appropriate amount of time (e.g., at least 36 hours after dosing). They should leave after meeting predetermined discharge criteria, e.g., a 48-hour 12-lead ECG without QTc prolongation. Upon physician discharge approval, the patient may be escorted home by a trusted adult.

G. Who Can Enroll

Potential participants could be adults 18 to 55 years old who have stopped

taking psychiatric medications. Likely exclusion criteria may include any of the following:

- structural cardiovascular disease, a baseline QTcF of 430 ms or greater, or abnormal heart rate or blood pressure;
- a personal or family history of arrhythmia or sudden cardiac death;
- a history of seizures, psychosis, or bipolar disorder;
- recent suicidal thoughts or behavior;
- a neurodegenerative or balance disorder;
- significant liver or kidney impairment; or
- pregnancy or breastfeeding.

Low serum potassium, calcium, or magnesium levels should be corrected before dosing.

H. Potential Study Populations

One prospective study population could include participants with moderate-to-severe PTSD for at least 6 months. For example, participants might have PTSD that has not responded to at least one adequate course of a selective serotonin reuptake inhibitor and one full course of PTSD-focused psychotherapy, with at least 12 months since the most recent course.

A second prospective study population could include participants with moderate or severe OUD. For example, participants might want to stop using opioids and have not achieved sustained remission in the years preceding study participation despite adequate treatment with an FDA-approved medication for OUD, including opioid agonist treatment, as well as multiple treatment attempts (outpatient, residential, inpatient).

I. Important Study Documents

FDA guidance documents, including two guidances for industry, "E6(R3) Good Clinical Practice" (September 2025) and "Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors" (August 2023), identify several essential documents that are fundamental to the planning, conduct, oversight, and evaluation of clinical trials. For this notice, the Agency highlights the following and requests comment on how these concepts should be applied in the context of ibogaine trials:

1. Informed consent. Participants must be given adequate information regarding the serious, potentially life-threatening risks of ibogaine drug products to provide informed consent for treatment.
2. Investigator's brochure. The investigator's brochure should provide an up-to-date summary of information

on the investigational product and clinical and nonclinical data on the ibogaine drug product. The investigator's brochure should provide sufficient information to facilitate an understanding of the rationale for the key elements of the protocol specific to the proposed use in the clinical trial (e.g., population, dosing, safety monitoring).

III. Topics for Public Input

FDA invites comment on every element described in section II. Comments are most useful if they identify the specific element addressed, state whether it should continue to be part of FDA's thinking, be modified, or if FDA should change its thinking about that element. Comments should also provide the data or clinical experience that supports that view. In addition to the preliminary thinking described above, FDA is particularly interested in comments on the following questions:

(1) General Study Design Considerations

a. Are there study populations for which a strong potential for benefit may justify the known risks of ibogaine drug products?

b. For trials enrolling participants with OUD, what approaches to discontinuing opioid agonist medications before dosing (including setting, duration, and measures to mitigate risks from loss of opioid tolerance) would best manage associated risks?

(2) Dose Selection and Escalation

a. Is a maximum dose of 10 mg/kg, reached through small, stepwise cohorts, appropriate for identifying a minimum pharmacologically active dose and an approximate MTD? Doses ranging from 5 to 20 mg/kg have been described in published clinical reports; however, these doses lack adequate safety margins based on available nonclinical data. Should dosing be based on total body weight, lean body weight, or a target exposure? Commenters are encouraged to consider the following:

i. What animal pharmacokinetic data, if any, are available or can be produced to correlate with no observed adverse effect levels in animal studies from published literature in order to determine whether adequate safety margins exist relative to anticipated human exposures to mitigate neurotoxicity risks?

ii. What threshold for neurotoxicity can be identified from animal studies across multiple species following both single and repeated dosing, and what role noribogaine, the metabolite of

ibogaine, may be playing in contributing to or modulating such effects?

iii. Given the significant limitations of published literature on clinical investigations with ibogaine, including inadequate characterization of the drug product and dose, how can clinical experience, which may include clinical neurological assessments, cognitive testing, brain imaging, or laboratory testing, be used in conjunction with animal study findings to inform appropriate monitoring strategies that would help detect, and ideally mitigate, neurotoxicity risks in clinical trials?

(3) Safety Considerations

a. Cardiac Safety Considerations. As ibogaine may have effects that last several days, it is anticipated that a multi-day cardiac safety monitoring period involving inpatient observation may be required. Potential safety monitoring requirements may include but are not limited to: (i) continuous cardiac rhythm monitoring; (ii) direct access to cardiac resuscitation; (iii) duration of electrocardiographic monitoring, given that ibogaine and its metabolite, noribogaine, are cleared slowly; and (iv) managing QTc prolongation when the full dose has already been given. Additional considerations include:

i. Given cardiac safety requirements (e.g., continuous electrocardiogram monitoring, staff trained to provide advanced cardiac life support interventions, resuscitation equipment), what care setting (e.g., intensive care unit or hospital telemetry) and safeguards would be needed to conduct an early phase trial of an ibogaine drug product in the United States?

ii. How should QTc prolongation be managed for a drug given as a single dose, and what potential pre-treatment to mitigate QTc prolongation and monitoring measures might inform dosing?

iii. What study design would best quantify and distinguish the effects on QTc interval change from baseline of ibogaine alone and ibogaine administered with pre-treatment with magnesium or other products intended to minimize delayed repolarization?

iv. What upper pre-treatment QTc threshold as an exclusion criterion for enrollment (e.g., greater than 430 ms) would best minimize the proportion of patients who experience marked QTc prolongation of greater than 500 ms?

v. What participant-level and study-wide stopping rules would best mitigate cardiac arrhythmia risks?

vi. What enrollment criteria would best minimize risk of cardiac arrhythmia in early-stage trials based on the known

risk factors for TdP (e.g., low serum potassium, calcium, or magnesium, bradycardia, structural heart disease, other QTc-prolonging medications, a personal or family history suggesting congenital long QT syndrome, and populations with known susceptibility to arrhythmia, including women)?

b. Central Nervous System Safety Considerations. Potential safety monitoring requirements may include but are not limited to: (i) monitoring for seizures and cerebellar abnormalities, such as ataxia; (ii) precautions to minimize risk of falls; (iii) assessment of the duration and persistence of neurologic and cognitive effects; and (iv) criteria for safe discharge.

i. What clinical safety outcomes or assessments are needed to inform acute neurologic and cognitive risks?

ii. What duration of follow-up and assessments are needed to characterize long-term neurologic and cognitive sequelae to inform benefit-risk assessment?

(4) Ethical and Oversight Considerations

a. What informed consent information would ensure prospective research participants understand the serious, potentially life-threatening risks of ibogaine drug products?

b. What factors might DSMBs and Institutional Review Boards need to consider?

c. What would make data from treatment settings outside the United States useful in designing a trial, including the individual-level pharmacokinetic, electrocardiographic, and product information that would be needed to interpret it?

FDA is not seeking comments on the following topics: (1) the safety or effectiveness of any specific ibogaine drug product, or the merits of any pending or anticipated application before the Agency; (2) the scheduling status of ibogaine drug products under the Controlled Substances Act, which is addressed through separate statutory processes; (3) the legalization or decriminalization of psychedelic substances, or the merits of state or local programs authorizing their use, although FDA welcomes input on data collection from such programs as described above; (4) religious, ceremonial, or personal (non-medical) use of psychedelic substances; or (5) individual disputes, enforcement matters, or complaints regarding specific practitioners or entities. Comments addressing these topics may not be considered.

FDA will review the comments received and expects to reflect them, as appropriate, in regulatory activities,

including review of protocols for federally supported and other clinical trials of ibogaine drug products and future guidance on their development.

IV. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff (see **ADDRESSES**) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at <https://www.regulations.gov>. References without asterisks are not on public display at <https://www.regulations.gov> because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. Although FDA verified the website addresses in this document, please note that websites are subject to change over time.

1. Alper, K.R., Stajić, M., and J.R. Gill, "Fatalities temporally associated with the ingestion of ibogaine," *J. Forensic Sci.*, 57(2):398–412 (2012), available at doi:10.1111/j.1556-4029.2011.02008.x.
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Hallak, J.E.C., and R.G. Dos Santos, "Identifying setting factors associated with improved ibogaine safety: a systematic review of clinical studies," *Eur. Arch. Psychiatry Clin. Neurosci.*, 273(7):1527–1542 (2023), available at doi:10.1007/s00406-023-01590-1.

9. * U.S. Food and Drug Administration guidance for industry "E14 and S7B Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential—Questions and Answers" (August 2022), available at <https://www.fda.gov/media/161198/download>.
10. * U.S. Food and Drug Administration guidance for industry "Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors" (August 2023), available at <https://www.fda.gov/media/88915/download>.
11. * U.S. Food and Drug Administration guidance for industry "E6(R3) Good Clinical Practice" (September 2025), available at <https://www.fda.gov/media/169090/download>.
12. * U.S. Food and Drug Administration guidance for industry "Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers" (July 2005), available at <https://www.fda.gov/media/72309/download>.
11. * U.S. Food and Drug Administration guidance for industry "QTc Information in Human Prescription Drug and Biological Product Labeling" (December 2025), available at <https://www.fda.gov/media/170814/download>.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2026–20427 Filed 10–5–26; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2026–N–4291]

Teva Pharmaceuticals USA, Inc., et al.; Withdrawal of Approval of 15 Abbreviated New Drug Applications; Correction

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; correction.

SUMMARY: The Food and Drug Administration (FDA) is correcting a notice that appeared in the **Federal Register** on May 7, 2026. The document announced the withdrawal of approval of 15 abbreviated new drug applications (ANDAs) from multiple applicants, withdrawn as of June 8, 2026. The document indicated that FDA was withdrawing approval of ANDA 210285 for dimethyl fumarate delayed-release

capsule, 120 milligrams (mg) and 240 mg, held by Upsher-Smith Laboratories, LLC., U.S. Agent for Sawai USA, Inc., 6701 Evenstad Dr. N, Suite 300, Maple Grove, MN 55369. Before FDA withdrew the approval of this ANDA, Upsher-Smith Laboratories, LLC., U.S. Agent for Sawai USA, Inc., informed FDA that they did not want the approval of the ANDA withdrawn. Because Upsher-Smith Laboratories, LLC., U.S. Agent for Sawai USA, Inc., timely requested that approval of the ANDA not be withdrawn, the approval is still in effect. This notice removes the entry for ANDA 210285.

FOR FURTHER INFORMATION CONTACT:

Martha Nguyen, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 1676, Silver Spring, MD 20993–0002, 301–796–3471, Martha.Nguyen@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of Thursday, May 7, 2026 (91 FR 24879), appearing on page 24879 in FR Doc. 2026–09012, the following correction is made:

On page 24879, in the table, the entry for ANDA 210285 is removed.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2026–20460 Filed 10–5–26; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2026–N–11259]

Issuance of Priority Review Voucher; Rare Pediatric Disease Product; FAYUVI (rebisufligene etisparvovec-hopf)

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the issuance of a priority review voucher to the sponsor of a rare pediatric disease product application. The Federal Food, Drug, and Cosmetic Act (FD&C Act) authorizes FDA to award priority review vouchers to sponsors of approved rare pediatric disease product applications that meet certain criteria. FDA is required to publish notice of the award of the priority review voucher. FDA has determined that FAYUVI (rebisufligene etisparvovec-hopf), approved on September 17, 2026, manufactured by Ultragenyx Pharmaceutical Inc., meets

the criteria for a priority review voucher.

FOR FURTHER INFORMATION CONTACT:

Myrna Hanna, Center for Biologics Evaluation and Research, Food and Drug Administration, industry.biologics@fda.hhs.gov, 240–402–7911.

SUPPLEMENTARY INFORMATION: FDA is announcing the issuance of a priority review voucher to the sponsor of an approved rare pediatric disease product application. Under section 529 of the FD&C Act (21 U.S.C. 360ff), FDA will award priority review vouchers to sponsors of approved rare pediatric disease product applications that meet certain criteria. FDA has determined that FAYUVI (rebisufligene etisparvovec-hopf), manufactured by Ultragenyx Pharmaceutical Inc., meets the criteria for a priority review voucher. FAYUVI (rebisufligene etisparvovec-hopf) is an adeno-associated virus (AAV) vector-based gene therapy indicated for the treatment of neurologic manifestations of mucopolysaccharidosis type IIIA (MPS IIIA, Sanfilippo syndrome type A) in pediatric patients with preserved neurodevelopmental function.

For further information about the Rare Pediatric Disease Priority Review Voucher Program and for a link to the full text of section 529 of the FD&C Act, go to <https://www.fda.gov/industry/developing-products-rare-diseases-conditions/rare-pediatric-disease-rpd-designation-and-voucher-programs>. For further information about FAYUVI (rebisufligene etisparvovec-hopf), go to the Center for Biologics Evaluation and Research's Approved Cellular and Gene Therapy Products website at <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products>.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2026–20434 Filed 10–5–26; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Meeting

Pursuant to section 1009 of the Federal Advisory Committee Act, as amended, notice is hereby given of a meeting of the President's Cancer Panel.