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Tony Evers, Governor
Dan Hereth, Secretary

HYBRID (IN-PERSON/VIRTUAL)
CONTROLLED SUBSTANCES BOARD
Room N208, 4822 Madison Yards Way, 2nd Floor, Madison
Contact: Tom Ryan (608) 266-2112
March 10, 2023

The following agenda describes the issues that the Board plans to consider at the meeting. At the time of the meeting, items may be removed from the agenda. Please consult the meeting minutes for a description of the actions and deliberations of the Board. Be advised that board members may attend meetings designated as "Hybrid" in-person or virtually.

AGENDA

9:30 A.M.
OR IMMEDIATELY FOLLOWING THE REFERRAL CRITERIA WORK GROUP MEETING

OPEN SESSION – CALL TO ORDER – ROLL CALL

A. Adoption of Agenda (1-3)

B. Approval of Minutes January 13, 2023 (4-8)

C. Reminders: Conflicts of Interests, Scheduling Concerns

D. Introductions, Announcements and Recognition

E. Administrative Matters – Discussion and Consideration

1) Department, Staff, and Board Updates
2) Board Members – Term Expiration Dates
   a. Alton, Troy
   b. Barman, Subhadeep – 5/1/2019
   c. Bellay, Yvonne
   d. Bloom, Alan – 5/1/2020
   e. Englebert, Doug
   f. Koresch, Sandy
   g. Weinman, Robert
   h. Weitekamp, John
   i. Yerby, Lemuel
3) Alternate Members
   a. Bistan, Matthew
   b. Ferguson, Kris
   c. McFarland, Rosalyn
   d. Parish, Michael
   e. Wasserman, Sheldon
   f. Zentz, Emily

F. Legislature Agenda Request: Status of Kratom – Discussion and Consideration (9-32)

G. Administrative Rule Matters – Discussion and Consideration

Review of Draft Biennial Report under S. 227.29, Wis. Stats (Added via Addendum)

1) Possible Affirmative Action Order: Excluding Fenfluramine from Schedule IV **(33-38)**
2) Possible Rulemaking Project for CSB 4 **(39-46)**
3) Pending and Possible Rulemaking Projects
    a. Rule Projects Chart **(47-48)**

H. Prescription Drug Monitoring Program (PDMP) Updates – Discussion and Consideration

1) WI ePDMP Operations
    a. Recent and Upcoming Releases **(49-52)**
    b. Status of Grant Projects:
        a. FY 2020 Harold Rogers Prescription Drug Monitoring Program
        b. FY 2021 Harold Rogers Prescription Drug Monitoring Program
        c. FY 2022 Harold Rogers Prescription Drug Monitoring Program
    c. EHR Integration Status **(53-55)**
2) WI ePDMP Outreach **(56)**

I. Board Member Reports – Discussion and Consideration

1) Medical Examining Board
2) Dentistry Examining Board
3) Board of Nursing
4) Pharmacy Examining Board

J. Liaison Reports

K. Report from the Referral Criteria Work Group – Discussion and Consideration

L. Deliberation on Special Use Authorizations – Discussion and Consideration

M. Discussion and Consideration of Items Received After Preparation of the Agenda

1) Introductions, Announcements, and Recognition
2) Administrative Matters
3) Election of Officers
4) Appointment of Liaisons and Alternates
5) Delegation of Authorities
6) Informational Items
7) Division of Legal Services and Compliance (DLSC) Matters
8) Education and Examination Matters
9) Credentialing Matters
10) Practice Matters
11) Legislative and Administrative Rule Matters
12) Liaison Reports
13) Public Health Emergencies
14) Appearances from Requests Received or Renewed
15) Speaking Engagements, Travel, or Public Relations Requests, and Reports
16) Consulting with Legal Counsel

N. Public Comments

CONVENE TO CLOSED SESSION to deliberate on cases following hearing (s. 19.85(1)(a), Stats.); to consider licensure or certification of individuals (s. 19.85(1)(b), Stats.); to consider individual histories or disciplinary data (s. 19.85(1)(f), Stats.); and to confer with legal counsel (s. 19.85(1)(g), Stats.).

O. Deliberation on Special Use Authorizations – Discussion and Consideration

P. Consulting with Legal Counsel

RECONVENE TO OPEN SESSION IMMEDIATELY FOLLOWING CLOSED SESSION

Q. Vote on Items Considered or Deliberated Upon in Closed Session if Voting is Appropriate

R. Open Session Items Noticed Above Not Completed in the Initial Open Session

ADJOURNMENT

NEXT MEETING: MAY 12, 2023

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MEETINGS AND HEARINGS ARE OPEN TO THE PUBLIC, AND MAY BE CANCELLED WITHOUT NOTICE.

Times listed for meeting items are approximate and depend on the length of discussion and voting. All meetings are held virtually unless otherwise indicated. In-person meetings are typically conducted at 4822 Madison Yards Way, Madison, Wisconsin, unless an alternative location is listed on the meeting notice. In order to confirm a meeting or to request a complete copy of the board's agenda, please visit the Department website at https:\\dsps.wi.gov. The board may also consider materials or items filed after the transmission of this notice. Times listed for the commencement of disciplinary hearings may be changed by the examiner for the convenience of the parties. Requests for interpreters for the hard of hearing, or other accommodations, are considered upon request by contacting the Affirmative Action Officer, or the Meeting Staff at 608-267-7213.

VIRTUAL/TELECONFERENCE
CONTROLLED SUBSTANCES BOARD
MEETING MINUTES
JANUARY 13, 2023

PRESENT: Troy Alton, Subhadeep Barman, Yvonne Bellay, Alan Bloom, Doug Englebert, Michael Parish *(excused at 10:55 a.m.)*, John Weitekamp

EXCUSED: Kris Ferguson, Sandy Koresch, Robert Weinman

STAFF: Adam Barr, Executive Director; Jameson Whitney, Legal Counsel; Nilajah Hardin, Administrative Rules Coordinator; Katlin Schwartz, Bureau Assistant; and other DSPS Staff

Michael Parish served as the Medical Examining Board Representative at this meeting.

CALL TO ORDER

Doug Englebert, Chairperson, called the meeting to order at 9:32 a.m. A quorum was confirmed with seven (7) members present.

ADOPTION OF AGENDA

MOTION: Alan Bloom moved, seconded by Michael Parish, to adopt the Agenda as published. Motion carried unanimously.

APPROVAL OF MINUTES OF NOVEMBER 11, 2022

MOTION: Troy Alton moved, seconded by John Weitekamp, to adopt the Minutes of November 11, 2022 as published. Motion carried unanimously.

LEGISLATURE AGENDA REQUEST: STATUS OF KRATOM

MOTION: Subhadeep Barman moved, seconded by Yvonne Bellay, to carry over the topic of the Scheduling of Kratom until the Boards next meeting in March of 2023. Motion carried unanimously.

ADMINISTRATIVE RULE MATTERS

Preliminary Rule Draft

MOTION: Michael Parish moved, seconded by Subhadeep Barman, to approve the preliminary rule draft for the following rules for posting for economic impact comments and submission to the Clearinghouse:

- CSB 2.92, Relating to Scheduling 38 Anabolic Steroids
- CSB 2.93, Relating to Scheduling Daridorexant
- CSB 2.94, Relating to Scheduling 7 Synthetic Benzimidazole-Opioids
- CSB 2.95, Relating to Scheduling Ganaxolone

Motion carried unanimously.

Affirmative Action Order

CSB 2.96, Relating to Scheduling Amineptine

MOTION: Alan Bloom moved, seconded by Yvonne Bellay, to schedule by affirmative action Amineptine as a schedule I controlled substance. The order shall take effect upon publication in the Administrative Register. Motion carried unanimously.

CSB 2.97, Relating to Scheduling Zipeprol

MOTION: John Weitekamp moved, seconded by Michael Parish, to schedule by affirmative action Zipeprol as a schedule I controlled substance. The order shall take effect upon publication in the Administrative Register. Motion carried unanimously.

CSB 2.98, Relating to Scheduling Excluding [^{18}F] FP-CIT

MOTION: Alan Bloom moved, seconded by Doug Englebert, to exclude by affirmative action [^{18} F] FP-CIT as a schedule II controlled substance. The order shall take effect upon publication in the Administrative Register. Motion carried unanimously.

CSB 2.99, Relating to Scheduling Mesocarb

MOTION: Michael Parish moved, seconded by Troy Alton, to schedule by affirmative action Mesocarb as a schedule I controlled substance. The order shall take effect upon publication in the Administrative Register. Motion carried unanimously.

CSB 2, Relating to Scheduling Methipropamine

MOTION: Yvonne Bellay moved, seconded by Troy Alton, to schedule by affirmative action Methiopropamine as a schedule I controlled substance. The order shall take effect upon publication in the Administrative Register. Motion carried unanimously.

Michael Parish was excused at 10:55 a.m.

Drafting Proposals

CSB 4, Relating to National Provider Identifier Requirements

MOTION: Alan Bloom moved, seconded by Doug Englebert, to designate Subhadeep Barman and John Weitekamp to serve as liaisons to DSPS staff for drafting CSB 4, relating to National Provider Identifier Requirement. Motion carried unanimously.

ADMINISTRATIVE MATTERS

Election of Officers

Slate of Officers

NOMINATION: Troy Alton nominated the 2022 slate of officers to continue in 2023. All officers accepted their nominations.

Adam Barr, Executive Director, called for nominations three (3) times.

The Slate of Officers was elected by unanimous voice vote.

ELECTION RESULTS	
Chairperson	Doug Englebert
Vice Chairperson	Alan Bloom
Secretary	Yvonne Bellay

Appointment of Liaison and Alternates

LIAISON APPOINTMENTS	
Special Use Authorization (SUA) Liaison(s)	Alan Bloom, Yvonne Bellay *Alternate:* Doug Englebert
PDMP Liaison(s)	Subhadeep Barman *Alternates:* Kris Ferguson, John Weitekamp-Pharmacy Issues, Doug Englebert
Legislative Liaison(s)	Doug Englebert *Alternates:* John Weitekamp
SCAODA Representative	Subhadeep Barman *Alternate:* Kris Ferguson
Referral Criteria Workgroup	Doug Englebert, John Weitekamp, Subhadeep, Barman, Robert Weinamn

Delegation of Authorities

Document Signature Delegations

MOTION: Alan Bloom moved, seconded by Subhadeep Barman, to delegate authority to the Chairperson (or in absence of the Chairperson, the highest-ranking officer

or longest serving board member in that succession) to sign documents on behalf of the Board in order to carry out its duties. Motion carried unanimously.

MOTION: John Weitekamp moved, seconded by Subhadeep Barman, in order to carry out duties of the Board, the Chairperson (or in absence of the Chairperson, the highest-ranking officer or longest serving board member in that succession) has the ability to delegate signature authority for purposes of facilitating the completion of assignments during or between meetings. The members of the Board hereby delegate to the Executive Director or DPD Division Administrator, the authority to sign on behalf of a board member as necessary. Motion carried unanimously.

Delegated Authority for Urgent Matters

MOTION: Alan Bloom moved, seconded by Troy Alton, that in order to facilitate the completion of urgent matters between meetings, the Board delegates its authority to the Chairperson (or, in the absence of the Chairperson, the highest-ranking officer or longest serving board member in that succession), to appoint liaisons to the Department to act in urgent matters. Motion carried unanimously.

Special Use Authorization Liaison(s) Delegation

MOTION: Troy Alton moved, seconded by John Weitekamp, to authorize the SUA Liaison(s) to review and make approval decisions regarding SUA applications and approve required training or credentialing on behalf of the Board. Furthermore, the Board authorizes DSPS staff to sign SUA permits on behalf of the Board. Motion carried unanimously.

MOTION: Doug Englebert moved, seconded by Troy Alton, to authorize the SUA Liaison(s) to make all decisions related to Special Use Authorizations. Motion carried unanimously.

Authorization for DSPS to Provide Board Member Contact Information to National Regulatory Related Bodies

MOTION: Doug Englebert moved, seconded by Alan Bloom, to authorize the Department staff to provide national regulatory related bodies with all board member contact information that the Department retains on file. Motion carried unanimously.

Legislative Liaison Delegation

MOTION: Yvonne Bellay moved, seconded by Subhadeep Barman, to delegate authority to the Legislative Liaisons to speak on behalf of the Board regarding legislative matters. Motion carried unanimously.

SCAODA Representative Delegation

MOTION: Yvonne Bellay moved, seconded by Doug Englebert, to authorize the SCAODA representative to vote on behalf of the Board at the State Council on Alcohol and Other Drug Abuse meetings. Motion carried unanimously.

PDMP Liaison(s) Delegation

MOTION: Doug Englebert moved, seconded by Troy Alton, to authorize PDMP Liaison(s) to make individual decisions on behalf of the Board when waiting for a Board meeting would unreasonably delay the development, testing, deployment, or operation of the PDMP. The Board also grants the PDMP liaison the authority to suspend access to the PDMP pursuant to CSB § 4.09(3). Motion carried unanimously.

Referral Criteria Workgroup Membership Delegation

MOTION: John Weitekamp moved, seconded by Doug Englebert, that in order to facilitate the completion of its duties between meetings, the Board delegates authority to the Chairperson (or, in the absence of the Chairperson, the highest-ranking officer or longest serving board member in that succession) to appoint members to the Referral Criteria Workgroup between meetings as necessary. Motion carried unanimously.

ADJOURNMENT

MOTION: John Weitekamp moved, seconded by Subhadeep Barman, to adjourn the meeting. Motion carried unanimously.

The meeting adjourned at 11:27 a.m.

Memorandum to Wisconsin Department of Public Safety
and Professional Services, Controlled Substances Board (CSB)

February 5, 2023

To:
Controlled Substances Board
Wisconsin Department of Public Safety and Professional Services
PO Box 8366
Madison, WI 53708-836
Sent via email: dsps@wi.gov

Attention:
Doug Englebert, Chairperson, CSB, Department of Health Services Designated Member; Alan Bloom, Ph.D., Vice Chairperson, CSB, Pharmacologist; Yvonne Bellay, Secretary, DATCP Designated Member; Troy A Alton, Dentistry Board Representative; Subhadeep Barman, Psychiatrist; Kris Ferguson, Medical Board Representative; Sandy Koresch, Attorney General Designee; Robert W. Weinman, Board of Nursing Representative; John G. Weitekamp, Pharmacy Board Representative
And others interested in the United States (US) Controlled Substances Act (CSA) Eight Factor Analysis (8FA) that was codified in the US CSA and adopted by Wisconsin

From:
Jack Henningfield, PhD, Vice President, Research, Health Policy and Abuse Liability, Pinney Associates, Inc. and Professor, Adjunct, Behavioral Biology, Johns Hopkins University School of Medicine
Michael Klein, PhD, Principal, Controlled Substance Scientific Solutions, LLC.
Frank Sapienza, Partner, The Drug and Chemical Advisory Group, LLC.
Frank Vocci, PhD, President & Senior Research Scientist, Friends Research Institute

Regarding: Consideration of factors 2 and 3 from the Eight Factor Analysis (8FA) of the Controlled Substances Act (CSA) in the development of scheduling recommendations including rescheduling and removal from control

Background: We are writing because we understand that on January 13, 2023**,** the Wisconsin CSB considered each of the eight factors of the CSA (see list at the end of this memo) to determine if those factors supported scheduling of the kratom alkaloids mitragynine and 7-hydroxymitragynine (a "yes" vote) or did not support scheduling (a "no" vote). We understand that the CSB voted "yes" that factors 2 and 3 supported scheduling and "no" that the remaining factors did not support scheduling. We understand that there has been discussion as to how such a mixed vote is addressed in scheduling recommendations in general and the typical role of factors 2 and 3 in CSA scheduling recommendations.

We understand that in 2013 the kratom alkaloids, mitragynine and 7-hydroxymitragyine, were placed in the Wisconsin CSA by an act of the legislature to more broadly control synthetic stimulants and cannabinoids, along with other substances, and not on the basis of an 8FA or

recommendation by the Wisconsin CSB. The CSB has recently been asked for its recommendation as to whether these kratom alkaloids should be removed from the CSA as the state legislature is considering legislation to allow consumer sale of kratom with regulatory oversight to ensure product purity, prohibit sales to minors, registration of products and vendors, and prohibit adulteration with unsafe substances or boosted levels of naturally occurring alkaloids.

This memorandum does not take a position on the legislation, on the abuse potential of kratom, or whether these alkaloids should be removed from control or the potential regulatory framework. Rather we are writing to clarify how such mixed votes are routinely approached in federal scheduling, including the many scheduling recommendations that we have been involved in during and since our respective federal agency positions. Our opinions do not represent any agency of the US federal government. Finally, we understand that state scheduling actions do not necessarily follow federal (i.e., Drug Enforcement Administration [DEA]) or international (i.e., World Health Organization Expert Committee on Drug Dependence and United Nations Commission on Narcotic Drugs) precedents, actions and recommendations.

Overview of the Eight Factor Analysis

This discussion follows FDA's 2017 Guidance for Industry, Assessment of Abuse Potential of Drugs (see https://www.fda.gov/media/116739/download), the legislative history of the CSA (specifically House Report 91-1444), and our own experience in 8FA guided scheduling recommendations.

The FDA Guidance provides an overview of the types of preclinical and clinical study evidence that are considered in scheduling recommendations and makes clear that abuse potential assessment is "conducted as a component of its safety evaluation." Similar to FDA, in the present memorandum the term "abuse related" will be used to designate nonclinical and clinical information that is related to the assessment of abuse potential of a new drug.

Section 21 U.S.C. 811(b) of the CSA, describes the eight factors but provides little detail as to what specific studies are used to inform each factor or how the final scheduling decision is made.

The evidence for many central nervous system (CNS) active substances, scheduled and not scheduled, is often mixed across factors, and it may be difficult to prove that a substance or product is without any abuse-related effects and has no abuse potential. In this context, the 8FA is used to provide a guide as to whether abuse-related risks and public health concerns are of sufficient concern to warrant scheduling, and, if scheduling is recommended for an approved medicine, which of the four schedules applicable to approved medicines (schedules II -V) is most appropriate. For substances and products that are not approved for therapeutic use and are considered of sufficient abuse-related risks to warrant scheduling, Schedule I is the only option. It is important to note that 21 U.S.C. 812, in addition to describing the eight factors, provides the criteria which must be met to place a drug or other substance into one of the five schedules. The criteria for Schedule I "no currently accepted medical use (e.g., FDA approval) and a high potential for abuse." Thus, Schedule I is the only option for substances that are not approved for medical use.

8FA-informed scheduling recommendations. Scheduling is a relative and comparative process, and not an absolute quantitative process, that considers the eight factors taken together and other considerations. Thus, there are many recreationally used substances that are known to have abuse potential, cause dependence and withdrawal in some people, and meet criteria for scheduling according to 8FAs but are not scheduled. Considerations leading to these decisions may have been because of a long history of consumer access and use that was sufficiently reassuring not to place the substance in the CSA, and determination that approaches such education, warnings, minimum age of purchase requirements and/or other regulatory approaches were more appropriate (e.g., as was concluded with respect to nicotine gum and dextromethorphan products). Because of the regulatory controls that are imposed by scheduling, the CSA specifies that only substances with "substantial" evidence of abuse potential "such as to warrant control" should be scheduled. (21 U.S.C.811(b).

Examples of nonscheduled substances that have abuse potential include caffeine and other methylxanthines, most antihistamines, pseudoephedrine, dextromethorphan, nicotine gum, many antidepressants, anticholinergics, and anti-diarrheals, in addition to widely available 'volatile substances', gases or chemicals that evaporate at room temperature, including various types of glue, gasoline, and nitrous oxide which is found in whipped cream making cartridges and dispensers and other propellant canisters. In some of these cases, states may impose public safety controls other than CSA scheduling such as minimum age of purchase, behind the counter access, and/or registration of retailers.

Thus, the question is not always *could* the substance or product be scheduled but rather *should* it be scheduled; and, if there are abuse-related and other safety concerns, are there other more appropriate and possibly more effective approaches to minimize risks than scheduling given consideration of all eight factors of the CSA and other considerations.

A commonly used term of art is whether the evidence indicates *meaningful* abuse potential based on clinical and nonclinical studies, chemistry, and pharmacology (factors 1, 2, 3 and 7). Only factors 1 and 7 specifically address whether there is actual or relative evidence of abuse potential (factor 1) and the level of "psychic or physiological dependence liability" (factor 7). Factors 4, 5 and 6 address whether there is evidence that the substance is known or expected to pose public or imminent threat to public health that outweighs the benefits of not being scheduled.

Factor 8 is the only factor that provides a basis for determining if a drug will be scheduled in the absence of any other factor if the substance is an immediate precursor of a substance that is already controlled. Control may also occur as a factual or administrative determination based on prior scheduling actions and chemical structures and synthesis of the substances regardless of scientific study outcomes. Substances that are derivatives of opium or thebaine are scheduled regardless of any other evidence. Thus, novel forms of naloxone (e.g., Naloxegol) were Schedule II during development and could only be removed from control following evaluation of the eight factors to determine if an exemption from scheduling was warranted.

The place of factors 2 and 3 in 8FAs and scheduling recommendations. The legislative history of the CSA (H.R. 91-1444) notes that Factor (1) – a substance's actual or relative potential for abuse – is the 'key' criterion for determining whether to control a substance.

What is the role of factors 2 and 3 in scheduling if they are not in themselves determinative of abuse-related effects such as reinforcement in animal studies, etc.? In practice, they contribute to the overall 8FA by ensuring that scientific evidence concerning mechanisms of action and receptor binding profiles are evaluated, and ensuring that the latest state of the science addressing its pharmacology, pharmacokinetic studies, and ease of chemical synthesis have been considered.

We are aware that there has been extensive recent study of kratom, largely funded by the National Institute on Drug Abuse (NIDA), that addressed the various pharmacological mechanisms of action, receptor binding profiles of kratom alkaloids and metabolites and more extensively addressed the long-understood fact that kratom and its various alkaloids have pharmacological effects. In many cases involving new chemical entities, factors 2 and 3 provide an understanding as to why substances with similar effects on some measures (e.g., providing relief of anxiety, depression, fatigue, and pain) may differ from one another on other measures and effects (e.g., abuse-related effects such as reward and euphoria, respiratory depression, and withdrawal). This is evident across a broad range of scheduled medicines and nonscheduled substances including natural and herbal products as well as FDA-approved medicinal products to manage pain, anxiety, depression, sleep, etc.

Thus, addressing questions related to factors 2 & 3 contributes to understanding the overall level of abuse potential and other risks (factor 3) but are not determinative of control decisions. Nor do those factors necessarily provide guidance as to the most appropriate regulatory and policy approach to address risks, including abuse related risks that may be real, but may not warrant CSA scheduling.

Rather, it is the totality of the eight factors that must be jointly considered to determine if a substance or product warrants CSA control, along with other considerations, to determine risk mitigation approaches other than CSA scheduling might be more effective and appropriate to address concerns.

We will be pleased to offer any additional assistance on this matter in writing or by teleconference.

Sincerely,

DocuSigned by:
Jack Henningfield
9B877158BD7C4BC...
Jack E. Henningfield, PhD
Vice President, Research, Health Policy and Abuse Liability, Pinney Associates, Inc.

DocuSigned by:
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Frank Sapienza, Partner, The Drug and Chemical Advisory Group, LLC.

DocuSigned by:
Frank Vocci
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Frank Vocci, PhD, President & Senior Research Scientist, Friends Research Institute

Correspondence may be sent to Jack Henningfield at jhenning@pinneyassociates.com.

Basis for expertise and disclosure. Each of us has several decades of experience in performing 8FAs for our former respective agencies. JH headed the Clinical Pharmacology as well as the Biology of Dependence and Abuse Potential Assessment section of NIDA that was created in 1985 to address NIDA's then authorized role in CSA scheduling. MK was involved in scheduling at DEA before he transferred to FDA where he headed FDA's Controlled Substance Staff, which performs FDA's 8FAs and develops FDA's scheduling recommendations. FS had several decades of scheduling experience at DEA including heading DEA's Drug and Chemical Evaluation Section in DEA's Office of Diversion Control. FV had several combined years of experience at FDA and then NIDA which included contributing to NIDA's advisory role in drug scheduling. All of us have given lectures, participated in panels, published peer review papers related to drug scheduling, and advise pharmaceutical developers in abuse potential assessments and 8FAs and scheduling recommendations.

The eight factors of the CSA that enable a medical and scientific analysis that are determinative of control of the drug under the CSA (21 U.S.C. 811(c)):

1. Its actual or relative potential for abuse.
2. Scientific evidence of its pharmacological effect, if known.
3. The state of current scientific knowledge regarding the drug or other substance.
4. Its history and current pattern of abuse.
5. The scope, duration, and significance of abuse.
6. What, if any, risk there is to the public health
7. Its psychic or physiological dependence liability.
8. Whether the substance is an immediate precursor of a substance already controlled

S8 - Mitragynine-only deaths in North Carolina

Justin Brower*, NMS Labs, Horsham, PA.

Introduction: Mitragynine is the primary active alkaloid present in Kratom, the herbal substance prepared from the leaves of the tropical evergreen tree *Mitragyna speciosa*, and it is being seen more frequently in postmortem cases. Pharmacologically, mitragynine is an opioid agonist with an activity of approximately one-fourth that of morphine, but at low doses exhibits stimulant-like properties. Its opioid activity is what fuels its recreational use, but it is also used to combat pain and prevent opioid withdrawal symptoms. Contributing to Kratom's popularity are vocal advocacy groups promoting its use and lobbying to keep it legal in the United States. These organizations often claim that no deaths can be attributed to Kratom because of the presence of other drugs. This is bolstered by the fact that very few mitragynine-only overdose deaths have been reported in the toxicology literature.

Objectives: This presentation will highlight 12 mitragynine-only overdose deaths from the statewide NC Office of the Chief Medical Examiner over a five-year period. These will be compared to similar mitragynine cases containing non-opioid prescription or OTC drugs in therapeutic concentrations and cases involving illicit drugs and opioids. Additionally, postmortem considerations will be discussed when presented with mitragynine-only cases.

Methods: Mitragynine was screened by a validated multi-analyte targeted assay using a high-resolution, accurate mass Thermo Orbitrap LC-MS/MS. Confirmation and quantitation were achieved by either NMS Labs or an in-house validated LC-MS/MS method. Confirmation is not reflexive, and the decision to confirm, and report either qualitatively or quantitatively, was based upon case history and other toxicological findings.

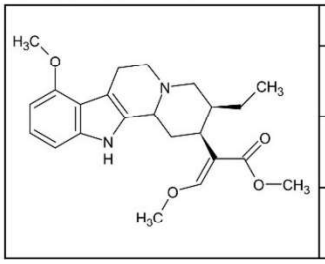
PLATFORM

Mitragynine results from a five-year period, from June 2017 through June 2022, were pulled from the toxicology laboratory's LIMS and separated into three bins: qualitative, less than 0.50 mg/L, and greater than or equal to 0.50 mg/L. Considering the pharmacological profile of mitragynine, and knowledge from a previously published analysis of over 1,000 blood specimens, data from the latter bin was used in the investigation of mitragynine-only deaths.

Results: In the five-year period, and from approximately 20,000 cases, the laboratory reported blood mitragynine in 396 cases. The breakdown of those cases was 242 reported qualitatively as "present," 90 less than 0.50 mg/L, and 64 greater than or equal to 0.50 mg/L.

From the 64 cases, 12 were mitragynine-only deaths with no other drugs or alcohol reported, 11 cases contained therapeutic concentrations of non-opioid prescription or OTC drugs, and 41 contained illicit drugs or opioids. The emphasis of this presentation is on the mitragynine-only cases, but a comparison with the other classes will be presented.

Table: Postmortem cases from NC OCME with blood mitragynine concentrations ≥0.50 mg/L.



Mitragynine	n	Mean (mg/L)	Range (mg/L)	Frequent other drugs
Mitragynine	12	2.36	0.73 – 5.9	---
+ prescription drugs	11	3.59	1.7 – 6.8	Gabapentin, SSRIs
+ illicit drugs/opioids	41	1.03	0.50 – 3.8	Fentanyl, Cocaine

Conclusion: The idea that Kratom is completely safe because it is natural and has centuries of ethnobotanical use is demonstrably false. Of the twelve mitragynine-only cases presented, all had a cause of death of mitragynine toxicity. In the 11 cases that included non-opioid prescription or OTC drugs, all but one included mitragynine in the cause of death. The remaining 41 cases involving illicit drugs, opioids, or ethanol, were most frequently listed as multi-drug toxicity.

Mitragynine-only fatalities exist, and to avoid missing these causes of death, laboratories should include mitragynine in their screening methods with a plan for confirmation and quantitation.

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Special Issue

OXFORD

Special Issue

The Trouble With Kratom: Analytical and Interpretative Issues Involving Mitragynine

Donna M. Papsun[1,*], Ayako Chan-Hosokawa[1], Laura Friederich[2], Justin Brower[2], Kristopher Graf[1] and Barry Logan[1,3]

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Abstract

Mitragynine is the primary active alkaloid in the leaves of the tropical tree *Mitragyna speciosa*, and goes by the popular names "Kratom", biak-biak and maeng da. Mitragynine is increasingly seen in forensic toxicology casework including driving under the influence of drugs and medicolegal death investigation cases. The toxicity of mitragynine continues to be debated in the scientific community as advocates highlight its long history of use in Southeast Asia and testimonials to its benefits by present-day users, while opponents point to an increasing number of adverse events tied to mitragynine use in Western societies. Quantitative reports of mitragynine in biological specimens from forensic investigations in the literature are sparse and may be influenced by poor analyte stability and inadequate resolution of mitragynine from its diastereomers, which could lead to falsely elevated concentrations and subsequently render those reported concentrations inappropriate for comparison to a reference range. Over the course of 27 months, 1,001 blood specimens submitted to our laboratory tested positive for mitragynine using a sensitive and specific quantitative LC-MS/MS method; concentrations ranged from 5.6–29,000 ng/mL, with mean and median concentrations of 410 ± 1,124 and 130 ng/mL, respectively. Mitragynine presents an analytical challenge that requires a method that appropriately separates and identifies mitragynine itself from its isomers and other related natural products. We describe a validated analytical method and present a short series of case reports that provide examples of apparent adverse events, and the associated range of mitragynine concentrations. This type of analytical specificity is required to appropriately interpret mitragynine concentrations detected in biological specimens from forensic casework and assess its potential toxicity.

Introduction

Mitragynine is the primary alkaloid of interest from the psychoactive plant *Mitragyna speciosa*, a tree most commonly referred to as Kratom, but other names include biak-biak, ketum and maeng da (1). Kratom has a long history of use in parts of Africa and Southeast Asia, where traditional practices include chewing leaves or brewed into a tea (2). The effects of Kratom are dose dependent; low doses (1–5 g), such as those obtained from chewing leaves or in Kratom-based tea, are associated with stimulant effects, whereas Kratom powders and leaf extracts deliver higher doses (5–15 g) and are associated with opioid-like effects due to agonist activity at the μ-opioid receptor (3). Although Kratom has a history of traditional and ceremonial use in some cultures, a grassroots following has developed in Western societies due to its accessibility, lack of regulation and psychoactive

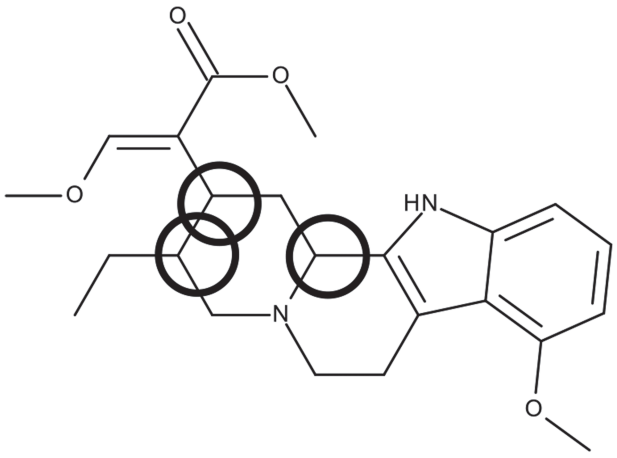

Figure 1. The structure of mitragynine (chiral centers are ringed).

effects, which are reported to include euphoria, relaxation, increased energy, analgesia and sensory enhancement (4). An additional consideration is that Kratom is often used as a treatment for opioid withdrawal symptoms and as an herbal alternative to opioids for pain management (5).

Mitragynine, as one of >20 different alkaloids in Kratom, is the predominant active indole-based alkaloid and has three chiral centers, resulting in a total of eight diastereomers; see Figure 1 for its structure (6). Mitragynine is reportedly 13 times more potent than morphine, and clinical research suggests that 7-hydroxymitragynine, another alkaloid present in Kratom, is four times more potent in its central nervous system (CNS) stimulant and depressant effects than mitragynine (7–9). Mitragynine makes up ~60% of the alkaloid content of the plant, with 7-hydroxymitragynine accounting for only 2% (10–11). The alkaloid content varies strain to strain, and is reflective of a number of environmental conditions, such as location where it was grown and soil content. In addition to μ-opioid receptor activity, mitragynine also has adrenergic receptor agonist activity (12). The other naturally occurring alkaloids in Kratom, each possibly acting upon other biological targets, may explain the wide range of reported effects (13).

Drug monitoring agencies are becoming more concerned about increasing reports of adverse effects associated with the use of mitragynine. In the United States, local, state and federal agencies are working to determine the safety and possible regulation of Kratom products, with several states issuing bans. In 2016, the US Drug Enforcement Administration released a notice of "Intent to Schedule" the active chemicals in Kratom (14); however, they retracted it following a public outcry as proponents argued about the medical benefits of Kratom and its role as a safe and legal psychoactive substance that improves mood, relieves pain and provides benefits in opiate addiction, which also provides a target for medicinal research (15).

Kratom has garnered the reputation of being minimally toxic due to its long history of use in certain cultures (16, 17). However, there is limited research to support an opinion one way or the other, with most available information being anecdotal. One study describes the administration of Kratom tea, containing 104, 166 and 192 mg/L of mitragynine, to 10 chronic Kratom users over 7 days; mitragynine plasma concentrations ranged from 18–105 ng/mL within ~1 h (18). No adverse effects were reported, aside from recorded elevated blood pressure and heart rate that were likely attributed to the stimulant effects of the low doses (~30 mg of mitragynine while chronic Kratom users in Malaysia reported using up to 276.5 mg) (19). Although Kratom has a historic, traditional use in Southeast Asia, it has been consumed recreationally as a "4×100" cocktail of Kratom tea, cough syrup, Coca-Cola and other illicit drugs prompting a ban in several countries (20). Further, Kratom products such as those marketed as nutritional supplements or opium substitutes are not regulated and therefore have unknown doses and purities of mitragynine and other Kratom alkaloids (21).

Mitragynine has been implicated in an increasing number of emergency room (ER) visits and calls to poison control centers (22–24). The number of calls to poison control centers in the United States increased 10-fold between 2010 and 2015 (n = 660), with moderate and severe outcomes due to Kratom exposure reported at 41.7% and 7.4%, respectively; the reported symptoms include tachycardia (n = 165, 25%), agitation or irritability (n = 157, 23.8%), drowsiness (128, 19.4%), nausea (97, 14.7%) and hypertension (n = 77, 11.7%). One death has been reported in a person exposed to lamotrigine and paroxetine in addition to mitragynine (25). A 26-year-old male arrived at the emergency department in cardiorespiratory arrest, with a history of taking Kratom 24 h prior; he died from cardiorespiratory failure and hypoxic brain damage 12 h later (13). Other adverse events include a 64-year-old male who suffered a seizure at home following Kratom consumption (26). Reported adverse effects include seizures, psychosis and liver toxicity including cholistastis and hyperthyroidism (19, 27–29). Naloxone was successfully used to reverse the respiratory depression in a 38-year-old female who presented to the ER with clinical symptoms of an opioid overdose (30). There is a concern for abuse potential with mitragynine, as there are reports of opioid-like withdrawal symptoms that required medical intervention and inpatient detoxification after "addiction to Kratom" (31–34).

Due to the increase in mitragynine use in the United States, it is not surprising that it has made its way into driving populations. In one reported driving under the influence of drugs (DUID) case, a 37-year-old female was stopped after almost striking an oncoming vehicle; standard field sobriety tests were administered with signs of impairment. The drug recognition expert observed leg tremors, continual clenching of the hands, fidgety and exaggerated movements, slurred and rapid speech and dilated pupils (35). Amphetamine was quantified at 52 ng/mL in the blood, while mitragynine and citalopram were qualitatively reported.

There have been a number of cases published in the literature along with mitragynine concentrations. A summary of these reports are listed in Table 1. Although most reports of mitragynine related fatalities include other drugs, there have been instances where other drugs and drug concentrations were determined to be insufficient to cause death. Many of the deaths involve autopsy findings consistent with opioid toxicity, including pulmonary congestion, cerebral edema and urinary retention. Blood mitragynine concentrations of 230, 600 and 1,060 ng/mL have been reported in cases where other substances were found to be insignificant or did not explain the autopsy findings, which were often consistent with opioid use (36–38). Conversely, there are some reported cases where an elevated mitragynine concentration was detected; however, the cause of death was unrelated to the ingested drugs. Mitragynine was confirmed at a concentration of 980 ng/mL in a case where the individual died from asphyxia (39).

As toxicologists and medical examiners work to understand what role mitragynine plays in medicolegal investigations and attempt to delineate incidental, contributory and fatal concentrations, it is important to gather quantitative information that is not falsely

Table 1. Summary of Published Reports

Case history	COD summary	Time	Matrix	Mitragynine	Other findings	Reference
A 20 y/o M discovered deceased at home with no signs of physical trauma. Pulmonary edema noted (chromatography discussed).	Propylhexedrine toxicity	NP	Heart blood	390	Propylhexedrine 1,700	40
A 17 y/o M found deceased in residence with no obvious signs of trauma. Decedent had a history of heroin abuse and chronic back pain and self-medicated with Kratom. Pulmonary congestion, edema and distended bladder were noted at autopsy. A box of Bali Kratom and bottle of liquid Kratom collected during investigation.	Possible Kratom toxicity	NP	Femoral blood	600	Dextromethorphan 280, diphenhydramine 330, temazepam 210, 7-amino-clonazepam 210	36
Middle aged M found deceased in bed after oral ingestion of Kratom purchased over the internet. History of substance abuse and psychiatric disease. Urine drug testing throughout employment.	Intoxication with Kratom, possibly in combination with other substances. Contributory pneumonia.	NP	Femoral blood	1,060	Zopiclone 43, citalopram 360, lamotrigine 5,400	38
A 24 y/o M found in bed unresponsive after alcohol and "sleeping pill". Attempted resuscitation unsuccessful. Vomitus present. History of EtOH[a] abuse, suicide attempts, depression and hospitalization for overdose.	Mixed drug toxicity (primarily mitragynine)	NP	Peripheral blood	230	Venlafaxine 1,100, O-desmethylvenlafaxine 1,600, diphenhydramine 450, mirtazepine 240, EtOH 20 mg/dL	37
A 28 y/o M found deceased in his residence. Scene investigation revealed recreational marijuana products, bags that contained green powders labeled "THAI" and "GREEN MAENG DA" and an unlabeled plastic bag that contained a crystalline white powder. Autopsy findings included pulmonary and cerebral edema, urinary retention and severe constipation.	Mixed drug intoxication of furanylfentanyl and mitragynine	<30 days	Leg blood	1,400	Furanylfentanyl 140	41
A 22 y/o M with history of drug addiction found deceased after ingestion of an herbal mixture ordered from the internet and an unknown tablet. Individual subsequently fell from a first floor window before going to bed. A 100 g[b] "Red Vein" package, Etizolam and fluoxetine were found at the scene. Mild pulmonary edema and urine retention noted.	Aspiration of chyme, possibly due to loss of consciousness	NP	Femoral blood	790	Etizolam 280, pregabalin 3 mg/L, pipamperon 7.4, lorazepam 6.9, triazolam 1.1, fluoxetine 89, quetiapine 18, olanzapine 5.8, 2-Methylmethcathinone ~5.2 (suspected)	42
A 20 y/o M was found with drug paraphernalia and various puncture wounds. Butane-1,4-diol and 250 g of brown colored powder (labeled Kratom) was collected; the powder was purchased over the internet. Urine retention noted.	Mixed drug intoxication with heroin, methamphetamine, MDMA[c] and GHB[d] (GHB may have partially resulted from postmortem decomposition)	NP	Femoral blood	10	Methamphetamine 3,300, Amphetamine 34, MDMA 1,400, MDA[e] 40, pseudoephedrine 8, codeine 24, morphine 210, 6-MAM[f] 41, acetaminophen 1.9 mg/L, GHB 480 mg/L	42

(Continued)

Table 1. Continued

Case history	COD summary	Time	Matrix	Mitragynine	Other findings	Reference
A 56 y/o F with history of chronic obstructive pulmonary disease (COPD) found deceased after recent complaints of dyspnea and cough. Prescriptions include oxycodone and lorazepam. Known to use cannabidiol oil drops and "methadone-like" powder obtained from Indonesia. Bilateral pneumonia noted at autopsy.	Mixed drug toxicity in conjunction with bronchopneumonia	<30 days	Femoral blood	2,500	Oxycodone 190, lorazepam 63	43
A 29 y/o M was found in a semi-seated position while partially suspended by a ligature. The decedent had a known history of drug and alcohol abuse. A package of Kratom pills was noted.	Asphyxia due to hanging; suicide	NP	Subclavian blood	980	EtOH 83 mg/dL	39

All units in ng/mL unless otherwise noted. Time refers to number of days between specimen collection and specimen testing. NP = not provided.
[a]EtOH = ethanol.
[b]g = gram.
[c]MDMA = 3,4-methylenedioxymethamphetamine.
[d]GHB = Gamma Hydroxybutyrate.
[e]MDA = 3,4-methylenedioxyamphetamine.
[f]6-MAM = 6-monoacetylmorphine.

elevated or underreported, or at least understand the limitations of the dataset. Since mitragynine has three chiral centers, four sets of enantiomers, composed of eight total stereoisomers, must be resolved chromatographically during analysis, not inclusive of other natural products contained within the leaves of Kratom (44). If this separation is not properly achieved, mitragynine concentrations could be artificially inflated, thereby skewing its interpretation. Further, stability of mitragynine in biological specimens also needs to be assessed, to understand how delays in time between specimen collection and sample analysis may affect the reported concentrations. Since the results of toxicological tests in forensic cases are used to interpret the potential lethality of a concentration, it is imperative to understand if any intoxicant concentrations, such as mitragynine, change between sample collection and analysis. The following analytical method was developed, validated and used to separate mitragynine diastereomers and analyze biological specimens for mitragynine; stability experiments were also performed. The method was applied to the analysis of authentic whole blood specimens in toxicological casework; case circumstances and concentration are reported for a subset.

Methods

Chemicals and reagents

Mitragynine in methanol and its deuterated internal standard, D3-Mitragynine in methanol, were purchased from Cerilliant (Round Rock, TX). Both were certified reference solutions, each at a concentration of 100 ng/mL. N-butyl chloride and ethyl acetate (HPLC grade) were purchased from Millipore (Billerica, MA). Acetonitrile (LCMS grade), ammonium hydroxide (Reagent ACS grade) and methanol (Optima grade) were purchased from Fisher Scientific (Fairlawn, NJ). Formic acid (Reagent grade, > 95%) and sodium borate (sodium tetraborate decahydrate) were purchased from Sigma-Aldrich (St Louis, MO). Concentrated sodium hydroxide, 10N was purchased from Avantor Materials (Center Valley, PA). Blank human whole blood with potassium oxalate/sodium fluoride preservative and human serum were purchased from BioIVT (Westbury, NY).

Table 2. MRM Method for Mitragynine and D3-mitragynine

Analyte	Parent Ion	Quantifier Ion	Qualifier Ion
Mitragynine	399.3	174.1	226.2
Mitragynine-d3	402.3	177.1	226.2

Calibrators and control preparation

Using pre-screened drug-free potassium oxalate/sodium fluoride preserved human whole blood, a calibration curve was prepared at concentrations of −5, 10, 50, 100, 250 and 500 ng/mL. Controls were prepared at 15 and 400 ng/mL.

Instrumentation

Quantitative analysis for mitragynine was performed using a Waters TQD® Tandem Mass Spectrometer with a Waters Acquity® Ultra Performance LC system (Waters Corp.®, Milford, MA). The mass spectrometer was operated in ESI positive ionization mode with a capillary voltage of 0.5 kV. The source temperature was 150°C and the desolvation temperature was 450°C. See Table 2 for MRM method.

The chromatographic separation was achieved with a Thermo Scientific® BETASIL Silica-100, 2.1 × 100 mm column with a 5.0-micron particle and EXP filter cartridge. The mobile phases used for LC-MS/MS analysis were ammonium formate, pH 4.0 and acetonitrile. The washes were acetonitrile and deionized water. An isocratic method of 10% ammonium formate buffer, pH 4.0 to 90% acetonitrile was used to separate mitragynine from its diastereomers. The total method run time was 3.5 min. Mitragynine is considered the primary toxicological target due to being the major constituent with pharmacological activity of the Kratom plant, but requires chromatographic separation from its diastereomers. Standard reference material may not be available for all isomers, and some analytical methods required isolation of alkaloids from the plant, typically provided by the National Center for Natural Products Research (6, 45).

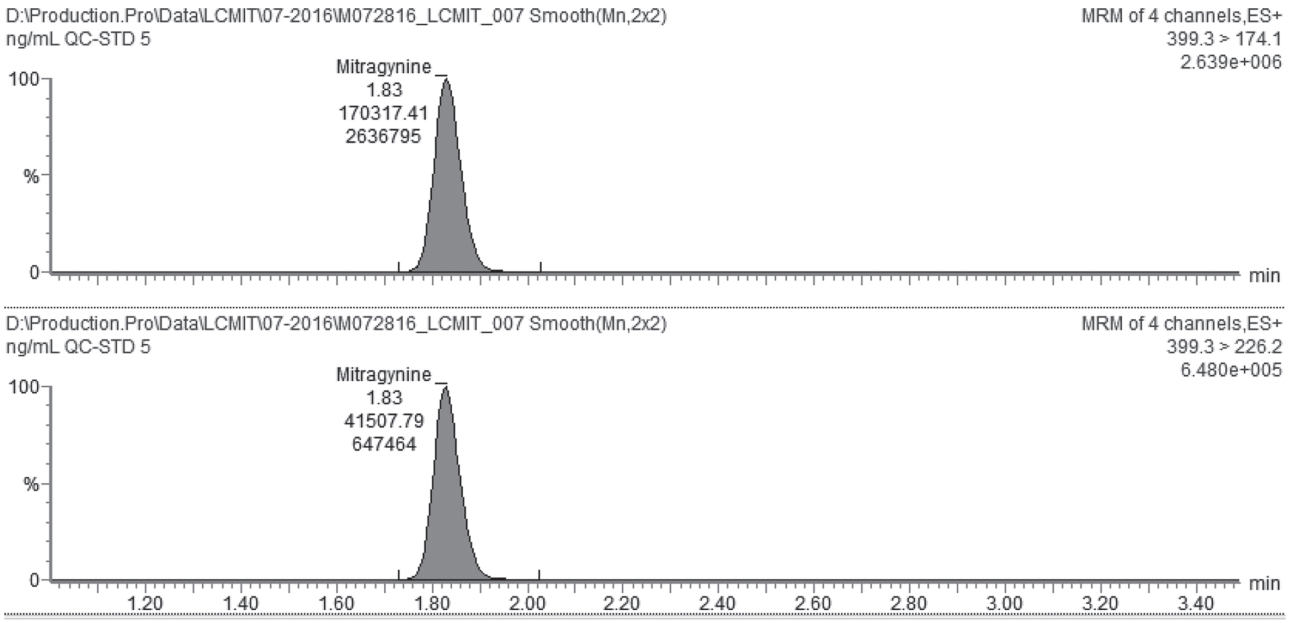

Figure 2. 500 ng/mL mitragynine standard.

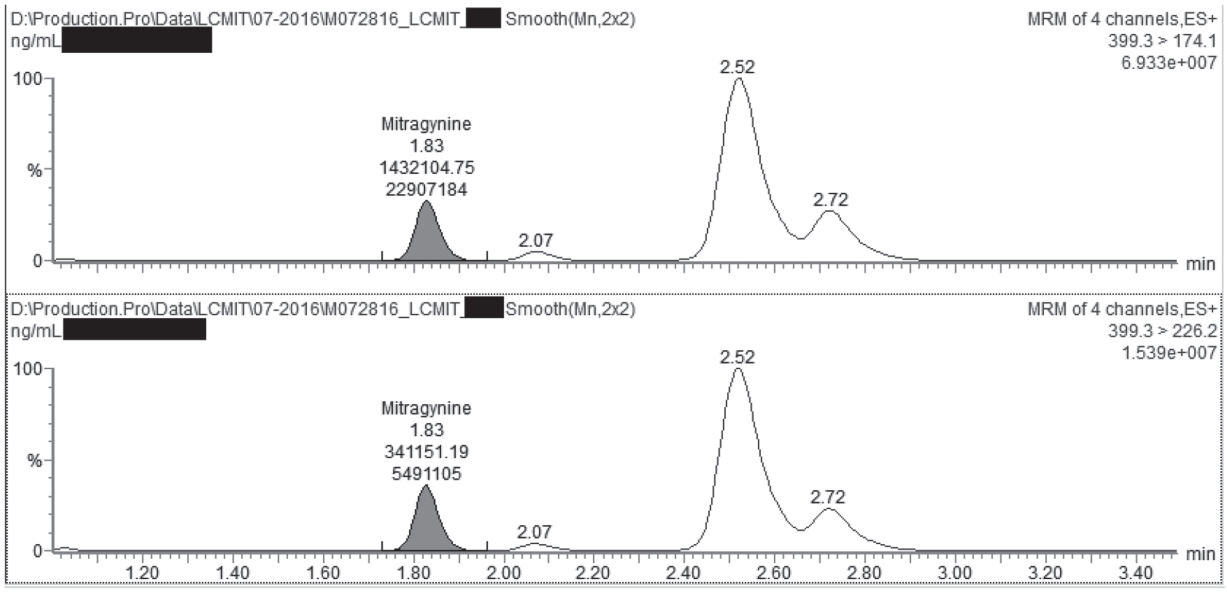

Figure 3. Chromatography of authentic mitragynine blood sample with presence of mitragynine diastereomers.

Therefore, it is not possible to properly identify which other isomers are present in mitragynine samples. Figure 2 depicts the chromatography of a 500 ng/mL standard of mitragynine. Figure 3 is a depiction of chromatography commonly seen in authentic blood specimens where mitragynine is present; the chromatography shows not only mitragynine, but chromatographic separation of mitragynine from compounds suspected of being its stereoisomers (by virtue of all possessing the same molecular formula and the same MRM transitions). However, these mitragynine-related compounds resolved from mitragynine in the final analytical method.

Sample preparation

D3-Mitragynine (50 µL at 0.5 ng/µL) internal standard was added to 500 µL aliquots of calibrators, controls and subject samples. A liquid–liquid extraction was performed, first alkalizing the blood with 0.1 M Borax Buffer, pH 10.4 (500 µL) vortex mixed and then adding 70:30 n-butyl chloride:ethyl acetate (4 mL). Samples were mixed on a rotomixer for 15 min, followed by centrifugation for 10 min. The top organic layer was decanted into a separate test tube after sitting in a cold-temperature bath to freeze the aqueous layer. The organic fraction was evaporated to dryness at 40 ± 5°C under

Table 3. Precision and Bias Estimates for Mitragynine[a]

Validation experiment	LLOQ	Low	High
Bias (%)	0.3	2.3	5.4
Within-run precision (% CV)	3.1	2	1
Between-run precision (% CV)	3.1	1.8	0.9

[a]Five replicates for the lower limit of quantiation (LLOQ); low and high quality controls were analyzed during three different analyses over three different days.

a gentle stream of nitrogen. Extracts were reconstituted with 0.1% formic acid in acetonitrile (500 µL) and extracts were analyzed using the described methodology.

Method validation

The validation protocol for this method was based on that described by the Scientific Working Group for Forensic Toxicology validation guidelines, and was performed as follows (46). The limit of detection for mitragynine was 0.16 ng/mL, and had a calibration range of 5–500 ng/mL. The calibration performance over 3 days of replicates resulted in an average correlation coefficient of 1.000, a slope of 0.999, with a bias of −0.18%. All calibration curves were second order, using 1/x weighted regression analysis of the ratio of the peak area of the analyte, to the peak area of the internal standard. Precision (%CV) and accuracy were <15% for all within-run and between-run data. The results of the validation bias, within-run and between-run precision are found in Table 3. A dilution experiment testing five replicates of the high control prepared at a 10-fold passed with a %CV of 1.0 and %Difference of 3.8; however, due to the use of a deuterated internal standard, further dilution is approved under this method.

Stability

Stability was assessed by spiking human whole blood with mitragynine at the control concentrations of 400 and 15 ng/mL. Aliquots of control material were stored at frozen (−70 and −20°C), refrigerated (4°C) and room temperature (25°C) conditions, in sodium fluoride/potassium oxalate preserved blood. Replicates from the fortified blood samples from each temperature condition were tested in triplicate at 1, 2, 7, 14, 30, and 90 days; frozen (−70°C) was not tested at 90 days. Mitragynine in blood is stable up to 7 days at room temperature and up to 30 days when refrigerated or frozen, with any deviation < 20%. See Figure 4 for a graph depicting the loss of mitragynine from the fortified low control in room temperature conditions within 30 days, while refrigerated and frozen conditions were relatively stable; data points are an average of the three replicates analyzed at each time point. However, stability experiments in blood demonstrated a loss of > 20% of mitragynine between 30 and 90 days across all temperature settings, with the most pronounced loss at room temperature and refrigerated settings. At 90 days, there was no detectable mitragynine in the refrigerated fortified low control, and the frozen (−20°C) declined to ∼10 ng/mL from a target of 15 ng/mL.

Since mitragynine stability declines markedly after 30 days, any analytical result obtained >30 days after specimen collection may underestimate the actual mitragynine concentration. The longer the period between specimen collection and testing, the greater the decrease from its original concentration.

Case samples

The method described above was used to analyze biological samples from toxicological casework in which mitragynine was specifically suspected from case investigative information and/or a positive screen for mitragynine using liquid chromatography time of flight mass spectrometry. This would be a mix of cases submitted for a variety of different reasons, including clinical investigations, impaired driving, drug facilitated sexual assault or postmortem investigations.

Over the course of 27 months (between October 2016 and December 2018) a total of 1,001 blood samples reported quantitative results for mitragynine by NMS Labs using the described method with appropriate stereoisomeric separation. Any results reported as less than reporting limit or greater than a specified concentration were excluded from the data set. Concentrations ranged from 5.6–29,000 ng/mL, with a mean and median concentrations of

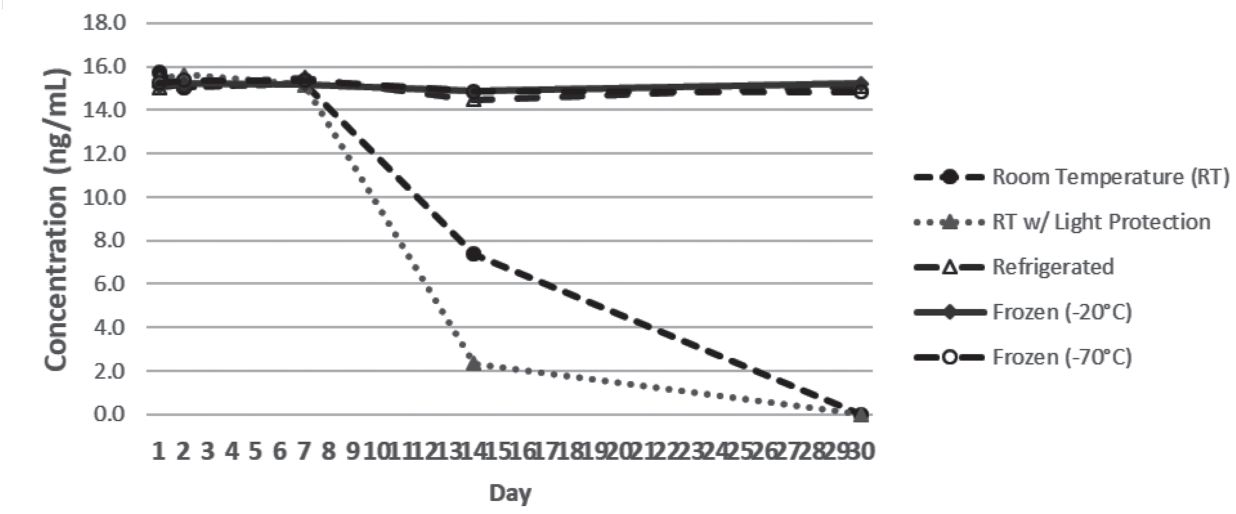

Figure 4. Stability of spiked low control (15 ng/mL) across conditions over 30 days. Data points are an average of three replicates.

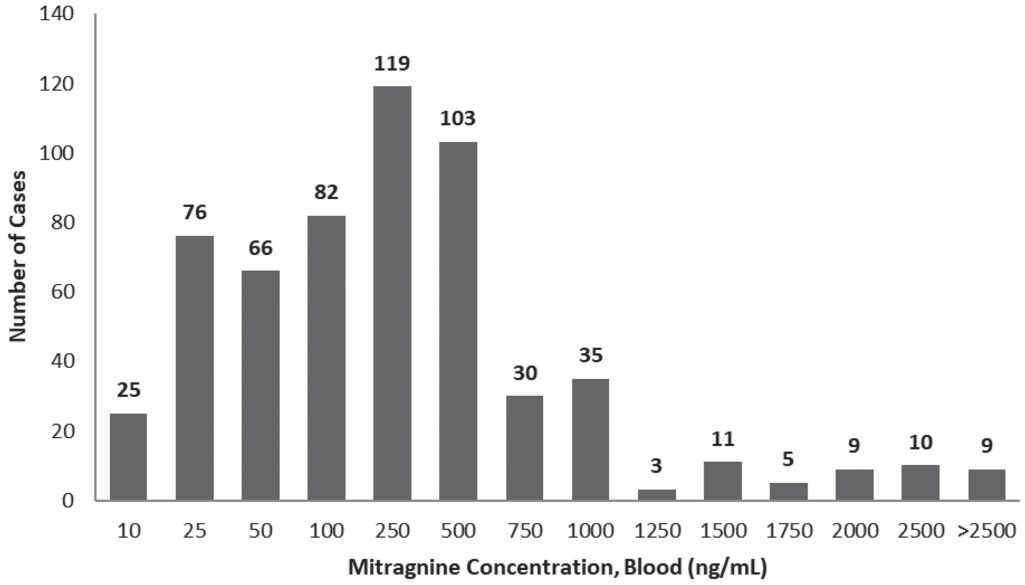

Figure 5. Histogram depicting positivity of reported blood samples for mitragynine where testing was completed within 35 days of specimen collection ($n = 583$).

410 ± 1,1240, and 130 ng/mL, respectively. When the 29,000 ng/mL postmortem blood outlier is removed from the dataset, the mean result decreases to 381 ± 668 ng/mL. Samples with initial concentrations greater than the highest calibrator of 500 ng/mL were subsequently re-analyzed and a dilution performed with a quantitative amount of blank solution so the diluted results would fall within the analytical measurable range. The concentration from the undiluted sample was then compared to the result from the diluted sample (corrected for the dilution factor).

Looking specifically at postmortem cases, these were defined as those submitted by a medical examiner and/or coroner, by using a designated postmortem test, and/or blood source was listed as femoral, iliac, subclavian or another collection site from autopsy. Using these criteria, 583 postmortem cases were identified with the assumption that the provided collection times were accurately reported. In addition, to obtain a better understanding of mitragynine concentrations seen in postmortem cases that are least likely to have suffered loss resulting from a delay between specimen collection and testing, the mitragynine cases were sorted to identify postmortem cases in which the case was reported within 35 days of specimen collection. The concentration range for these postmortem cases where mitragynine was analyzed within 35 days of specimen collection was 5.9–4,400 ng/mL, with mean and median concentrations of 372 ± 594 and 140 ng/mL, respectively. Figure 5 shows the distribution of concentrations seen in these postmortem cases. The highest reported mitragynine blood result from the original dataset is 29,000 ng/mL. This result stems from a postmortem case where the report was issued >60 days after sample collection. The case history provided by Detective T. Pike (email communication, March 2019) involved a 29-year-old male who was found deceased in a bathroom; packages of Kratom products labeled "MAENG DA KRATOM POWDER, 60 g", "mitragyna speciosa KRATOM" and "Mitragyna speciosa KRATOM SEM 20g" were located in the room along with a drinking cup containing a green-colored liquid. An electronic cigarette was also located with suspected methamphetamine in the cartridge. The death was ruled an accidental overdose from mitragynine.

Detailed case histories for a subset of postmortem cases from North Carolina are provided in Table 4. Cases from North Carolina screened positive for mitragynine by gas chromatography-mass spectrometry and were forwarded to the laboratory for directed testing for mitragynine. Concentrations for this subset ($n = 31$) ranged from 11–3,300 ng/mL, with mean and median results of 582 ± 822 and 230 ng/mL.

Between 2014 and 2017, mitragynine was reported in a total of six DUID cases when routine toxicology was also performed. In 2018, the frequency of mitragynine finding in DUID population increased significantly; mitragynine confirmed in 20 cases out of ~17,500 submissions. Of the 20 cases, 18 reported mitragynine results < 35 days of specimen collection. The concentration range for these cases is 11–490 ng/mL, with average and median concentrations of 106 ± 117 and 75 ng/mL. In one case, a 38-year-old male was stopped after making an abrupt steering correction and crossing the yellow line; when police interacted with the individual, he appeared anxious and had bloodshot eyes and a disheveled appearance. He was deemed to be impaired based on the fact that he displayed clues on the horizontal gaze nystagmus test (lack of smooth pursuit, distinct and sustained nystagmus at maximum deviation, onset of nystagmus prior to 45°, resting nystagmus), and on the walk-and-turn (started too soon prior to instruction, stopped while walking, improper turns, incorrect number of steps); information was provided by P. Yates, J.D. (email communication, October 2018). Mitragynine was confirmed at 99 ng/mL in blood, and therapeutic amphetamine was also present at a concentration of 140 ng/mL, which was consistent with the prescribed dosage. In a second case of a 39-year-old male, police officers observed a box truck swerving between lanes and the shoulder, almost striking another vehicle. Police officers found a bottle of "Kratom Supplement Capsules" upon vehicle search; the driver admitted to being a recovering opioid user and was using Kratom daily to help with his withdrawal. His eyes were noted

Table 4. Case Histories From North Carolina Office of the Chief Medical Examiner With Quantitative Mitragynine From Reported Method

Case	Age	Sex	Case history	COD summary	Source of blood	Mitragynine	Additional toxicological findings (ng/mL)	Time delay (days)[a]
1	33	M	Found down in bathroom by wife after reportedly drinking 10+ malt drinks and then taking two Adderall®. History of alcohol and prescription drug abuse. No non-prescribed meds found at the scene.	Acute fentanyl, mitragynine and EtOH toxicity	Femoral blood	85	Fentanyl 2.4, EtOH 180 mg/dL (aortic blood)	44
2	35	M	Found deceased in bedroom. History of back injury, prescribed methadone and gabapentin. According to spouse, decedent had stopped methadone. Gabapentin pill count off.	Acute methadone, mitragynine, gabapentin and metham-phetamine toxicity	Iliac blood	290	Methamphetamine 170, amphetamine 49, gabapentin 3.3 mg/L, methadone 470	290
3	35	M	Found unresponsive on couch wrapped in blanket next to unmarked baggie with 20 Xanax® and empty bottle of vodka. History of hydrocodone abuse.	Oxymorphone, mitragynine, alprazolam and EtOH toxicity	Iliac Blood	42	Alprazolam 200, diazepam 130, nordiazepam 90, oxymorphone 36, EtOH 90 mg/dL (vena cava blood)	46
4	20	F	Found in a motel room with white powder and a rolled up dollar bill when she failed to check out.	Heroin, fentanyl and cocaine toxicity with additive MDMA, hydrocodone and mitragynine	Iliac blood	200	MDMA 300, MDA 42, cocaine 53, BZE[b] >4,000, fentanyl 8.8, hydrocodone 5, hydromorphone 1, morphine 86, 6-MAM present	52
5	28	M	Found deceased on futon in unlocked house. A rolled up dollar bill with white powder on it was at the scene. Decedent is a known drug user. Urinary drug screen positive for oxycodone.	Fentanyl and mitragynine toxicity	Femoral blood	680	Fentanyl 26	53
6	47	F	Found unresponsive, with vomitus, after laying down for a nap. Pronounced dead at the scene. History of illicit and prescription drug abuse.	Loperamide, gabapenti and mitragynine toxicity	Iliac blood	100	Fluoxetine 620, norfluoxetine 680, gabapentin 28 mg/L, loperamide 58	54
7	41	M	Decedent found unresponsive with no medical issues. Had used opioids in the past. Prescriptions for alprazolam, sertraline, and buspirone.	Mixed drug toxicity (mitragynine and sertraline)	Femoral blood	3,300	Sertraline 450, norsertraline 930	39
8	33	M	Discovered by wife non-responsive lying on floor of their living room. EMS was called; decedent was eventually pronounced at the residence. Tramadol script filled 2 days earlier for 120 pills, when inventoried there were 10 pills present.	Mixed drug toxicity (mitragynine, tramadol, cyclobenzaprine and diphenhy-dramine)	Iliac blood	2,300	Cyclobenzaprine 180, diphenhydramine 3,400, duloxetine 300, lamotrigine 8.1 mg/L, tramadol 7,500, O-desmethyltramadol 660	27

(Continued)

Table 4. Continued

Case	Age	Sex	Case history	COD summary	Source of blood	Mitragynine	Additional toxicological findings (ng/mL)	Time delay (days)[a]
9	34	M	Found unresponsive and supine on bedroom floor by family, $20 bill and white powdery substance on scene. History of abusing heroin, marijuana and "illegal pills".	Fentanyl and mitragynine toxicity	Iliac blood	220	Bupropion 310, threo bupropion 1,100, sertraline 350, desmethylsertraline 670, fentanyl 16	30
10	49	M	Found face down on right side in front of the couch. Small laceration above left eyelid, coffee table leg broken, looked like he may have passed out or fallen. Had constant shoulder pain, headaches and tremors due to an assault 2 months prior. Wife was concerned about mitragynine usage, 15 empty packages in trash can with 2 tablets/package.	Mitragynine and alprazolam toxicity	Iliac blood	2,900	Alprazolam 31	25
11	39	M	History of hypertension, hyperlipidemia, anxiety with cyclic vomiting, pancreatitis, Rocky Mountain Spotted Fever, unknown heart surgery at 17 years old, two back surgeries due to an accidental injury and foot drop after back surgery. Did not want to take narcotics so started taking Kratom powder, turmeric and kava. History of alcoholism, marijuana and cocaine use (5 years ago). Decedent was prescribed clonazepam. which he had not picked up yet, and Lyrica®. Taking wife's clonazepam (filled 6 days earlier for 60, 47 missing); wife stated she only took 5. Lyrica® was filled 7 days earlier for 90, with 23 missing at the time of death. He was complaining of bloating when he went to bed, but no complaints earlier in the day. Wife woke up the next morning and he was cold.	Acute mitragynine, phenibut, pregabalin and clonazepam toxicity	Iliac blood	1,100	7-Aminoclonazepam 67, phenibut 64 mg/L, pregabalin 13 mg/L	37
12	24	M	Found leaning over bed by roommate. History of substance abuse. Several empty pill bottles prescribed to other people and fentanyl patches present.	Acute mixed drug intoxication with fentanyl, butalbital, mitragynine and temazepam.	Femoral blood	24	Butalbital 2.5 mg/L, fentanyl 33, fluoxetine 530, norfluoxetine 510, lamotrigine 2.5 mg/L, promethazine 340, temazepam 410, topiramate 1.3 mg/L	25

(Continued)

Table 4. Continued

Case	Age	Sex	Case history	COD summary	Source of blood	Mitragynine	Additional toxicological findings (ng/mL)	Time delay (days)[a]
13	56	F	Found lying on floor with clear plastic bag over head closed by a soft cloth ligature, detached hose to a helium tank nearby. Suicide instructions present on the nearby bed.	Asphyxia due to insufflation of plastic bag over head with contributing morphine and mitragynine toxicity	Iliac blood	800	Amphetamine 29, hydromorphone 9, morphine 280	28
14	27	M	Found unresponsive with heroin and Kratom. Straws located on scene. History of heroin abuse. Suicide attempt within last 6 months, unknown method.	Multidrug toxicity	Femoral blood	510	Methamphetamine 320, amphetamine < 120, cocaine 230, cocaethylene 170, BZE 1,000, furanylfentanyl 54, fluoroisobutyrylfentanyl 5.2, U-47700 1, U-49900 20, EtOH 170 mg/dL (aortic blood)	43
15	44	M	History of heroin abuse. Found dead on his bed. Had been seen to be acting high the night before.	Fentanyl toxicity with additive mitragynine	Iliac blood	440	Fentanyl 10 ng/g, morphine 7	46
16	46	M	History of heroin abuse with cardiac arrest due to overdose, found unresponsive in bathroom by roommate. Track marks and venipunctures in right antecubital fossa.	Fentanyl, heroin and cocaine toxicity, with contributing mitragynine use	Iliac blood	120	Cocaine 12, BZE 230, codeine < 10, morphine 100, fentanyl 33, 6-MAM present in urine	44
17	30	M	Heard snorting something in bathroom prior to going unresponsive with pinpoint pupils.	Fentanyl, etizolam and mitragynine toxicity	Femoral blood	550	Etizolam 50, fentanyl 10	41
18	34	M	History of HIV[c] and heroin abuse, found deceased at home on his bed by his mother. Mother reports deceased was depressed and she was keeping tabs on him. Single unidentified white pill on bed, box of Narcan® on kitchen table. No other drugs or paraphernalia on scene. Autopsy showed pulmonary and cerebral edema, hepatosplenomegaly.	Methadone, gabapentin, clonazepam, mitragynine, phentermine and zolpidem toxicity	Iliac blood	1,600	Clonazepam 12, 7-aminoclonazepam 260, citalopram 270, gabapentin 18 mg/L, methadone 160, phentermine 160, zolpidem 130	44
19	48	F	History of Charcot-Marie-Tooth disease, smoking and COPD[d]. Found unresponsive at home in living room.	Diazepam, gabapentin, mitragynine, morphine and oxycodone toxicity	Iliac blood	160	Diazepam 84, nordiazepam 170, gabapentin 32 mg/L, hydromorphone < 5, morphine 95, oxycodone 16, oxymorphone < 5	39

(Continued)

Table 4. Continued

Case	Age	Sex	Case history	COD summary	Source of blood	Mitragynine	Additional toxicological findings (ng/mL)	Time delay (days)[a]
20	25	M	Found next to Waffle House. Found syringe and tourniquet and known to abuse drugs.	Heroin, fentanyl and mitragynine toxicity	Femoral blood	780	Fentanyl 19, morphine 18, 6-MAM present in urine	67
21	22	M	Found unresponsive in bedroom by grandmother. Extensive substance abuse history, found with grocery bag full of loperamide and multiple bags of a powdery substance from an online company.	Methadone toxicity with additive mitragynine	Iliac blood	370	Methadone 330	47
22	29	M	Used heroin with roommate/friend. Roommate passed out immediately and discovered decedent unresponsive on floor of bathroom when he awoke. There are needles on the sink counter and an empty can of coke that was dismantled to create a heating tray with the bottom of the can. There is residue in the can. No obvious injuries.	Acute fentanyl, mitragynine and EtOH toxicity	Iliac blood	150	Fentanyl 22, EtOH 30 mg/dL (aorta blood)	48
23	22	M	Found dead in bed at home after argument with mother over substance abuse. Adjacent medication for bottle for amitriptyline contains 22 Xanax ®. History of asthma, depression and ETOH/drug abuse. Autopsy: pulmonary edema.	EtOH, alprazolam and mitragynine toxicity	Iliac blood	230	Alprazolam 110, amitriptyline 350, nortriptyline 230, EtOH 130 mg/dL (heart blood)	52
24	50	F	Likely smoked heroin immediately prior to death. Known history of substance abuse.	Acute fentanyl toxicity with additive mitragynine	Iliac blood	100	Fentanyl 4.9, 4-ANPP[c] present	38
25	41	M	Allegedly used heroin prior to death, no anatomic cause of death.	Fentanyl and mitragynine toxicity	Iliac blood	350	Fentanyl 34, EtOH 70 mg/dL (aorta blood)	55
26	28	M	Undergoing gender reassignment surgery. Has a history of drug abuse. Found at home apneic, pulseless and unresponsive. History of suicide attempt within last 2 years.	Amphetamine, memantine, mitragynine, phenibut, fluorophenmetrazine, clonazepam and gabapentin toxicity	Subclavian blood	43	3-Fluorophenmetrazine Present, 7-Aminoclonazepam 75, amitriptyline < 250, amphetamine 1,100, gabapentin 18 mg/L, memantine 1,800, nortriptyline < 250, phenibut < 1.0 mg/L	55

(Continued)

Table 4. Continued

Case	Age	Sex	Case history	COD summary	Source of blood	Mitragynine	Additional toxicological findings (ng/mL)	Time delay (days)[a]
27	30	M	Found almost unconscious in Walgreens bathroom with syringe and packets nearby.	Fentanyl, mitragynine, metham-phetamine and EtOH intoxication	Femoral blood	230	Methamphetamine 360, EtOH 120 mg/dL (aorta blood), fentanyl 3.7 (aorta blood)	56
28	52	M	Found on floor next to couch. History of "huffing" or "injecting" sublingual Suboxone® strips (knife, blade, tweezers and spoon with burn marks and suboxone in liquid form next to several empty boxes of Suboxone® strips). It is believed that the decedent is melting down his Suboxone® and huffing the vapors. There is no evidence of needles or track marks.	Acute mitragynine and buprenorphine toxicity	Iliac blood	66	Buprenorphine 1.9, norbuprenorphine 4.6	57
29	28	F	Was found unresponsive on bathroom floor.	Drug (fentanyl, mitragynine and morphine) toxicity with contributing alprazolam, clonazepam and diazepam use	Femoral blood	190	Clonazepam < 5, 7-aminoclonazepam 57, alprazolam 8, diazepam 300, nordiazepam 38, fentanyl 11, morphine 21	59
30	43	M	Was working on his vehicle and was found unresponsive with his head on open drawer and body on floor. Past history of drug abuse. Heart disease noted on autopsy.	Heroin, fentanyl and mitragynine toxicity	Femoral blood	11	Amphetamine < 120, fentanyl 5.7, morphine 22. 6-MAM present in urine.	63
31	38	M	Found kneeling outside of vehicle with head on floorboard. History of EtOH and polysubstance misuse.	Furanylfentanyl and U-47700 toxicity with contributing mitragynine and alprazolam	Femoral blood	120	Alprazolam 120, furanylfentanyl 1.0, morphine 16, U-47700 3	63

[a]Time delay is listed as the difference in time (in days) between specimen collection and reporting of case.
[b]BZE = Benzoylecgonine.
[c]HIV=Human immunodeficiency virus.
[d]COPD = Chronic Obstructive Pulmonary Disease.
[e]4-ANPP=N-phenethyl-4-piperidinone.

to be pinpoint as well as bouncing/twitching, and was unable to focus. He also estimated passage of 30 s in 19 s. In addition to 69 ng/mL of mitragynine in the blood, cocaine and benzoylecgonine were confirmed at 360 and 2,000 ng/mL. Case history was shared by S. Knickel (email communication March 2019). The majority of the cases positive for mitragynine presented poly-pharmacy; most frequently concomitant findings were opioids ($n = 8$) and benzodiazepine ($n = 8$). Of those, 50% ($n = 4$) were reported with both opioid and benzodiazepines. There is one case where a 27-year-old female was arrested for DUID twice in the same jurisdiction nearly 2 months apart. In the first incident, mitragynine was the only finding at a concentration of 65 ng/mL. Clonazolam at less than a reporting limit of 5.0 ng/mL in addition to mitragynine at 160 ng/mL were the finding in the second incident.

These data demonstrate that mitragynine results in living and deceased individuals span a large concentration range with a significant amount of overlap.

Discussion

Overall, mitragynine detection in toxicological casework has been increasing over time, with the first blood results reported in 2012

Table 5. Number of Submitted Mitragynine Blood Cases Between 2012 and 2018[a]

Year	Qualitative	Quantitative	Sum
2012	2	NA	2
2013	25	NA	25
2014	55	NA	55
2015	86	NA	86
2016	189	23	212
2017	303	209	512
2018	11	774	785

[a]There are five results categorized under the quantitative method that are reported as "less than" or "greater than".

from this laboratory. Table 5 details the number of blood samples reported each year and Figure 6 shows the increase in submitted blood samples from the laboratory between 2012 and 2018. Mitragynine was only included in the scope of a single esoteric panel in 2012; in the spring of 2013 mitragynine was included in the scope of a routine expanded panel with qualitative reporting. The quantitative assay for mitragynine was available in October 2016. In 2018, all mitragynine blood testing was reported quantitatively; 1.24% of postmortem cases under a routine expanded panel screened positive for mitragynine, with 785 total blood samples being submitted and reported positive for mitragynine. When evaluating the frequency of reported concentrations in Figure 5, 81% of cases had a result of <500 ng/mL, with 92% of cases <1,000 ng/mL.

The role of mitragynine in a medicolegal investigation has challenged toxicologists due to the lack of clinical studies with accompanying drug monitoring data, and other confounding variables that may include non-specific analysis and poly-pharmacy. There is a need to evaluate each case individually, taking into account scene investigation, medical history and autopsy findings, as the diagnosis becomes one of exclusion (47).

Geographic distribution of the original 1,001 blood cases with quantitative results were from 46 different states in the United States and 3 Canadian provinces. Florida accounted for almost 14% of the reported cases, with 88 cases reported from Pennsylvania, 72 from Michigan and 64 from Illinois. Ten additional states reported between 25 and 30 cases for mitragynine in blood, representing different geographical areas; these states included California, Louisiana, New York and Texas. A limitation to this information is that it only reflects the geographical distribution of cases that were sent to the laboratory and is not a comprehensive assessment of how prevalent mitragynine is in a certain state or region.

In the postmortem case series from North Carolina described in Table 4, all 31 cases involved other substances in addition to mitragynine. Opioids, both pharmaceutical and illicit, were detected in 84% of the cases. The opioids included fentanyl as the most prevalent, ($n = 14$), but also included morphine, heroin, furanylfentanyl, parafluoroisobutyrylfentanyl, U-47700, U-49900, methadone, buprenorphine, tramadol, oxycodone, oxymorphone, hydrocodone, hydromorphone and loperamide. Since mitragynine has opioid-like effects at higher doses, some recreational users may simply be using mitragynine as an additional substance at their disposal. There are other situations in which the decedent may have been using mitragynine to manage pain, or to try to reduce their opioid dosage since it also has a reputation as a natural alternative to other pharmaceutical opioids. Case 7 reported a mitragynine level of 3,300 ng/mL, which is one of the highest concentrations reported to date; a sertraline concentration of 450 ng/mL was also present, but typically only sertraline concentrations in excess of 1,500 ng/mL are considered to be a contributing factor in death (48). In case 10, 31 ng/mL of alprazolam was found, which is consistent with therapeutic administration of alprazolam, in addition to 2,900 ng/mL of mitragynine.

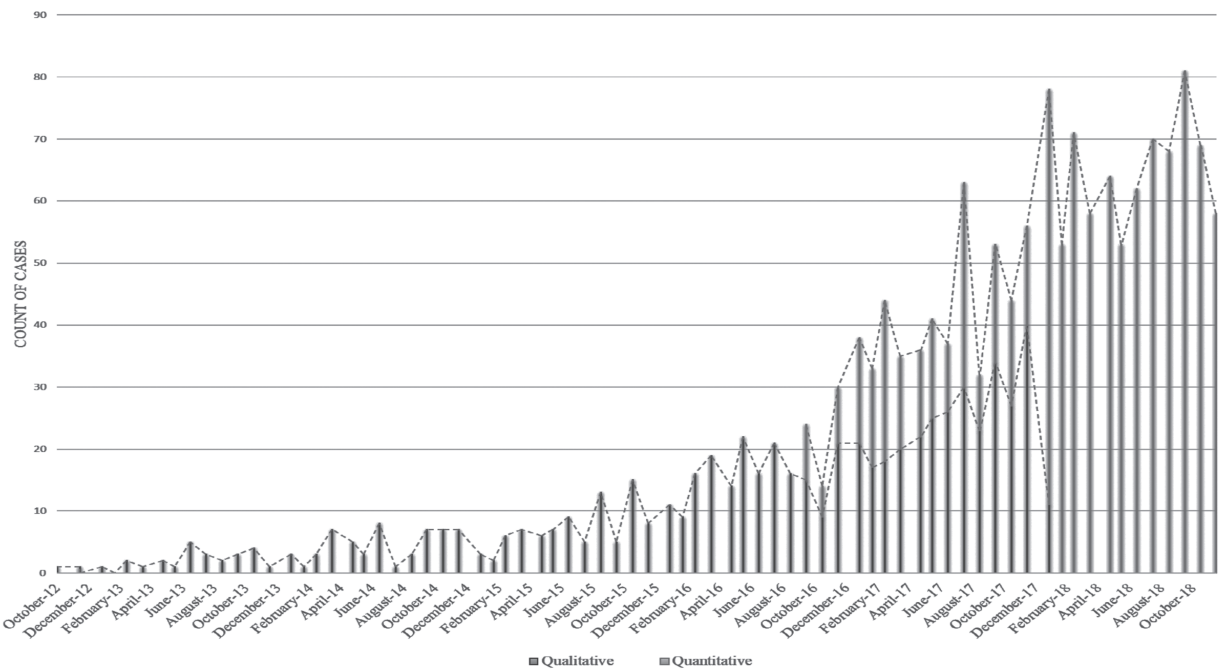

Figure 6. Frequency of positive mitragynine test results submitted by month between 2012 and 2018; mitragynine was reported qualitatively from an NPS screen prior to being included in the scope of a routine drug panel. A quantitative assay became available October 2016, with all blood mitragynine being reported starting January 2018.

There have been previous case reports of fatalities documenting blood mitragynine concentrations in addition to other toxicological findings (see Table 1). The ability of some of those methods to resolve mitragynine isomers is unknown, so the reported concentrations may not be directly comparable to the concentrations reported in our subjects. Some of the published articles specify the various mitragynine species and the need for separation, such as those described by Holler *et al.* (40), Domingo *et al.* (42) and Holler *et al.*, but some do not, which may then adversely affect the reported concentration, such as Neerman *et al.* (36), Karinen *et al.* (37) and McIntyre *et al.* (38). Reported concentrations are not only a product of the precision and accuracy of the analytical method, but are affected by a large number of pre-analytical variables, which include sample integrity, site differences and drug instability. The instability of mitragynine documented in our validation experiments described above may also account for differences in apparent lethal concentrations, since the length of time between death, specimen collection and specimen testing is often not documented.

Of the 31 cases described in Table 4, all but one case was ruled a multi-drug toxicity. Case 13 was a suicide by asphyxia and had reported concentration of 800 ng/mL of mitragynine in the blood. This concentration is in line with the 980 ng/mL reported in a separate suicide by asphyxia (39). Blood mitragynine concentrations of 800 and 980 ng/mL are considered elevated and within range of other reported fatalities attributed to mitragynine, but were clearly not related to the cause of death in these two instances.

Based on consideration of the cases reported here and previous published reports, mitragynine poses a risk to recreational users and those using it as a natural remedy or nutritional supplement due to lack of medical supervision or oversight/regulation of the dose. The risks are greatly increased when it is taken with other drugs, particularly opioids or other CNS depressants, and when taken in large doses. Mitragynine content of various Kratom products and preparations can vary widely, and the user will most likely not know the specific dose they are ingesting (49). For example, red vein Kratom is popularly believed to be more sedative, while green and white vein are considered more stimulatory (50). Since there is no regulation of Kratom sales, recreational users will not know the strength of the strain used or the dosage of mitragynine they are truly ingesting. There are no guidelines regarding dosages, routes of exposure or permitted mitragynine content as these products are not evaluated by any kind of agency for quality and proper representation. Further, some of these products may be contaminated with other substances, which may increase the risk of adverse effects. A series of nine unintentional overdose deaths were linked to a product called *Krypton*; O-desmethyltramadol, a potent μ-opioid receptor agonist, was detected with mitragynine, which ranged from 0.02 to 0.18 mcg/g (51). Another report suggests that there may be products on the market fortified with 7-OH mitragynine, which has higher potency than mitragynine (52).

Conclusions

Since data are limited, it can be difficult to understand what role mitragynine plays in a human performance or medicolegal death investigation. As with most drugs, it is impossible to give clear quantitative guidance as to what concentrations should be considered therapeutic, toxic or fatal. The optimal approach is to look at the totality of the circumstances of the case, including the patient history, the scene and circumstances, prescription or illicit drug evidence at the scene, autopsy findings and histology and toxicology results, including mitragynine and other drugs in combination. Once that information is obtained, and in the absence of a competing cause of death such as trauma or disease, consideration could be given to the emerging substance(s) detected, such as mitragynine. Comparison of the case with other reported cases (such as those described here) helps to support that conclusion about most likely cause of death. As the body of data supporting the investigation of mitragynine cases continues to grow, the process should become gradually easier.

Mitragynine is increasingly being detected in postmortem cases but rarely seen on its own. These cases appear to be separated between recreational poly-substance cases and potentially chronic pain management cases. Mitragynine is frequently encountered with other opioids, which makes it exceedingly difficult to determine the effect mitragynine had on a case relative to another opioid. Although opioids are typically the most frequently encountered drug class with mitragynine, the same difficulty with interpretation will occur with other CNS depressants such as benzodiazepines.

Although each case has to be evaluated on its own merits since drug concentrations vary widely and are affected by a large number of variables such as route of administration, time of sample collection, stability of drug in a sample, accuracy of laboratory measurement and poly-pharmacy, mitragynine concentrations between 100 and 500 ng/mL may need to be scrutinized as contributory, while concentrations > 1,000 ng/mL are more frequently being associated with fatalities and may be more causative in nature.

In attempting to establish toxic ranges for mitragynine, it is imperative that the data is not improperly influenced by pre-analytical and analytical variables. Due to the public debate regarding mitragynine's safety profile, and demonstrated instability in biological samples, it is necessary to obtain accurate quantitation in a timely manner so an appropriate assessment can be made regarding mitragynine's role in human performance and death investigations.

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WISCONSIN LEGISLATURE
P.O. Box 7882 • Madison, WI 53707-7882

March 3, 2023

VIA ELECTRONIC MAIL AND U.S. POSTAL SERVICE

Wisconsin Controlled Substances Board
DSPS
PO Box 836
Madison, WI 53708-8366

Dear Chair Engelbart and Members:

We want to thank the Controlled Substances Board (CSB) for the time and effort put into our request that the CSB conduct an 8-factor analysis to determine whether natural kratom meets the statutory criteria to be scheduled under the law. We appreciate the CSB's premise of doing the analysis as though kratom were a new substance being reviewed and relying on the most recent peer-reviewed data and information rather than outdated research, unsubstantiated claims or news articles that are not viewed as credible evidence.

The 8-factors are intended to ensure that current, accurate research and science are the basis for scheduling decisions, and we hope your final decision will be based on the statutory factors and the science on kratom. We also recommend you consider the conclusions of the Assistant Secretary of Health at the Department of Health and Human Services (HHS), who stated after their decision to forgo scheduling kratom that the "decision is based on many factors, in part on new data, and in part on the relative lack of evidence, combined with an unknown and potentially substantial risk to public health if these chemicals were scheduled at this time." It is an assessment we wish the Wisconsin Legislature had available to us at the time the initial discussions about scheduling kratom took place in Wisconsin.

Over the last year, we know that in addition to the CSB, several other examining boards and agencies were involved in reviewing the extensive amount of data provided. We look forward to the decision at your March meeting where a final "yes or no" judgement on whether natural kratom meets the statutory requirements will be provided. As you know, the 2023-2024 Legislative Session has begun and we will commence a review of needed legislation, so your input will be welcomed prior to any legislative action.

We reviewed the January 13, 2023 meeting where each of the 8-factors was discussed in open session and members were asked for their initial vote on each factor. Below is our observation and short summary of the discussion and the votes taken during the meeting.

Wisconsin Controlled Substances Board
January 13, 2023

FACTOR 1	The actual or relative potential for abuse Summary: Abuse potential liability not proven	No
FACTOR 2	The scientific evidence of its pharmacological effect, if known Summary: Pharmacologic effects seem to be well understood and kratom does have pharmacologic effects; adulterated products implicated in adverse events; Safe dosages questioned	Yes
FACTOR 3	The state of current scientific knowledge regarding the substance Summary: Research shows kratom has opioid-like effects, but minor compared to Schedule I substances; where adverse events do occur, they are usually reported to be from adulterated products	Yes
FACTORS 4 & 5	The history and current pattern of abuse and the scope, duration, and significance of abuse Summary: There is no clear evidence of any pattern of abuse; some reports have been made, but not to a level of scientific conclusions and unknown if data is attributable to adulterated products	No
FACTOR 6	The risk to the public health Summary: There is some data showing adverse events, but they are few and at low level risk compared to other illegal products	No
FACTOR 7	The potential of the substance to produce psychological or physical dependence liability Summary: Kratom can produce dependence, but a review of the available literature shows it is mild	No
FACTOR 8	Whether the substance is an immediate precursor of a substance already controlled under this chapter Summary: Unanimous that no evidence exists on this issue	No

(The summary above are observations from notes taken during the meeting and do not reflect any official document of the CSB. It is based on our review and conversations with others who attending the meeting.)

Although other regulatory bodies like the US Department of Health and Human Services, the World Health Organization, the Rhode Island Department of Health and most recently Wisconsin's own Concordia University School of Pharmacy have done this analysis and determined that kratom did not warrant scheduling, we appreciate the CSB's review as Wisconsin's regulatory body for these matters.

Thank you again and please let us know if you have any questions or need additional information from us.

Sincerely,

Robin Vos
Speaker of the Wisconsin State Assembly

David Murphy
State Representative

John Macco
State Representative

Michael Schraa
State Representative

Mary Felzkowski
State Senator

Rachael Cabral-Guevara
State Senator

State of Wisconsin
Department of Safety & Professional Services
AGENDA REQUEST FORM

1) Name and title of person submitting the request:	2) Date when request submitted:
Nilajah Hardin **Administrative Rules Coordinator**	**02/27/23** **Items will be considered late if submitted after 12:00 p.m. on the deadline date which is 8 business days before the meeting**

3) Name of Board, Committee, Council, Sections:

Controlled Substances Board

4) Meeting Date:	5) Attachments:	6) How should the item be titled on the agenda page?
03/10/23	☒ Yes ☐ No	**Administrative Rule Matters – Discussion and Consideration** **1. Possible Affirmative Action Order: Excluding Fenfluramine from Schedule IV** **2. Pending or Possible Rulemaking Projects** **a. Rule Projects Chart**

7) Place Item in:	8) Is an appearance before the Board being scheduled? *(If yes, please complete **Appearance Request** for Non-DSPS Staff)*	9) Name of Case Advisor(s), if required:
☒ Open Session ☐ Closed Session	☐ Yes ☒ No	**N/A**

10) Describe the issue and action that should be addressed:

Attachments:

- Fenfluramine Federal Rule
- Wis. Stats. Chapter 961 section 20 (Schedule IV)
- Rule Projects Chart

(All Board Rule Projects can be Viewed Here if Needed: https://dsps.wi.gov/Pages/RulesStatutes/PendingRules.aspx)

11) Authorization

Nilajah D. Hardin — 02/27/23

Signature of person making this request — **Date**

Supervisor (if required) — **Date**

Executive Director signature (indicates approval to add post agenda deadline item to agenda) — **Date**

Directions for including supporting documents:

1. This form should be attached to any documents submitted to the agenda.
2. Post Agenda Deadline items must be authorized by a Supervisor and the Policy Development Executive Director.
3. If necessary, provide original documents needing Board Chairperson signature to the Bureau Assistant prior to the start of a meeting.

Authority: 50 U.S.C. 4801–4852; 50 U.S.C. 4601 *et seq.;* 50 U.S.C. 1701 *et seq.;* 22 U.S.C. 3201 *et seq.;* 42 U.S.C. 2139a; 22 U.S.C. 7201 *et seq.;* 22 U.S.C. 7210; E.O. 12058, 43 FR 20947, 3 CFR, 1978 Comp., p. 179; E.O. 12851, 58 FR 33181, 3 CFR, 1993 Comp., p. 608; E.O. 12938, 59 FR 59099, 3 CFR, 1994 Comp., p. 950; E.O. 13026, 61 FR 58767, 3 CFR, 1996 Comp., p. 228; E.O. 13099, 63 FR 45167, 3 CFR, 1998 Comp., p. 208; E.O. 13222, 66 FR 44025, 3 CFR, 2001 Comp., p. 783; E.O. 13224, 66 FR 49079, 3 CFR, 2001 Comp., p. 786; Notice of September 19, 2022, 87 FR 57569 (September 21, 2022); Notice of November 8, 2022, 87 FR 68015 (November 10, 2022).

■ 2. Supplement No. 4 to part 744 is amended under RUSSIA by revising the entry for ''Private Military Company 'Wagner' '' to read as follows:

Supplement No. 4 to Part 744—Entity List

* * * * *

Country	Entity	License requirement	License review policy	**Federal Register** citation
*	*	*	*	*
RUSSIA	*	*	*	*
	Private Military Company 'Wagner', a.k.a., the following five aliases: —Chastnaya Voennaya Kompaniya 'Vagner'; —Chvk Vagner; —PMC Wagner; —Wagner Group; *and* —Vagner Group. 15 Zolnaya Street, Saint Petersburg, 195213, Russia	For all items subject to the EAR. (See §§ 734.9(g),[3] 746.8(a)(3), and 744.21(b) of the EAR). The license requirements under this entry also extend to any export, reexport and transfer (in-country) to the entity wherever located worldwide	Policy of denial for all items subject to the EAR apart from food and medicine designated as EAR99, which will be reviewed on a case-by-case basis. See §§ 746.8(b) and 744.21(e).	82 FR 28408, 6/22/17. 87 FR [INSERT FR PAGE NUMBER] 12/23/22.
	*	*	*	*
*	*	*	*	*

* * * * *

Thea D. Rozman Kendler,

Assistant Secretary for Export Administration.

[FR Doc. 2022–28033 Filed 12–21–22; 4:15 pm]

BILLING CODE 3510–JT–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 130 and 131

[Docket No. FDA–2000–P–0126 (formerly Docket No. 2000P–0658)]

RIN 0910–AI40

International Dairy Foods Association and Chobani, Inc.: Response to the Objections and Requests for a Public Hearing on the Final Rule To Revoke the Standards for Lowfat Yogurt and Nonfat Yogurt and To Amend the Standard for Yogurt; Correction

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; response to objections and denial of public hearing requests; removal of administrative stay; correction.

SUMMARY: The Food and Drug Administration is correcting a final rule entitled ''International Dairy Foods Association and Chobani, Inc.: Response to the Objections and Requests for a Public Hearing on the Final Rule To Revoke the Standards for Lowfat Yogurt and Nonfat Yogurt and To Amend the Standard for Yogurt'' that appeared in the **Federal Register** of December 15, 2022. The final rule revoked the standards of identity for lowfat yogurt and nonfat yogurt and amended the standard of identity for yogurt in numerous respects. The document was published with an errant reference to its effective date in the preamble discussion. This document corrects that error.

DATES: This correction is effective January 17, 2023, and applicable December 15, 2022.

FOR FURTHER INFORMATION CONTACT: Andrea Krause, Center for Food Safety and Applied Nutrition (HFS–820), Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, 240–402–2371, or Joan Rothenberg, Center for Food Safety and Applied Nutrition, Office of Regulations and Policy (HFS–024), Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, 240–402–2378.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of Wednesday, December 15, 2022 (87 FR 765590), appearing on page 76567, in FR Doc. 2022–27040, the following correction is made:

1. On page 76567, in the third column, in the fifth sentence of the third paragraph under IV. Summary and Conclusions, ''[DATE OF PUBLICATION IN THE **FEDERAL REGISTER**]'' is corrected to read ''January 17, 2023''.

Dated: December 16, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2022–27816 Filed 12–22–22; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA–945]

Schedules of Controlled Substances: Removal of Fenfluramine From Control

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final rule.

SUMMARY: With the issuance of this final rule, the Drug Enforcement Administration removes fenfluramine (chemical name: *N*-ethyl-α-methyl-3-(trifluoromethyl)phenethylamine), including its salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts is possible, from the schedules of the Controlled Substances Act. Prior to the effective date of this rule, fenfluramine was a

schedule IV controlled substance. This action removes the regulatory controls and administrative, civil, and criminal sanctions applicable to controlled substances, including those specific to schedule IV controlled substances, on persons who handle (manufacture, distribute, reverse distribute, dispense, engage in research, import, export, conduct instructional activities or chemical analysis with, or possess) or propose to handle fenfluramine.

DATES: Effective December 23, 2022.

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

SUPPLEMENTARY INFORMATION:

Legal Authority

Under the Controlled Substances Act (CSA), each controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause.[1] The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c) and the current list of scheduled substances is published at 21 CFR part 1308.

Pursuant to 21 U.S.C. 811(a)(2), the Attorney General may, by rule, ''remove any drug or other substance from the schedules if he finds that the drug or other substance does not meet the requirements for inclusion in any schedule.'' The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the Drug Enforcement Administration (DEA).[2]

The CSA provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General on the petition of any interested party.[3] This action was initiated by a petition to remove fenfluramine from the list of scheduled controlled substances of the CSA, and is supported by, *inter alia,* a recommendation from the Assistant Secretary for Health of the Department of Health and Human Services (HHS) and an evaluation of all relevant data by DEA. This action removes the regulatory controls and administrative, civil, and criminal sanctions applicable to controlled substances, including those specific to schedule IV controlled substances, on persons who handle or propose to handle fenfluramine.

Background

Fenfluramine (chemical name: *N*-ethyl-α-methyl-3-(trifluoromethyl)phenethylamine), including its salts, isomers, and salts of such isomers, has been controlled under 21 CFR 1308.14(d) as a schedule IV substance of the CSA since June 15, 1973.[4] On September 25, 2019, Zogenix, Inc. (Zogenix; the Sponsor) submitted to the Food and Drug Administration (FDA) a New Drug Application (NDA) for Fintepla (fenfluramine), for the treatment of seizures associated with Dravet syndrome (DS) in patients two years of age and older. FDA approved the NDA on June 25, 2020, with the labelling listing fenfluramine as a schedule IV controlled substance.

On October 18, 2018, Zogenix submitted to DEA a petition requesting that fenfluramine be removed from schedule IV of the CSA. The petition complied with the requirements of 21 CFR 1308.43(b) and DEA accepted the petition for filing on November 13, 2018.

Notice of Proposed Rulemaking To Decontrol Fenfluramine

On July 19, 2022, DEA published a notice of proposed rulemaking (NPRM) to remove fenfluramine from the schedules of the CSA.[5] The NPRM provided an opportunity for interested persons to file a request for a hearing in accordance with DEA regulations by August 18, 2022. No requests for such a hearing were received by DEA. The NPRM also provided an opportunity for interested persons to submit comments on the proposal on or before August 18, 2022.

Comment Received

DEA received one comment on the NPRM to remove fenfluramine from control.

Opposition to rulemaking: One commenter opposed decontrol of fenfluramine, however the comment was at times ambiguous. The commenter seemed to be concerned about children using fenfluramine illicitly and the potential harm related to the combined use with a stimulant, specifically noting the fenfluramine-phentermine (''fen-phen'') combination and noting ''Stimulants+Psychedelics=Psychosis.''

DEA Response: DEA acknowledges the commenter's concerns about relative harm, especially related to children. DEA notes FDA approved Fintepla (fenfluramine) on June 25, 2020, for the treatment of DS in patients two years of age and older. Currently Fintepla is the only FDA-approved drug product with fenfluramine. HHS considered the harms the fenfluramine-phentermine combination produced in their April 2021 scientific and medical evaluation, which was provided to DEA as part of this rulemaking process, pursuant to 21 U.S.C. 811(b).

DEA notes that the combination historically produced serious cardiac effects, not psychological effects. The FDA-approved labeling for Fintepla indicates that patients must be enrolled in the Fintepla risk evaluation and mitigation strategy (REMS) program and undergo cardiac monitoring before, during, and after treatment with Fintepla to monitor for serious heart valve changes or high blood pressure in the arteries of the lungs. The FDA-required REMS program for Fintepla, including ongoing cardiac monitoring, would still be applicable under the FDA rules even after fenfluramine is decontrolled by DEA.

Based on FDA's scientific and medical review of the eight factors and findings related to the substance's abuse potential, legitimate medical use, and dependence liability, HHS recommended that fenfluramine and its salts be removed from all schedules of the CSA. Pursuant to 21 U.S.C. 811(b), the recommendations of HHS shall be binding on DEA as to such scientific and medical matters and if the Secretary recommends that a drug or other substance not be controlled, DEA shall not control the drug or other substances. As stated in the NPRM, after careful review of all relevant data including HHS' scientific and medical evaluation and scheduling recommendation, DEA is therefore promulgating this final rule to remove fenfluramine, including its salts, isomers, and salts of such isomers whenever the existence of such salts, isomers, and salts of isomers is possible, from control under the CSA.

Determination To Decontrol Fenfluramine

Based on consideration of the comment, and the rationale set forth in the NPRM, the Administrator finds that fenfluramine does not meet the requirements for inclusion in any schedule. As such, DEA is removing fenfluramine, including its salts, isomers, and salts of such isomers whenever the existence of such salts, isomers, and salts of isomers is possible, from control under the CSA.

[1] 21 U.S.C. 812.

[2] 28 CFR 0.100.

[3] 21 U.S.C. 811(a).

[4] 38 FR 15719, May 9, 1973.

[5] 87 FR 42979.

Regulatory Analyses

Executive Orders 12866 (Regulatory Planning and Review) and 13563 (Improving Regulation and Regulatory Review)

In accordance with 21 U.S.C. 811(a), this scheduling action is subject to formal rulemaking procedures done ''on the record after opportunity for a hearing,'' which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the criteria for removing a drug or other substance from the list of controlled substances. Such actions are exempt from review by the Office of Management and Budget pursuant to section 3(d)(1) of Executive Order (E.O.) 12866 and the principles reaffirmed in E.O. 13563.

Executive Order 12988, Civil Justice Reform

This regulation 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. This rule does not have substantial direct effects on the States, on the relationship between the Federal government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination With Indian Tribal Governments

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

Regulatory Flexibility Act

The Administrator, in accordance with the Regulatory Flexibility Act (5 U.S.C. 601–612), has reviewed this rule and by approving it certifies that it will not have a significant economic impact on a substantial number of small entities. The purpose of this rule is to remove fenfluramine from the list of schedules of the CSA. This action will remove regulatory controls and administrative, civil, and criminal sanctions applicable to controlled substances for handlers and proposed handlers of fenfluramine. Accordingly, it has the potential for some economic impact in the form of cost savings.

Fenfluramine as a pharmaceutical product (Fintepla) is currently available and marketed in the U.S. Because fenfluramine is currently a schedule IV drug, all legal handling of fenfluramine is currently done under appropriate DEA license. In such instances, DEA's knowledge of its registrant population forms the basis for estimating the number of affected entities and small entities that are affected by this rulemaking. There are currently 40 unique registrations authorized to handle fenfluramine specifically, as well as a number of registered analytical labs that are authorized to handle schedule IV controlled substances generally. From review of entity names, DEA estimates these 40 registrations represent 27 entities. Some of these entities are likely to be small entities. However, since DEA does not have information of registrant size and the majority of DEA registrants are small entities or are employed by small entities, DEA estimates a maximum of 27 entities are small entities. Therefore, DEA conservatively estimates as many as 27 small entities are affected by this final rule. However, because this rule would remove fenfluramine from regulatory controls of the CSA, it is likely to result in some cost savings. Any person planning to handle fenfluramine will realize cost savings in the form of saved DEA registration fees, and the elimination of physical security, recordkeeping, and reporting requirements. Because of these factors, DEA projects that this rule will not result in a significant economic impact on a substantial number of small entities.

Administrative Procedure Act

The Administrative Procedure Act requires the publication of a substantive rule to be made not less than 30 days before its effective date.[6] However, this requirement need not apply for ''a substantive rule which . . . relieves a restriction.'' [7] Therefore, DEA makes this rule effective immediately upon publication.

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 that this action would not result in any Federal mandate that may result ''in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year.'' 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 the final rule 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, 21 CFR part 1308 is amended to read 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.

§ 1308.14 [Amended]

■ 2. In § 1308.14, remove and reserve paragraph (d).

Signing Authority

This document of the Drug Enforcement Administration was signed on December 12, 2022, by Administrator Anne Milgram. 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**.

Scott Brinks,

Federal Register Liaison Officer, Drug Enforcement Administration.

[FR Doc. 2022–27400 Filed 12–22–22; 8:45 am]

BILLING CODE 4410–09–P

[6] 5 U.S.C. 553(d).

[7] 5 U.S.C. 553(d)(1).

(dg) Boldenone.
(dr) Boldione.
(e) Calusterone.
(eg) 4–chlorotestosterone, which is also called clostebol.
(er) Dehydrochloromethyltestosterone.
(f) Desoxymethyltestosterone.
(fg) Delta1–dihydrotestosterone.
(fr) 4–dihydrotestosterone, which is also called stanolone.
(g) Drostanolone.
(gg) Ethylestrenol.
(gr) Fluoxymesterone.
(h) Formebulone, which is also called fromebolone.
(hg) Furazabol.
(hr) 13beta–ethyl–17beta–hydroxygon–4–en–3–one.
(i) 4–hydroxytestosterone.
(ig) 4–hydroxy–19–nortestosterone.
(ir) Mestanolone.
(j) Mesterolone.
(jg) Methandienone, which is also called methandrostenolone.
(jr) Methandriol.
(k) Methasterone.
(kg) Methenolone.
(kr) 17alpha–methyl–3beta, 17beta–dihydroxy–5alpha–androstane.
(L) 17alpha–methyl–3alpha,17beta–dihydroxy–5alpha–androstane.
(Lg) 17alpha–methyl–3beta,17beta–dihydroxyandrost–4–ene.
(Lr) 17alpha–methyl–4–hydroxynandrolone.
(m) Methyldienolone.
(mg) Methyltestosterone.
(mr) Methyltrienolone.
(n) Mibolerone.
(ng) 17alpha–methyl–delta1–dihydrotestosterone, which is also called 17–alpha–methyl–1–testosterone.
(nr) Nandrolone.
(o) 19–nor–4–androstenediol (3beta, 17beta–dihydroxyestr–4–ene; 3alpha, 17beta–dihydroxyestr–4–ene).
(og) 19–nor–5–androstenediol (3beta, 17beta–dihydroxyestr–5–ene; 3alpha, 17beta–dihydroxyestr–5–ene).
(or) 19–nor–4,9(10)–androstadienedione.
(p) 19–nor–4–androstenedione (estr–4–en–3,17–dione).
(pg) 19–nor–5–androstenedione (estr–5–en–3,17–dione).
(pr) Norbolethone.
(q) Norclostebol.
(qg) Norethandrolone.
(qr) Normethandrolone.
(r) Oxandrolone.
(rg) Oxymesterone.
(rr) Oxymetholone.
(s) Prostanozol.
(sg) Stanozolol.
(sr) Stenbolone.
(t) Testolactone.
(tg) Testosterone.
(tr) Tetrahydrogestrinone.
(u) Trenbolone.

History: 1971 c. 219; 1981 c. 6; 1981 c. 206 ss. 32 to 40, 57; 1995 a. 448 ss. 181 to 200, 475, 476; Stats. 1995 s. 961.18; 1997 a. 220; 2009 a. 180; 2013 a. 351; ss. CSB 2.19, 2.21, 2.25, 2.29, 2.30, 2.37, 2.87, 2.89, 2.92, Wis. adm. code.

NOTE: See 1993–94 stats. for notes on actions by the Controlled Substances Board under s. 161.11 (1), 1993 stats.

961.19 Schedule IV tests. (1m) The controlled substances board shall add a substance to schedule IV upon finding that:

(a) The substance has a low potential for abuse relative to substances included in schedule III;

(b) The substance has currently accepted medical use in treatment in the United States; and

(c) Abuse of the substance may lead to limited physical dependence or psychological dependence relative to the substances included in schedule III.

(2m) The controlled substances board may add a substance to schedule IV without making the findings required under sub. (1m) if the substance is controlled under schedule IV of 21 USC 812 (c) by a federal agency as the result of an international treaty, convention or protocol.

History: 1971 c. 219; 1995 a. 448 ss. 201, 202, 477; Stats. 1995 s. 961.19.

961.20 Schedule IV. Unless specifically excepted by state or federal law or regulation or more specifically included in another schedule, the following controlled substances are listed in schedule IV:

(2) DEPRESSANTS. Any material, compound, mixture or preparation which contains any quantity of any of the following substances having a depressant effect on the central nervous system, including any of their salts, isomers and salts of isomers that are theoretically possible within the specific chemical designation:

(a) Alfaxalone;
(ak) Alprazolam;
(am) Barbital;
(ap) Brexanolone;
(ar) Bromazepam;
(av) Camazepam;
(ax) Carisoprodol;
(b) Chloral betaine;
(c) Chloral hydrate;
(cd) Clobazam;
(cg) Clotiazepam;
(cm) Chlordiazepoxide;
(cn) Clonazepam;
(co) Cloxazolam;
(cp) Clorazepate;
(cpm) Daridorexant;
(cq) Delorazepam;
(cr) Diazepam;
(cs) Dichloralphenazone;
(cu) Estazolam;
(d) Ethchlorvynol;
(e) Ethinamate;
(ed) Ethyl loflazepate;
(ef) Flualprazolam;
(eg) Fludiazepam;
(ej) Flunitrazepam;
(em) Flurazepam;
(en) Fospropofol;
(eo) Halazepam;
(ep) Haloxazolam;
(eq) Ketazolam;
(eqm) Lemborexant;
(er) Lorazepam;
(es) Loprazolam;
(eu) Lormetazepam;
(ew) Mebutamate;
(ey) Medazepam;
(f) Methohexital;
(g) Meprobamate;
(h) Methylphenobarbital, which is also called mephobarbital;
(hg) Midazolam;

(hh) Nimetazepam;
(hj) Nitrazepam;
(hk) Nordiazepam;
(hm) Oxazepam;
(hr) Oxazolam;
(j) Paraldehyde;
(k) Petrichloral;
(m) Phenobarbital;
(md) Pinazepam;
(mg) Prazepam;
(mm) Quazepam;
(mo) Remimazolam;
(mr) Suvorexant;
(n) Temazepam;
(ng) Tetrazepam;
(nm) Triazolam;
(o) Zaleplon;
(p) Zolpidem;
(q) Zopiclone.

(2m) STIMULANTS. Any material, compound, mixture, or preparation which contains any quantity of any of the following substances having a stimulant effect on the central nervous system, including any of their salts, isomers and salts of isomers that are theoretically possible within the specific chemical designation:

(a) Diethylpropion.
(ad) Cathine.
(ag) N,N−dimethyl−1,2−diphenylethylamine, commonly known as "SPA".
(ak) Ephedrine, if ephedrine is the only active medicinal ingredient or if there are only therapeutically insignificant quantities of another active medicinal ingredient.
(ar) Fencamfamine.
(at) Fenproporex.
(bm) Mazindol.
(br) Mefenorex.
(bu) Modafinil.
(c) Pemoline, including its organometallic complexes and chelates.
(d) Phentermine.
(e) Pipradrol.
(em) Serdexmethylphenidate.
(f) Sibutramine.
(g) Solriamfetol.

(3) NARCOTIC DRUGS CONTAINING NONNARCOTIC ACTIVE MEDICINAL INGREDIENTS. Any compound, mixture or preparation containing any of the following narcotic drugs or their salts, isomers or salts of isomers, in limited quantities as set forth below, calculated as the free anhydrous base or alkaloid, which also contains one or more nonnarcotic, active medicinal ingredients in sufficient proportion to confer upon the compound, mixture or preparation valuable medicinal qualities other than those possessed by the narcotic drug alone:

(a) Not more than 1.0 milligrams of difenoxin and not less than 25 micrograms of atropine sulfate per dosage unit.

(4) OTHER SUBSTANCES. Any material, compound, mixture or preparation which contains any quantity of any of the following substances or their salts:

(a) Dextropropoxyphene (Alpha−(+)−4−dimethylamino−1, 2−diphenyl−3−methyl−2−propionoxybutane).
(am) Fenfluramine, including any of its isomers and salts of isomers.
(b) Pentazocine, including any of its isomers and salts of isomers.
(c) Butorphanol, including any of its isomers and salts of isomers.
(cm) Eluxadoline, including any of its isomers, and salts of isomers.
(d) Lorcaserin, including any of its isomers and salts of isomers.
(e) Tramadol, including any of its isomers and salts of isomers.

(5) EXCEPTIONS. The controlled substances board may except by rule any compound, mixture or preparation containing any depressant substance included in sub. (2) from the application of all or any part of this chapter if the compound, mixture or preparation contains one or more active medicinal ingredients not having a depressant effect on the central nervous system, and if the admixtures are in combinations, quantity, proportion or concentration that vitiate the potential for abuse of the substances which have a depressant effect on the central nervous system.

History: 1971 c. 219; 1979 c. 32; 1981 c. 206 ss. 34m, 41 to 52; 1993 a. 468; 1995 a. 448 ss. 203 to 220, 478, 479; Stats. 1995 s. 961.20; 2013 a. 351; 2015 a. 195 s. 83; 2021 a. 239 s. 74; ss. CSB 2.15, 2.19, 2.21, 2.24, 2.25, 2.28, 2.36, 2.38, 2.48, 2.67, 2.74, 2.77, 2.79, 2.82, 2.84, 2.86, 2.93, Wis. adm. code.

NOTE: See 1979−80 stats. and 1993−94 stats. for notes on actions by the Controlled Substances Board under s. 161.11 (1), 1993 stats.

961.21 Schedule V tests. (1m) The controlled substances board shall add a substance to schedule V upon finding that:

(a) The substance has low potential for abuse relative to the controlled substances included in schedule IV;
(b) The substance has currently accepted medical use in treatment in the United States; and
(c) The substance has limited physical dependence or psychological dependence liability relative to the controlled substances included in schedule IV.

(2m) The controlled substances board may add a substance to schedule V without making the findings required by sub. (1m) if the substance is controlled under schedule V of 21 USC 811 (c) by a federal agency as the result of an international treaty, convention or protocol.

History: 1971 c. 219; 1995 a. 448 ss. 221, 222, 480; Stats. 1995 s. 961.21.

961.22 Schedule V. Unless specifically excepted by state or federal law or regulation or more specifically included in another schedule, the following controlled substances are listed in schedule V:

(2) NARCOTIC DRUGS CONTAINING NONNARCOTIC ACTIVE MEDICINAL INGREDIENTS. Any compound, mixture or preparation containing any of the following narcotic drugs or their salts, isomers or salts of isomers, in limited quantities as set forth below, calculated as the free anhydrous base or alkaloid, which also contains one or more nonnarcotic, active medicinal ingredients in sufficient proportion to confer upon the compound, mixture or preparation, valuable medicinal qualities other than those possessed by the narcotic drug alone:

(a) Not more than 200 milligrams of codeine per 100 milliliters or per 100 grams.
(b) Not more than 100 milligrams of dihydrocodeine per 100 milliliters or per 100 grams.
(c) Not more than 100 milligrams of ethylmorphine per 100 milliliters or per 100 grams.
(d) Not more than 2.5 milligrams of diphenoxylate and not less than 25 micrograms of atropine sulfate per dosage unit.
(e) Not more than 100 milligrams of opium per 100 milliliters or per 100 grams.
(f) Not more than 0.5 milligrams of difenoxin and not less than 25 micrograms of atropine sulfate per dosage unit.

(2m) PSEUDOEPHEDRINE. Pseudoephedrine or any of its salts, isomers, or salts of isomers.

(3) OTHER STIMULANTS. Any material, compound, mixture or preparation which contains any quantity of any of the following substances having a stimulant effect on the central nervous system, including any of their salts, isomers and salts of isomers that

State of Wisconsin
Department of Safety & Professional Services

AGENDA REQUEST FORM

1) Name and title of person submitting the request: Whitney DeVoe, Board Counsel		2) Date when request submitted: 02/27/23 Items will be considered late if submitted after 12:00 p.m. on the deadline date which is 8 business days before the meeting	
3) Name of Board, Committee, Council, Sections: Controlled Substances Board			
4) Meeting Date: 03/10/2023	5) Attachments: ☒ Yes ☐ No	6) How should the item be titled on the agenda page? Possible rulemaking project for CSB 4 – Discussion and Consideration	
7) Place Item in: ☒ Open Session ☐ Closed Session	8) Is an appearance before the Board being scheduled? ☐ Yes ☒ No	9) Name of Case Advisor(s), if applicable: N/A	
10) Describe the issue and action that should be addressed: Discussion of possible rulemaking project related to CSB 4 and methods of obtaining monitored prescription drug history reports.			
11) Authorization Whitney DeVoe — Signature of person making this request		02/27/23 — Date	
Supervisor (Only required for post agenda deadline items)		Date	
Executive Director signature (Indicates approval for post agenda deadline items)		Date	

Directions for including supporting documents:
1. This form should be saved with any other documents submitted to the Agenda Items folders.
2. Post Agenda Deadline items must be authorized by a Supervisor and the Policy Development Executive Director.
3. If necessary, provide original documents needing Board Chairperson signature to the Bureau Assistant prior to the start of a meeting.

Chapter CSB 4

PRESCRIPTION DRUG MONITORING PROGRAM

Note: Chapter Phar 18 was renumbered chapter CSB 4 under s. 13.92 (4) (b) 1., Stats., Register September 2015 No. 717.

CSB 4.01 Authority and scope. The rules in this chapter are adopted under authority in ss. 227.11 (2) (a) and 961.385, Stats., for the purpose of creating a prescription drug monitoring program to collect and disclose information relating to the prescribing and dispensing of monitored prescription drugs.

History: CR 12–009: cr. Register October 2012 No. 682, eff. 1–1–13; correction made under s. 13.92 (4) (b) 7., Stats., Register September 2015 No. 717; EmR1706: emerg. am., eff. 4–1–17; CR 17–028: am. Register December 2017 No. 744, eff. 1–1–18.

CSB 4.02 Definitions. As used in this chapter:

(1) "Access" means to have the ability to view monitored prescription drug history reports, audit trails, and PDMP data as authorized by s. CSB 4.09.

(2) "Administer" has the meaning given in s. 961.385 (1) (a), Stats.

(2m) "Agent" has the meaning given in s. 961.385 (1) (ab), Stats.

(3) "Animal" has the meaning given in s. 89.02 (1m), Stats.

(3m) "ASAP" means the American Society for Automation in Pharmacy.

Note: Contact: American Society for Automation in Pharmacy, 492 Norristown Road, Suite 160; Blue Bell, PA 19422; phone: (610) 825–7783; fax: (610) 825–7641; webpage: http://asapnet.org/index.html.

(3s) "Audit trail" means the log that contains information about each time the PDMP system discloses PDMP data, monitored prescription drug history reports, and prescribing metrics reports.

(4) "Board" means the Controlled Substances Board.

(4m) "Business day" has the meaning given in s. 961.385 (1) (ad), Stats.

(5) "Controlled substance" means a drug, substance, analog, or precursor described in any of the following:

(a) Schedule I, II, III, IV, or V in the federal controlled substances act, 21 USC 812 (b) (1) to (b) (5) and (c), as changed and updated by 21 CFR 1308.

(b) Schedule I, II, III, IV, or V in subch. II of ch. 961, Stats., as amended by ch. CSB 2.

(5k) "DEA registration number" means the registration number issued to a dispenser or practitioner by the federal department of justice, drug enforcement administration.

(5m) "Deliver" or "delivery" has the meaning in s. 961.385 (1) (ae), Stats.

(6) "Department" means the department of safety and professional services.

(7) "Dispense" has the meaning given in s. 961.385 (1) (af), Stats.

(8) "Dispenser" means all of the following:

(a) A pharmacy.

Note: A site of remote dispensing authorized under s. 450.062, Stats., is under the supervision of a pharmacy.

(b) A practitioner who dispenses a monitored prescription drug.

(9) "Dispenser delegate" means any of the following:

(a) A managing pharmacist of a pharmacy.

(b) An agent or employee of a practitioner who has been delegated the task of satisfying the data compilation and submission requirements of ss. CSB 4.04 and 4.05.

(10) "Dispensing data" means data compiled pursuant to s. CSB 4.04.

(11) "Drug" has the meaning given in s. 450.01 (10), Stats.

(11c) "Healthcare Professional" means a pharmacist, practitioner, registered nurse licensed under s. 441.06, Stats., substance abuse counselor, as defined in s. 440.88 (1) (b), Stats., or individual authorized under s. 457.02 (5m), Stats., to treat alcohol or substance dependency or abuse as a specialty.

(11g) "Hospital" has the meaning given in s. 50.33 (2), Stats.

(11n) "Law enforcement agency" has the meaning given in s. 165.77 (1) (b), Stats.

(11r) "Managing pharmacist" means a pharmacist designated by the pharmacy owner to have responsibility for and direct control of pharmaceutical operations in a pharmacy.

(11w) "Medical coordinator" means a person who medically coordinates, directs, supervises, or establishes standard operating procedures for a healthcare professional.

(12) (a) "Monitored prescription drug" means all of the following:

1. A controlled substance included in s. 961.385 (1) (ag), Stats.

2. A drug identified by the board as having a substantial potential for abuse in s. CSB 4.03.

(b) "Monitored prescription drug" does not mean a controlled substance that by law may be dispensed without a prescription order.

(12m) "Monitored prescription drug history report" means all of the following information about a patient, patient address, practitioner, or dispenser compiled by the PDMP system and disclosed as authorized in ss. CSB 4.09 and 4.11:

(a) PDMP data.

(b) Reports submitted to the program pursuant to s. 961.37, Stats.

(c) Information submitted to the program by a healthcare professional.

(d) Information from the analytics platform.

(13) "Patient" has the meaning given in s. 961.385 (1) (aj), Stats.

(14e) "PDMP" means the Wisconsin prescription drug monitoring program.

(15) "PDMP data" means the information compiled and analyzed by the PDMP system from dispensing data submitted to it by dispensers.

(15b) "PDMP system" means the web−based application, analytics platform, and all related hardware and software that facilitates the submission of dispensing data and the access to and disclosure of PDMP data, monitored prescription drug history reports, audit trails, and prescribing metrics reports.

(15e) "Personally identifiable information" means information that can be associated with a particular person through one or more identifiers or other information or circumstances.

(15g) "Pharmacist" has the meaning given in s. 961.385 (1) (aL), Stats. For the purposes of this program, the board recognizes a pharmacist licensed by another state that engages in the practice of pharmacy within the contiguous borders of this state or who practices at a pharmacy licensed under s. 450.065, Stats. as a person authorized to engage in the practice of pharmacy.

(15r) "Pharmacist delegate" means an agent of a pharmacist to whom the pharmacist has delegated the task of accessing monitored prescription drug history reports.

(16) "Pharmacy" has the meaning given in s. 961.385 (1) (an), Stats., including a pharmacy that chooses to solely dispense to animal patients.

(17) "Practitioner" has the meaning given in s. 961.385 (1) (ar), Stats. For the purposes of this program, the board recognizes a practitioner licensed by another state that engages in the practice of their credentialed profession within the contiguous borders of this state as a person authorized to prescribe and administer drugs.

(18) "Practitioner delegate" means an agent of a practitioner to whom the practitioner has delegated the task of accessing monitored prescription drug history reports.

(18m) "Prescribing metrics report" means all of the following information about a practitioner compiled by the PDMP system and disclosed as authorized in s. CSB 4.09:

(a) PDMP data.

(b) Audit trails.

(c) Reports submitted to the program pursuant to s. 961.37, Stats., about a patient to whom the practitioner has issued a prescription order.

(d) Information from the analytics platform.

(19) "Prescription" has the meaning given in s. 450.01 (19), Stats.

(20) "Prescription order" has the meaning given in s. 961.385 (1) (b), Stats.

(21) "Program" means the prescription drug monitoring program established under this chapter.

(21m) "Prosecutorial unit" has the meaning given in s. 978.001 (2), Stats.

(23) "Zero report" means a report that indicates that a dispenser has not dispensed a monitored prescription drug since the previous submission of dispensing data or a zero report.

History: CR 12−009: cr. Register October 2012 No. 682, eff. 1−1−13; correction in (5) (b) made under s. 13.92 (4) (b) 7., Stats., Register October 2012 No. 682; CR 13−065: cr. (3m), (13e), am. (16), (17), r. (22) Register February 2014 No. 698, eff. 3−1−14; (13e) renum. to (14e) under s. 13.92 (4) (b) 1., Stats., Register February 2014 No. 698; correction in (17) made under s. 13.92 (4) (b) 7., Stats., Register February 2014 No. 698; CR 14−003: am. (8) (a), renum. (9) to (9) (intro.) and am., cr. (9) (a), (b), (11g), (11r), am. (15) (intro.), cr. (15g), (15r), am. (17) Register August 2014 No. 704, eff. 9−1−14; correction in (3), (9) (b), (10), (12) (a) 1., 2., (15) (b), (15g), (17), (20) made under s. 13.92 (4) (b) 7., Stats., Register September 2015 No. 717; CR 15−101: am. (4) Register June 2016 No. 726, eff. 7−1−16; EmR1706: emerg. am. (1), (2), cr. (2m), (3s), (4m), (5m), am. (7), cr. (11c), (11n), am. (11r), cr. (11w), am. (12) (a) 1., cr. (12m), am. (13), r. (14), cons. and renum. (15) (intro.) and (a) to (15) and am., r. (15) (b), cr. (15b), (15e), am. (15g), (15r), (16), (17), (18), cr. (18m), (21m), eff. 4−1−17; CR 17−028: am. (1), (2), cr. (2m), (3s), (4m), (5m), am. (7), cr. (11c), (11n), am. (11r), cr. (11w), am. (12) (a) 1., cr. (12m), am. (13), r. (14), cons. and renum. (15) (intro.) and (a) to (15) and am., r. (15) (b), cr. (15b), (15e), am. (15g), (15r), (16), (17), (18), cr. (18m), (21m) Register December 2017 No. 744, eff. 1−1−18; **(5k) renumbered from CSB 4.04 (1) (a) under s. 13.92 (4) (b) 1., Stats., Register August 2021 No. 788.**

CSB 4.03 Drugs that have a substantial potential for abuse. Pursuant to s. 961.385 (1) (ag), Stats., the board has identified all of the following drugs as having a substantial potential for abuse:

(1) A controlled substance identified in schedule II, III, IV or V in the federal controlled substances act, 21 USC 812 (b) (2) to (b) (5) and (c), as changed and updated by 21 CFR 1308.

(2) Gabapentin.

History: CR 12−009: cr. Register October 2012 No. 682, eff. 1−1−13; correction in (2) made under s. 13.92 (4) (b) 7., Stats., Register October 2012 No. 682; CR 13−065: am. (intro.) Register February 2014 No. 698, eff. 3−1−14; correction in (intro.) made under s. 13.92 (4) (b) 7., Stats., Register February 2014 No. 698; correction in (intro.) made under s. 13.92 (4) (b) 7., Stats., Register September 2015 No. 717; CR 15−101: r. (3) Register June 2016 No. 726, eff. 7−1−16; EmR1706: emerg. r. (2), eff. 4−1−17; CR 17−028: r. (2) Register December 2017 No. 744, eff. 1−1−18; **CR 20−080: cr. (2) Register August 2021 No. 788, eff. 9−1−21.**

CSB 4.04 Compilation of dispensing data. (1) As used in this section, "NDC number" means national drug code number, the universal product identifier used in the U.S. to identify a specific drug product.

(2) Subject to s. CSB 4.08, a dispenser shall compile dispensing data that contains all of the following information each time the dispenser dispenses a monitored prescription drug:

(a) The dispenser's full name.

(b) The dispenser's DEA registration number.

(c) The date dispensed.

(d) The prescription number.

(e) The NDC number of the monitored prescription drug.

(f) The quantity dispensed.

(g) The estimated number of days of drug therapy.

(gb) The drug dosage units.

(gd) The partial fill indicator.

(ge) The classification code for payment type.

(gm) The number of refills authorized by the prescriber.

(gs) The refill number of the prescription.

(h) The practitioner's full name.

(i) The practitioner's DEA registration number.

(j) The date prescribed.

(L) The patient's full name or if the patient is an animal, the animal's name and the owner's last name.

(m) The patient's address, or if the patient is an animal, patient's owner's address, including street address, city, state, and ZIP code.

(n) The patient's date of birth, or if the patient is an animal, patient's owner's date of birth.

(o) The patient's gender.

(p) The name recorded under s. 450.11 (1b) (bm), Stats.

(4) The board may refer a dispenser and dispenser delegate that fail to compile dispensing data as required by sub. (2) to the appropriate licensing or regulatory board for discipline.

History: CR 12−009: cr. Register October 2012 No. 682, eff. 1−1−13; CR 13−065: am. (1) (b), (e), (3) (b), (d), (i), (k) Register February 2014 No. 698, eff. 3−1−14; CR 14−003: am. (title), renum. (2) to (2) (intro.) and am., cr. (2) (ge), (gm), (gs), renum. (3) (a) to (g) and (h) to (j) to (2) (a) to (g) and (h) to (j), r. (3) (k), renum. (3) (L) to (o) to (2) (L) to (o) and am. (L) to (n), am. (4) Register August 2014 No. 704, eff. 9−1−14; correction in (2) (intro.) made under s. 35.17, Stats., and in (4) made under s. 13.92 (4) (b) 7., Stats., Register August 2014 No. 704; correction in (2) (intro.) made under s. 13.92 (4) (b) 7., Stats., Register September 2015 No. 717; CR 15−070: cr. (2) (p) Register April 2016 No. 724, eff. 4−9−17; numbering correction in (2) (p) under s. 13.92 (4) (b) 1. Register April 2016 No. 724; republished to correct CR 15−070: cr. (2) (p) effective date Register May 2016 No. 725; EmR1706: emerg. r. (1) (b), (d), (e), am. (2) (b), (e), (i), (4), eff. 4−1−17; CR 17−028: r. (1) (b), (d), (e), am. (2) (b), (e), (i), (4) Register December 2017 No. 744, eff. 1−1−18; CR 19−156: cr. (2) (gb), (gd) Register August 2020 No. 776, eff. 9−1−20; **(1) (a) renumbered to CSB 4.02 (5k), and (1) (intro.) and (c) consolidated and renumberd to (1) under s. 13.92 (4) (b) 1., Stats., correction in (1) made under s. 35.17, Stats., Register August 2021 No. 788.**

CSB 4.05 Electronic submission of dispensing data. (1) Unless exempt under s. CSB 4.08, a dispenser shall electronically submit dispensing data to the PDMP in any of the following ways:

(a) As a file that complies with the data standards identified in version 4 and release 2 of ASAP implementation guide for prescription monitoring programs.

(b) Using the prescription record entry functions of the PDMP system.

Note: The guide for dispensers which specifies the data standards in version 4 release 2 of the ASAP implementation guide for prescription monitoring programs and other electronic formats identified by the board may be obtained online at https://pdmp.wi.gov or obtained at no charge from the Department of Safety and Professional Services, 1400 East Washington Avenue, P.O. Box 8366, Madison, WI 53708.

(4) The board may refer a dispenser and dispenser delegate that fail to submit dispensing data as required by sub. (1) to the appropriate licensing or regulatory board for discipline.

History: CR 12–009: cr. Register October 2012 No. 682, eff. 1–1–13; CR 13–065: am. (2) Register February 2014 No. 698, eff. 3–1–14; CR 14–003: am. (1), (4) Register August 2014 No. 704, eff. 9–1–14; correction in (intro.) made under s. 13.92 (4) (b) 7., Stats., Register September 2015 No. 717; EmR1706: emerg. renum. (1) to (1) (intro.), cr. (1) (a), (b), r. (2), (3), r. and recr. (4), eff. 4–1–17; CR 17–028: renum. (1) to (1) (intro.), cr. (1) (a), (b), r. (2), (3), r. and recr. (4) Register December 2017 No. 744, eff. 1–1–18.

CSB 4.06 Frequency of submissions. (1) A dispenser shall submit dispensing data to the PDMP no later than 11:59 p.m. of the next business day after the monitored prescription drug is dispensed.

(2) If a dispenser does not dispense a monitored prescription drug on a business day, the dispenser shall submit no later than 11:59 p.m. of the next business day a zero report to the PDMP that accounts for each business day on which the dispenser did not dispense a monitored prescription drug.

(3) If a dispenser is not able to submit dispensing data zero report before 11:59 p.m. of the next business day as required by subs. (1) or (2), the board may grant an emergency waiver to a dispenser who satisfies all of the following conditions:

(a) The dispenser is not able to submit dispensing data or a zero report because of circumstances beyond its control.

(b) The dispenser files with the board a written application for an emergency waiver on a form provided by the board prior to the required submission of dispensing data or zero report.

Note: The application for an emergency waiver may be obtained online at www.dsps.wi.gov or obtained at no charge from the Department of Safety and Professional Services, 1400 East Washington Avenue, P.O. Box 8366, Madison, WI 53708.

(4) Unless otherwise specified by the board, an emergency waiver granted under sub. (3) shall only be effective for 7 days.

(5) The board may refer a dispenser and dispenser delegate that fail to submit dispensing data or a zero report as required by subs. (1) and (2), or be granted an emergency waiver under sub. (3), or a dispenser and a dispenser delegate that submit false information to the PDMP to the appropriate licensing or regulatory board for discipline.

History: CR 12–009: cr. Register October 2012 No. 682, eff. 1–1–13; CR 13–065: am. (1), (2), (3) (intro.), r. (4) to (6), (9), renum. (7) to (4) and am., renum. (8) to (5) Register February 2014 No. 698, eff. 3–1–14; CR 14–003: am. (2), (5) Register August 2014 No. 704, eff. 9–1–14; EmR1706: emerg. am. (1), (2), (3), (5), eff. 4–1–17; CR 17–028: am. (1), (2), (3), (5) Register December 2017 No. 744, eff. 1–1–18.

CSB 4.07 Correction of dispensing data. (1) A dispenser shall electronically correct dispensing data in the PDMP system within 5 business days of discovering an omission, error, or inaccuracy in previously submitted dispensing data.

(2) The board may refer a dispenser and dispenser delegate that fail to correct dispensing data as required by sub. (1) to the appropriate licensing or regulatory board for discipline.

Note: The written notice to the board may be submitted through an account with the board, sent by electronic mail or sent by U.S. mail to the Department of Safety and Professional Services 1400 East Washington Avenue, P.O. Box 8366, Madison, WI 53708.

History: CR 12–009: cr. Register October 2012 No. 682, eff. 1–1–13; CR 14–003: am. Register August 2014 No. 704, eff. 9–1–14; EmR1706: emerg. r. and recr. eff. 4–1–17; CR 17–028: r. and recr. Register December 2017 No. 744, eff. 1–1–18.

CSB 4.08 Exemptions from compiling and submitting dispensing data. (1) The board shall exempt a dispenser from compiling and submitting dispensing data and from submitting a zero report as required under this chapter until the dispenser is required to renew its license, or until the dispenser dispenses a monitored prescription drug, if the dispenser satisfies all of the following conditions:

(a) The dispenser provides evidence sufficient to the board that the dispenser does not dispense monitored prescription drugs.

(b) The dispenser files with the board a written request for exemption on a form provided by the board.

Note: The application for an exemption may be obtained online at www.dsps.wi.gov or at no charge from the Department of Safety and Professional Services 1400 East Washington Avenue, P.O. Box 8366, Madison, WI 53708. A dispenser who is already exempt can renew his or her exemption as part of the licensure renewal process.

(2) A dispenser is not required to compile or submit dispensing data when the monitored prescription drug is administered directly to a patient.

(2m) A dispenser is not required to compile or submit dispensing data when the monitored prescription drug is compounded, packaged, or labeled in preparation for delivery but is not delivered.

(3) A dispenser is not required to compile or submit dispensing data when the monitored prescription drug is a substance listed in the schedule in s. 961.22, Stats., and is not a narcotic drug, as defined in s. 961.01 (15), Stats., and is dispensed pursuant to a prescription order for a number of doses that is intended to last the patient 7 days or less.

(4) A dispenser who is not otherwise required to have a DEA registration number is not required to compile or submit dispensing data when dispensing Gabapentin.

History: CR 12–009: cr. Register October 2012 No. 682, eff. 1–1–13; CR 14–003: am. (1) (a), cr. (3) Register August 2014 No. 704, eff. 9–1–14; CR 15–101: am. (1) Register June 2016 No. 726, eff. 7–1–16; EmR1706: emerg. cr. (2m), eff. 4–1–17; CR 17–028: cr. (2m) Register December 2017 No. 744, eff. 1–1–18; **CR 20–080: cr. (4) Register August 2021 No. 788, eff. 9–1–21.**

CSB 4.09 Access to monitored prescription drug history reports and PDMP data about a patient. (1) Healthcare professionals may access monitored prescription drug history reports about a patient for any of the following reasons:

(a) The healthcare professional is directly treating or rendering assistance to the patient.

(b) The healthcare professional is being consulted regarding the health of the patient by an individual who is directly treating or rendering assistance to the patient.

(c) Scientific research purposes if all of the following requirements are met:

1. The patient is a direct patient of the healthcare professional.

2. The healthcare professional has obtained informed consent from the patient to access monitored prescription drug history reports for scientific research purposes.

(d) Purposes of conducting an overdose fatality review.

(2) Pharmacist delegates and practitioner delegates may access monitored prescription drug history reports about a patient for any of the following reasons:

(a) A pharmacist or practitioner who is directly treating or rendering assistance to the patient has delegated the task of obtaining monitored prescription drug history reports about the patient to the pharmacist delegate or practitioner delegate.

(b) A pharmacist or practitioner who is being consulted regarding the health of the patient by an individual who is directly treating or rendering assistance to the patient has delegated the task of obtaining monitored prescription drug history reports about the patient to the pharmacist delegate or practitioner delegate.

(3) Healthcare professionals, pharmacist delegates, and practitioner delegates may only disclose a monitored prescription drug history report about a patient obtained pursuant to sub. (1) or (2) in the following situations:

(a) To the patient as part of treating or rendering assistance to the patient.

(b) To another healthcare professional or a medical coordinator for consultation about the health of the patient or as part of treating or rendering assistance to the patient.

(c) To the pharmacist or practitioner who is directly treating or rendering assistance to the patient.

(d) To a law enforcement agency as required by s. 146.82, Stats.

(4) To obtain access to monitored prescription drug history reports as authorized in subs. (1) and (2), healthcare professionals, pharmacist delegates, and practitioner delegates shall do one of the following:

(a) Create an account with the PDMP system.

(b) Create an account with a prescription monitoring program operated by a relevant agency in another jurisdiction with which the board exchanges monitored prescription drug history reports or PDMP data pursuant to s. CSB 4.14.

(c) Create an account with a pharmacy or other entity at which pharmacists dispense or administer monitored prescription drugs in the course of professional practice with which the board has determined to have at least equivalent capability to maintain the confidentiality of monitored prescription drug history reports or that is connected to and lawfully obtains data from the state−designated entity under ch. 153, Stats.

(d) Create an account with a hospital or other entity at which practitioners prescribe, dispense, or administer monitored prescription drugs in the course of professional practice with which the board has determined to have at least equivalent capability to maintain the confidentiality of monitored prescription drug history reports or that is connected to and lawfully obtains data from the state−designated entity under ch. 153, Stats.

History: CR 12−009: cr. Register October 2012 No. 682, eff. 1−1−13; CR 14−003: am. (1), renum. (2) to (2) (intro.) and am., cr. (2) (a) to (d), am. (3) Register August 2014 No. 704, eff. 9−1−14; corrections in (1), (2) (b), (3) (a) Register September 2015 No. 717; EmR1706: emerg. r. and recr., eff. 4−1−17; CR 17−028: r. and recr. Register December 2017 No. 744, eff. 4−1−17; s. 35.17 corrections in (3) (intro.), (4) (intro.), Register December 2017 No. 744; CR 19−156: cr. (1) (c), (d) Register August 2020 No. 776, eff. 9−1−20.

CSB 4.093 Monitored prescription drug history reports and audit trails about healthcare professionals. (1) Healthcare professionals may access audit trails about themselves and their practitioner delegates or pharmacist delegates.

(2) A practitioner may access the audit trails accessible to healthcare professionals and a prescribing metrics report about themself.

(2m) Department staff who are charged with investigating dispensers, dispenser delegates, pharmacists, pharmacist delegates, practitioners, and practitioner delegates may access the audit trails related to s. CSB 4.12 (3) (f) and (g).

(3) Medical coordinators may access prescribing metrics reports and audit trails about a healthcare professional whom the medical coordinator coordinates, directs, or supervises or for whom the medical coordinator establishes standard operating procedures that contain no personally identifiable information about a patient if the medical coordinator is conducting any of the following activities:

(a) Evaluating the job performance of the healthcare professional.

(b) Performing quality assessment and improvement activities, including outcomes evaluation or development of clinical guidelines for the healthcare professional.

(4) To obtain access to prescribing metrics reports and audit trails as authorized in subs. (1) and (2), healthcare professionals, pharmacist delegates, and practitioner delegates shall create an account with the PDMP system.

(5) To obtain access to prescribing metrics reports, and audit trails about a healthcare professional, a medical coordinator shall create an account with the PDMP system.

History: EmR1706: emerg. cr. eff. 4−1−17; CR 17−028: cr. Register December 2017 No. 744, eff. 4−1−17; s. 35.17 correction in (4), Register December 2017 No. 744; CR 19−156: cr. (2m) Register August 2020 No. 776, eff. 9−1−20.

CSB 4.097 Deny, suspend, revoke or otherwise restrict or limit access. (1) The board may deny, suspend, revoke, or otherwise restrict or limit a healthcare professional's, pharmacist delegate's, practitioner delegate's, or medical coordinator's access to monitored prescription drug history reports, prescribing metrics reports, PDMP data, and audit tails for any of the following reasons:

(a) The healthcare professional, pharmacist delegate, practitioner delegate, or medical coordinator is suspected of attempting to access, accessing, or disclosing a monitored prescription drug history report, prescribing metrics report, PDMP data, or audit trail in violation of s. 146.82 or 961.385, Stats., this chapter, or other state or federal laws or regulations relating to the privacy of patient health care records.

(b) The healthcare professional is no longer licensed in this state or in another state and recognized by this state as a person to whom the board may grant access pursuant to s. CSB 4.09 or 4.093.

(c) The board, or other licensing board, or regulatory agency takes adverse action against the healthcare professional, pharmacist delegate, practitioner delegate, or medical coordinator.

(d) A licensing board or equivalent regulatory agency in another jurisdiction takes adverse action against the healthcare professional, pharmacist delegate, practitioner delegate, or medical coordinator.

(e) The federal department of justice, drug enforcement administration takes adverse action against the healthcare professional, pharmacist delegate, practitioner delegate, or medical coordinator.

(f) The healthcare professional, pharmacist delegate, practitioner delegate, or medical coordinator is convicted of a crime substantially related to the prescribing, administering, or dispensing of a monitored prescription drug.

(g) The pharmacist delegate or practitioner delegate is no longer delegated the task of accessing monitored prescription drug history reports.

(h) The medical coordinator no longer coordinates, directs, supervises, or establishes standard operating procedures for a healthcare professional.

(2) The board may temporarily suspend access to monitored prescription drug history reports, prescribing metrics reports, PDMP data, and audit trails upon discovering circumstances that indicate a healthcare professional, pharmacist delegate, practitioner delegate, or medical coordinator has performed any of the actions identified in sub. (1) (a).

History: EmR1706: emerg. cr., eff. 4−1−17; CR 17−028: cr. Register December 2017 No. 744, eff. 1−1−18.

CSB 4.10 Requests for review. (1) A dispenser, healthcare professional, pharmacist delegate, practitioner delegate, or medical coordinator may request that the board review any of the following:

(b) The denial of an emergency waiver requested pursuant to s. CSB 4.06 (3).

(c) The denial, suspension, revocation or other restriction or limitation imposed on the healthcare professional's, pharmacist delegate's, practitioner delegate's, or medical coordinator's account pursuant to s. CSB 4.097.

(2) To request a review, the dispenser, health care professional, pharmacist delegate, practitioner delegate, or medical coordinator shall file a written request with the board within 20 days after the mailing of the notice of the action in sub. (1). The request shall be in writing and include all of the following:

(a) The dispenser's, healthcare professional's, pharmacist delegate's, practitioner delegate's, or medical coordinator's name and address, including street address, city, state and ZIP code.

(b) The citation to the specific statute or rule on which the request is based.

(3) The board shall conduct the review at its next regularly scheduled meeting and notify the dispenser, healthcare professional, pharmacist delegate, practitioner delegate, or medical coordinator of the time and place of the review.

(4) No discovery is permitted.

(5) The board shall preside over the review. The review shall be recorded by audio tape unless otherwise specified by the board.

(6) The board shall provide the dispenser, healthcare professional, pharmacist delegate, practitioner delegate, or medical coordinator with an opportunity to submit written documentation, make a personal appearance before the board and present a statement. The board may establish a time limit for making a presentation. Unless otherwise determined by the board, the time for making a personal appearance shall be 20 minutes.

(7) If the dispenser, healthcare professional, pharmacist delegate, practitioner delegate, or medical coordinator fails to appear for a review, or withdraws the request for a review, the board may note the failure to appear in the minutes and affirm its original decision without further action.

History: CR 12–009: cr. Register October 2012 No. 682, eff. 1–1–13; correction in (1) (b) made under s. 13.92 (4) (b) 7., Stats., Register February 2014 No. 698; CR 14–003: am. (1) (intro.), (2) (intro.), (b), (3), (6), (7) Register August 2014 No. 704, eff. 9–1–14; correction in (1) (a) to (c) made under s. 13.92 (4) (b) 7., Stats., Register September 2015 No. 717; CR 15–101: am. (1) (c), (2) (a) Register June 2016 No. 726, eff. 7–1–16; s. 35.17 correction in (1) (c), Register June 2016 No. 726; EmR1706: emerg. am. (1) (intro.), r. (1) (a), am. (1) (c), (2) (intro.), (a), (3), (6), (7), eff. 4–1–17; CR 17–028: am. (1) (intro.), r. (1) (a), am. (1) (c), (2) (intro.), (a), (3), (6), (7) Register December 2017 No. 744, eff. 1–1–18; correction in (1) (c) made under s. 13.92 (4) (b) 7., Stats., December 2017 No. 744.

CSB 4.105 Practitioners' requirement to review monitored prescription drug history reports. (1) A practitioner, or a practitioner delegate assisting the practitioner in accordance with the standards of practice for the practitioner's profession, shall review the monitored prescription drug history report about a patient before the practitioner issues a prescription order for the patient unless any of the following conditions are met:

(a) The patient is receiving hospice care, as defined in s. 50.94 (1) (a).

(b) The prescription order is for a number of doses that is intended to last the patient 3 days or less and is not subject to refill.

(c) The monitored prescription drug is lawfully administered to the patient.

(d) The practitioner is unable to review the patient's monitored prescription drug history reports before issuing a prescription order for the patient due to an emergency.

(e) The practitioner is unable to review the patient's records under their program because the PDMP system is not operational or due to other technological failure that the practitioner reports to the board.

(2) Reviews of reports or other information not provided by the board as part of the program that summarize or analyze PDMP data do not satisfy the requirement to review a monitored prescription drug history report under sub. (1).

(3) The board may refer a practitioner that fails to review a monitored prescription drug history report about a patient prior to issuing a prescription order for that patient to the appropriate licensing or regulatory board for discipline.

History: EmR1706: emerg. cr., eff. 4–1–17; CR 17–028: cr. Register December 2017 No. 744, eff. 1–1–18.

CSB 4.11 Methods of obtaining monitored prescription drug history reports. (1) The board shall disclose the monitored prescription drug history report about a patient to the patient if he or she does all of the following:

(a) Appears in person at the department with two forms of valid proof of identity, one of which is valid government–issued photographic identification or mails to the department copies of two forms of valid proof of identity, one of which is valid government–issued photographic identification.

(b) Makes a request for the monitored prescription drug history reports about the patient on a form provided by the board. If the request is mailed, the form shall be notarized.

(2) The board shall disclose the monitored prescription drug history report about a patient to a person authorized by the patient if the person authorized by the patient does all of the following:

(a) Appears in person at the department with two forms of valid proof of identity, one of which is valid government–issued photographic identification.

(b) Provides proof sufficient to the board of the authorization or delegation from the patient.

(c) Makes a request for the monitored prescription drug history report on a form provided by the board.

(5) The board shall disclose the minimum necessary amount of information in a monitored prescription drug history report about a patient, patient address, practitioner, or dispenser to designated staff of a federal or state governmental agency in the same or similar manner, and for the same or similar purposes, as those persons are authorized to access similar confidential patient health care records under ss. 146.82 and 961.385, Stats., this chapter, and other state or federal laws and regulations relating to the privacy of patient health care records if the designated staff does all of the following:

(a) Creates an account with the PDMP system.

(b) Provides proof sufficient to the board that the federal or state governmental agency is entitled to the information under s. 146.82 (2) (a) 5., Stats.

(c) Makes a request for the monitored prescription drug history report through its PDMP system account.

(d) If the PDMP system is unable to fulfill a request from designated staff through their account with the PDMP system, the board may disclose the minimum necessary amount of information necessary to designated staff of a federal or state governmental agency upon written request that cites the agency's specific authorization to access similar confidential patient health care records under ss. 146.82 and 961.385, Stats., this chapter, and other state or federal laws and regulations relating to the privacy of patient health care records.

(6) The board shall disclose the minimum necessary amount of PDMP data or information in a monitored prescription drug history report about a patient, patient address, practitioner, or dispenser to designated staff of the department who is charged with investigating dispensers, dispenser delegates, pharmacists, pharmacist delegates, practitioners, and practitioner delegates in the same or similar manner, and for the same or similar purposes, as those persons are authorized to access similar confidential patient health care records under ss. 146.82 and 961.385, Stats., this chapter, and other state or federal laws and regulations relating to the privacy of patient health care records if the designated staff does all of the following:

(a) Creates an account with the PDMP system.

(b) Provides proof sufficient to the board that the department is entitled to the information under s. 146.82 (2) (a) 5., Stats.

(c) Makes a request for the monitored prescription drug history report through its PDMP system account.

(7) The board shall disclose the minimum necessary amount of information in a monitored prescription drug history report about a patient or patient address to a prisoner's health care provider, the medical staff of a prison or jail in which a prisoner is confined, the receiving institution intake staff at a prison or jail to which a prisoner is being transferred or a person designated by a jailer to maintain prisoner medical records or designated staff of the department of corrections in the same or similar manner, and for the same or similar purposes, as those persons are authorized to access similar confidential patient health care records under ss. 146.82 and 961.385, Stats., this chapter, and other state or federal

laws and regulations relating to the privacy of patient health care records if the person does all of the following:

(a) Creates an account with the PDMP system.

(b) Provides proof sufficient to the board that the person is entitled to the information under s. 146.82 (2) (a) 21., Stats.

(c) Makes a request for the monitored prescription drug history report through its PDMP system account.

(8) The board shall disclose the minimum necessary amount of information in a monitored prescription drug history report about a patient to a coroner, deputy coroner, medical examiner, or medical examiner's assistant following the death of a patient in the same or similar manner, and for the same or similar purposes, as those persons are authorized to access similar confidential patient health care records under ss. 146.82 and 961.385, Stats., this chapter, and other state or federal laws and regulations relating to the privacy of patient health care records if the person does all of the following:

(a) Creates an account with the PDMP system.

(b) Provides proof sufficient to the board that the person is entitled to the information under s. 146.82 (2) (a) 18., Stats.

(c) Makes a request for the monitored prescription drug history report through its PDMP system account with the board.

(9) The board may disclose PDMP data without personally identifiable information that could be reasonably used to identify any patient, healthcare professional, practitioner delegate, pharmacist delegate, or dispenser for public health and scientific research purposes. The board may require evidence of institutional review board approval.

(10) The board shall disclose the minimum necessary amount of information in a monitored prescription drug history report about a patient, patient address, practitioner, or dispenser to designated staff of a law enforcement agency or prosecutorial unit if the designated staff does all of the following:

(a) Creates an account with the PDMP system.

(b) Provides documentation demonstrating the law enforcement agency or prosecutorial unit is engaged in one of the following activities:

1. An active and specific investigation or prosecution of a violation of any state or federal law involving a monitored prescription drug and that the information being requested is reasonably related to that investigation or prosecution.

2. The monitoring of a patient as part of a drug court, as defined in s. 165.955 (1).

(c) Makes a request for the monitored prescription drug history report through its account with the PDMP system.

History: CR 12–009: cr. Register October 2012 No. 682, eff. 1–1–13; CR 14–003: r. (3), (4), am. (6) (intro.), renum. (9) (intro.) to (9) and am., r. (9) (a) to (c) Register August 2014 No. 704, eff. 9–1–14; correction in (5) (intro.), (6) (intro.), (7) (intro.), (8) (intro.), (10) (intro.) Register September 2015 No. 717; CR 15–101: am. (1) (intro.), (b), (2) (intro.), (c), (7) (intro.), (c), (8) (intro.), (c) Register June 2016 No. 726, eff. 7–1–16; EmR1706: emerg. am (Title), (1), (2) (intro.), (c), (5) (intro.), (a), (c), cr. (d), am. (6) (intro.), (a), (c), (7) (intro.), (a), (c), (8) (intro.), (a), (c), (9), (10) eff. 4–1–17; CR 17–028: (Title), (1), (2) (intro.), (c), (5) (intro.), (a), (c), cr. (d), am. (6) (intro.), (a), (c), (7) (intro.), (a), (c), (8) (intro.), (a), (c), (9), (10) Register December 2017 No. 744, eff. 1–1–18; CR 19–156: am. (9) Register August 2020 No. 776, eff. 9–1–20.

CSB 4.12 Use of PDMP data by the board and department. (1) The board shall develop and maintain a PDMP database to store dispensing data and PDMP data in a secure environment and an encrypted format.

(2m) The board shall develop and maintain a PDMP system to facilitate all of the following:

(a) The submission of dispensing data to the PDMP database.

(b) The creation of monitored prescription drug history reports about specific patients, practitioners, and dispensers.

(c) The access to and the obtaining of monitored prescription drug history reports, prescribing metrics reports, and audit trails.

(3) The board shall maintain audit trails that contain all of the following information:

(a) A log of dispensing data submitted to the PDMP database by each dispenser.

(b) A log of persons to whom the Board has granted direct access to the PDMP system under ss. CSB 4.09 or 4.093 and a log of each time a person attempts to access PDMP data or a monitored prescription drug history report.

(c) A log of prescription monitoring programs operated by a relevant agency in another jurisdiction with which the board exchanges PDMP data pursuant to s. CSB 4.14 and a log of each time a person from another jurisdiction attempts to access PDMP data.

(d) A log of pharmacies or other entities at which pharmacists dispense or administer monitored prescription drugs in the course of professional practice with which the board has determined to have at least equivalent capability to maintain the confidentiality of monitored prescription drug history reports and a log of each time a person from a pharmacy or other entity attempts to access PDMP data or a monitored prescription drug history report.

(e) A log of hospitals or other entities at which practitioners prescribe, dispense, or administer monitored prescription drugs in the course of professional practice with which the board has determined to have at least equivalent capability to maintain the confidentiality of monitored prescription drug history reports and a log of each time a person from a hospital or other entity attempts to access PDMP data or a monitored prescription drug history report.

(f) A log of monitored prescription drug history reports and PDMP data disclosed pursuant to s. CSB 4.11, including the name of the person to whom the information was disclosed.

(g) A log of requests for PDMP data or monitored prescription drug history reports even when no information was disclosed.

(6) Staff assigned administrative duties over the PDMP, vendors, contractors, and other agents of the board shall only have access to the minimum amount of PDMP data necessary for all of the following purposes:

(a) The design, implementation, operation, and maintenance of the program, including the PDMP database, PDMP system, the disclosure of information via other entities pursuant to s. CSB 4.09 (4), and the exchange of information pursuant to s. CSB 4.15 as part of the assigned duties and responsibilities of their employment.

(am) The operation of an analytics platform that provides data cleansing and standardization, data integration, advanced analytics, and alert management capabilities as part of the PDMP database and PDMP system.

(b) The collection of dispensing data as part of the assigned duties and responsibilities under s. 961.385, Stats., and this chapter.

(c) Evaluating and responding to legitimate requests for monitored prescription drug history reports, audit trails, and PDMP data.

(cg) Preparing monitored prescription drug history reports, audit trails, and PDMP data for the board to determine whether suspicious or critically dangerous conduct or practices has occurred or is occurring pursuant to s. CSB 4.15.

(cr) Conducting a review of the program as required by s. 961.385 (5), Stats.

(d) Other legally authorized purposes.

History: CR 12–009: cr. Register October 2012 No. 682, eff. 1–1–13; CR 14–003: am. (4), cr. (4g), (4r) Register August 2014 No. 704, eff. 9–1–14; correction in (6) (b) made under s. 13.92 (4) (b) 7., Stats., Register September 2015 No. 717; EmR1706: emerg. am. (title), (1), r. (2), cr. (2m), r. and recr. (3), r. (4), (4g), (4r), (5), am. (6) (intro.), (a), cr. (6) (am), am. (6) (c), cr. (6) (cg), (cr), eff. 4–1–17; CR 17–028: am. (title), (1), r. (2), cr. (2m), r. and recr. (3), r. (4), (4g), (4r), (5), am. (6) (intro.), (a), cr. (6) (am), am. (6) (c), cr. (6) (cg), (cr), Register December 2017 No. 744, eff. 1–1–18; ; correction in (3) (b) made under s. 13.92 (4) (b) 7., Stats., December 2017 No. 744.

CSB 4.13 Confidentiality of PDMP records. (1) The dispensing data, PDMP data, audit trails, monitored prescription drug history reports, and prescribing metrics reports maintained,

created, or stored as a part of the program are not subject to inspection or copying under s. 19.35, Stats.

(2) A person who discloses or a person whose delegate discloses dispensing data, PDMP data, audit trails, monitored prescription drug history reports, or prescribing metrics reports in violation of s. 146.82 or 961.385, Stats., this chapter, or other state or federal laws or regulations relating to the privacy of patient health care records, may be referred to the appropriate licensing or regulatory board for discipline, or the appropriate law enforcement agency for investigation and possible prosecution if the board determines that a criminal violation may have occurred.

History: CR 12–009: cr. Register October 2012 No. 682, eff. 1–1–13; correction in (2) made under s. 13.92 (4) (b) 7., Stats., Register September 2015 No. 717; EmR1706: emerg. am., eff. 4–1–17; CR 17–028: am. Register December 2017 No. 744, eff. 1–1–18.

CSB 4.14 Exchange of PDMP data. (1) The board may exchange monitored prescription drug history reports and PDMP data with a prescription monitoring program operated by a relevant agency in another state or jurisdiction if the prescription monitoring program satisfies all of the following conditions:

(a) The prescription monitoring program is compatible with the program.

(b) The relevant agency operating the prescription monitoring program agrees to exchange similar information with the program.

(2) In determining the compatibility of a prescription monitoring program to the program, the board may consider any of the following:

(a) The safeguards for privacy of patient records and the prescription monitoring program's success in protecting patient privacy.

(b) The persons authorized to access the information stored by the prescription monitoring program.

(c) The schedules of controlled substances monitored by the prescription monitoring program.

(d) The information required by the agency to be submitted regarding the dispensing of a prescription drug.

(e) The costs and benefits to the board of sharing information.

(3) The board may assess a prescription monitoring program's continued compatibility with the program at any time.

History: CR 12–009: cr. Register October 2012 No. 682, eff. 1–1–13; CR 14–003: am. (1) (intro.) Register August 2014 No. 704, eff. 9–1–14; EmR1706: emerg. am. (title), (1) (intro.), eff. 4–1–17; CR 17–028: am. (title), (1) (intro.) Register December 2017 No. 744, eff. 1–1–18.

CSB 4.15 Disclosure of suspicious or critically dangerous conduct or practices. (1) The board may review dispensing data, monitored prescription drug history reports, PDMP data, and data compiled pursuant to s. CSB 4.12 to determine whether circumstances indicate suspicious or critically dangerous conduct or practices of a pharmacist, pharmacy, practitioner, or patient.

(2) The board may include any of the following factors when determining whether circumstances indicate suspicious or critically dangerous conduct or practices of a pharmacist or pharmacy:

(a) The pharmacist or pharmacy's monitored prescription drug dispensing practices deviate from accepted pharmacist or pharmacy practices.

(b) There are unusual patterns in the payment methodology used by patients to whom monitored prescription drugs are dispensed by the pharmacist or pharmacy.

(c) The history of actions taken against the pharmacist or pharmacy by other state agencies, agencies of another state, or law enforcement.

(d) The type and number of monitored prescription drugs dispensed by the pharmacist or at the pharmacy.

(e) The pharmacist or pharmacy has dispensed forged prescription orders for a monitored prescription drug.

(f) The distance patients travel to have monitored prescription drugs dispensed at the pharmacy.

(g) The number of patients dispensed monitored prescription drugs at the pharmacy or by the pharmacist who satisfy any of the criteria identified in sub. (4).

(3) The board may include any of the following factors when determining whether circumstances indicate suspicious or critically dangerous conduct or practices of a practitioner:

(a) The practitioner's monitored prescription drug prescribing practices deviate from accepted prescribing practices.

(b) The practitioner prescribes potentially dangerous combinations of monitored prescription drugs to the same patient.

(c) The type and number of monitored prescription drugs prescribed by the practitioner.

(d) The history of actions taken against the practitioner by other state agencies, agencies of another state, or law enforcement.

(e) The distance patients travel to obtain monitored prescription drug prescriptions from the practitioner.

(f) The number of patients to whom the practitioner prescribed a monitored prescription who satisfy any of the criteria identified in sub. (4).

(4) The board may include any of the following factors when determining whether circumstances indicate suspicious or critically dangerous conduct or practices of a patient:

(a) The number of practitioners from whom the patient has obtained a prescription for a monitored prescription drug.

(b) The number of pharmacies from where the patient was dispensed a monitored prescription drug.

(c) The number of prescriptions for a monitored prescription drug obtained by the patient.

(d) The number of monitored prescription drug doses dispensed to the patient.

(e) Whether the monitored prescription drugs dispensed to the patient include dangerous levels of any drug.

(f) The number of times the patient is prescribed or dispensed a monitored prescription drug before the previously dispensed amount of the same or a similar monitored prescription drug would be expected to end.

(g) The payment methodology used by the patient to obtain controlled substances at a pharmacy.

(5) Upon determining that circumstances indicate suspicious or critically dangerous conduct or practices of a pharmacy, practitioner, or patient, the Board may disclose monitored prescription drug history reports, audit trails, and PDMP data to any of the following:

(a) A relevant patient.

(b) A relevant pharmacist or practitioner.

(c) A relevant state board or agency.

(d) A relevant agency of another state.

(e) A relevant law enforcement agency.

(6) Upon determining that a criminal violation may have occurred, the board may refer a pharmacist, pharmacy, or practitioner to the appropriate law enforcement agency for investigation and possible prosecution. The board may disclose monitored prescription drug history reports, audit trails, and PDMP data to the law enforcement agency as part of the referral.

History: CR 15–101: cr. Register June 2016 No. 726, eff. 7–1–16; CR 17–028: am. (1), (5) (intro.), cr. (6) Register December 2017 No. 744, eff. 1–1–18.

Controlled Substances Board
Rule Projects (updated 02/27/23)

CH Rule Number	Scope Number	Scope Expiration Date	Code Chapter Affected	Relating Clause	Stage of Rule Process	Next Step
22-011	070-21	02/29/2024	CSB 2.78	Scheduling Crotonyl Fentanyl	Legislative Review	Adoption
22-014	071-21	02/29/2024	CSB 2.79	Scheduling Remimazolam	Legislative Review	Adoption
22-016	072-21	02/29/2024	CSB 2.81	Scheduling Brorphine	Legislative Review	Adoption
22-032	088-21	04/18/2024	CSB 2.82	Scheduling Serdexmethylphenidate	Legislative Review	Adoption
22-033	089-21	04/18/2024	CSB 2.83	Scheduling 10 Fentanyl Related Substances	Legislative Review	Adoption
22-034	090-21	04/18/2024	CSB 2.84	Scheduling Alfaxalone	Legislative Review	Adoption
22-035	091-21	04/18/2024	CSB 2.85	Excluding 6-beta-Naltrexol	Legislative Review	Adoption
22-036	092-21	04/18/2024	CSB 2.86	Scheduling Fospropofol	Legislative Review	Adoption
22-037	093-21	04/18/2024	CSB 2.87	Scheduling Embutramide	Legislative Review	Adoption
22-039	094-21	04/18/2024	CSB 2.88	Scheduling Lacosamide	Legislative Review	Adoption
22-038	095-21	04/18/2024	CSB 2.89	Scheduling Perampanel	Legislative Review	Adoption
22-040	096-21	04/18/2024	CSB 2.90	Transferring 1-phenylcyclohexylamine and 1-piperidinocyclohexanecarbonitrile, Immediate Precursors to Phencyclidine, Also Known as PCP	Legislative Review	Adoption
22-054	015-22	08/28/2024	CSB 2.91	Scheduling 4,4'-Dimethylaminorex	Legislative Review	Adoption

Controlled Substances Board
Rule Projects (updated 02/27/23)

CH Rule Number	Scope Number	Scope Expiration Date	Code Chapter Affected	Relating Clause	Stage of Rule Process	Next Step
Not Assigned Yet	091-22	05/21/2025	CSB 2.92	Scheduling 38 Anabolic Steroids	Fiscal Estimate and Clearinghouse Review	Draft Final Rule and Legislative Report
Not Assigned Yet	092-22	05/21/2025	CSB 2.93	Scheduling Daridorexant	Fiscal Estimate and Clearinghouse Review	Draft Final Rule and Legislative Report
Not Assigned Yet	093-22	05/21/2025	CSB 2.94	Scheduling 7 Synthetic Benzimidazole-Opioids	Fiscal Estimate and Clearinghouse Review	Draft Final Rule and Legislative Report
Not Assigned Yet	094-22	05/21/2025	CSB 2.95	Scheduling Ganaxolone	Fiscal Estimate and Clearinghouse Review	Draft Final Rule and Legislative Report
Not Assigned Yet	Not Assigned Yet	Not Assigned Yet	CSB 2.96	Scheduling Amineptine	Affirmative Action Order Submitted for Publication	Scope Statement Review
Not Assigned Yet	Not Assigned Yet	Not Assigned Yet	CSB 2.97	Scheduling Zipeprol	Affirmative Action Order Submitted for Publication	Scope Statement Review
Not Assigned Yet	Not Assigned Yet	Not Assigned Yet	CSB 2.98	Excluding [^{18} F] FP-CIT	Affirmative Action Order Submitted for Publication	Scope Statement Review
Not Assigned Yet	Not Assigned Yet	Not Assigned Yet	CSB 2.99	Scheduling Mesocarb	Affirmative Action Order Submitted for Publication	Scope Statement Review
Not Assigned Yet	Not Assigned Yet	Not Assigned Yet	TBD	Scheduling Methiopropamine	Affirmative Action Order Reviewed at 01/13/2023 Meeting	Scope Statement Review
Not Assigned Yet	Not Assigned Yet	Not Assigned Yet	TBD	Excluding Fenfluramine	Affirmative Action Order Requested at 03/10/23 Meeting	Affirmative Action Order Drafting and Publication
Not Assigned Yet	095-22	05/21/2025	CSB 4	National Provider Identifier Requirement	Drafting	Board Review of Preliminary Rule Draft

State of Wisconsin
Department of Safety & Professional Services

AGENDA REQUEST FORM

1) Name and title of person submitting the request:	2) Date when request submitted:
Marjorie Liu **Program Lead, PDMP**	02/28/2023 Items will be considered late if submitted after 12:00 p.m. on the deadline date which is 8 business days before the meeting

3) Name of Board, Committee, Council, Sections:

Controlled Substances Board

4) Meeting Date:	5) Attachments:	6) How should the item be titled on the agenda page?
03/10/2023	☒ Yes ☐ No	Prescription Drug Monitoring Program (PDMP) Updates – Discussion and Consideration

7) Place Item in:	8) Is an appearance before the Board being scheduled? *(If yes, please complete Appearance Request for Non-DSPS Staff)*	9) Name of Case Advisor(s), if required:
☒ Open Session ☐ Closed Session	☐ Yes ☒ No	

10) Describe the issue and action that should be addressed:

1. WI ePDMP Operations
    a. Recent and Upcoming Releases
    b. Status of Grant Projects:
        i. FY 2020 Harold Rogers Prescription Drug Monitoring Program
        ii. FY 2021 Harold Rogers Prescription Drug Monitoring Program
        iii. FY 2022 Harold Rogers Prescription Drug Monitoring Program
    c. EHR Integration Status
2. WI ePDMP Outreach

11) Authorization

Marjorie Liu — Feb 28, 2023

Signature of person making this request — Date

Supervisor (if required) — Date

Executive Director signature (indicates approval to add post agenda deadline item to agenda) — Date

Directions for including supporting documents:
1. This form should be attached to any documents submitted to the agenda.
2. Post Agenda Deadline items must be authorized by a Supervisor and the Policy Development Executive Director.
3. If necessary, provide original documents needing Board Chairperson signature to the Bureau Assistant prior to the start of a meeting.

2021-2023 Development and Release Summary

Updated 02.27.2023

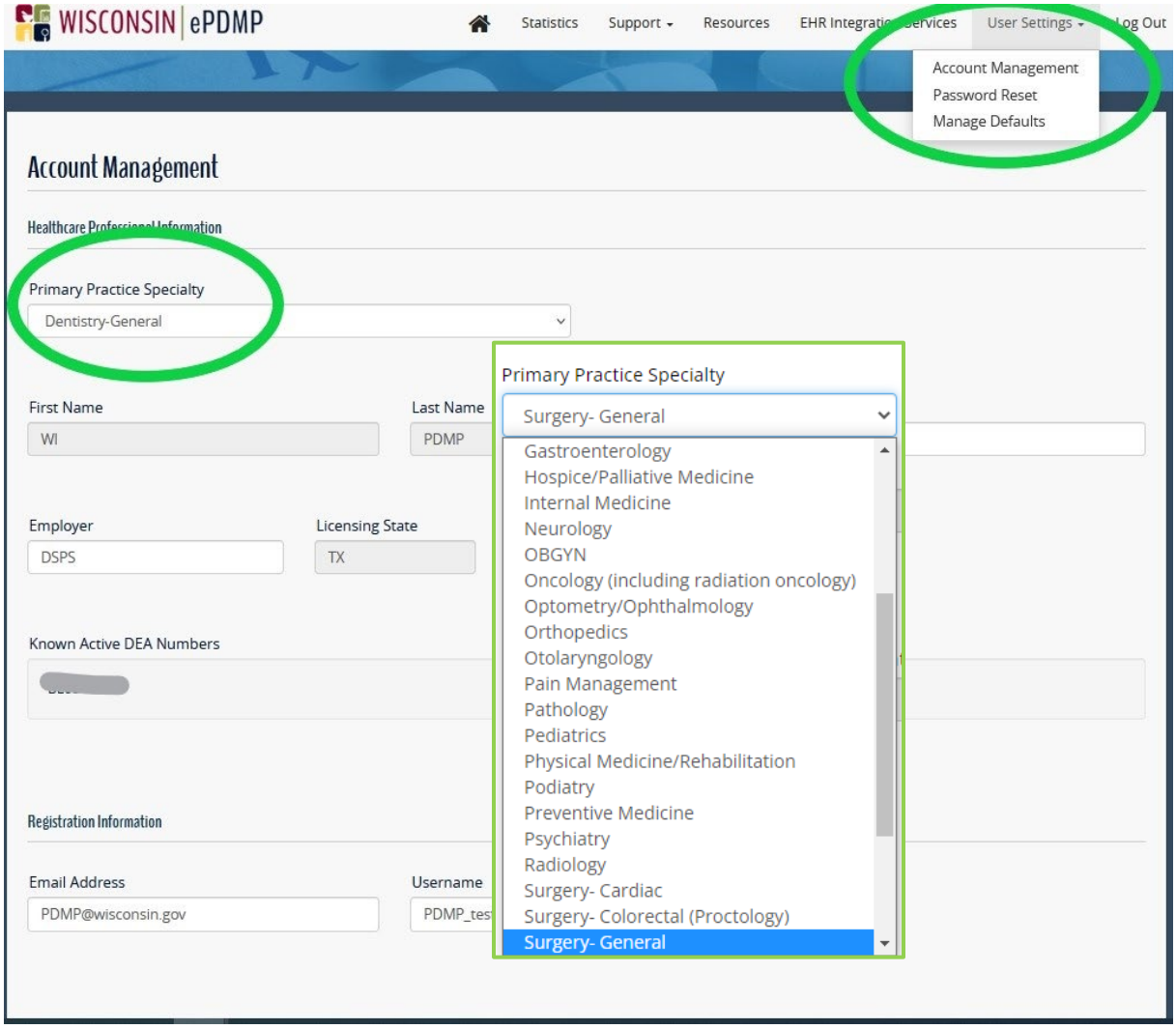
Release Date	Description
Pending	
Harold Rogers Grant 2020 Component 3 Release date TBD	• Automation of top prescribing provider reports • Site reskin/redesign • Ability for users to change the order in which the sections of the patient report are presented. • Adding a Buprenorphine Naïve Alert section to the patient report.
Harold Rogers Grant 2020 Component 2 Release date TBD	Infrastructure and Technology stack changes to improve performance in the following areas: • Patient Matching • Dispensing Matching • Reporting Statistics
Completed	
R30 February 2022	Iframe support Prescriber Practice Metric User Interface Text updates Maintenance Updates
R29 October 2022	Updated mapping tool Adjusted language for expired temporary licenses Modified file processing
R28 July 2022	Adding language related to Buprenorphine Alert Override • Minor text changes to submission error emails • Minor language changes around alert messaging Maintenance Updates
Harold Rogers Grant 2021 Promotional Materials May 2022	Promotional Materials for free EHR Integrations Maintenance Updates
R26 April 2022	Buprenorphine Alert Override • Ability to override prescriber facing alerts, metrics, and MME calculations for certain drugs. Maintenance Updates RxCheck 3.0 Upgrades
Harold Rogers Grant 2020 Component 1 December 2021	Security Enhancements • Two-Factor Authentication • Compromised Email Address Check Patient Report and other User Experience Updates

R25 **November 2021**	Maintenance Updates • Adjustments to triggering Annual Terms and Conditions prompt • Enhanced EHR Integration Testing capabilities Chatbot display changes
R24 **August 2021**	Text Updates • Gabapentin related text changes to the Submitter Error Email. Security-Related Enhancements
R23 **July 2021**	Text Updates • Gabapentin related text changes to the Submitter Error Email.
R22 **July 2021**	Pharmacy-Related Enhancements • Missing DEA Number Error Process Updates Administrative-Related Enhancements
R21 **May 2021**	New Design Enhancements • Proactive MC/HCP linkage renewals • Search enhancements Administrative-Related Enhancements Additional administrator tools
R20 **March 2021**	WI DOJ-Medical College of Wisconsin DataShare Project • Automatically send data extracts to DOJ-MCW • Automatically receive data extracts from DOJ-MCW Administrative-Related Enhancements • Additional improvements to query process • Additional administrator tools

Automation of Top Prescribing Provider Reports

- Buprenorphine used to treat drug use disorder is excluded from Prescribing Percentile Ranking.
- Percentile ranking is by "Specialty."

"Specialty" is self-elected at ePDMP registration and may be updated via **User Setting> Account Management** in the Prescribing Healthcare Professional account.



WI ePDMP Integration Services Summary

Current as of 02.27.2023

Pending Health Systems and EHR Platforms	Status			Notes
Advent Health	Pending Implementation			
Marshfield	Pending - Kickoff			
Bluestone Physician Services	In discussion			
OCHIN	**Went live on 12/21/2022**			
Time 4 U MD	Pending - Sign Agreement			
Marshfield Medical Center - Dickinson	Pending - Sign Agreement			
SRS Pharmacy Systems	Pending - Sign Agreement			
Chet Johnson Drug	Pending - Kickoff			
Wisconsin Statewide Health Information Network (New Platform)	Pending Implementation			
Clark County	Pending Implementation			
CompuGroup Medical	Pending - Sign Agreement			
Mindy's Place	Pending CSB Approval			
Allina Health	In discussion			
Connected Health Systems (approx. 57% of monthly patient queries)	**Free Pricing Model**	**Implementation Date**	**Est. Total # of Users**	**Notes**
Ascension Wisconsin				
Aspirus Health Care				
Aurora Health Care				
Children's Hospital of Wisconsin	Y	09/01/2022	300	
Clean Slate	Y	09/01/2022	26	
DrFirst				
Froedtert & the Medical College of Wisconsin				Pending signed Free agreement
GHC of South Central Wisconsin				
Gundersen Health System				Pending signed Free agreement
HealthPartners				
HSHS / Prevea Health				

M Health Fairview	Y	08/01/2022	30	
Marshfield Clinic	Y	09/01/2022	100	
Mayo Clinic				
Mercy Health	Y	08/01/2022	766	
Monroe Clinic				
NOVO Health Technology Group				
ProHealth Care				
SSM Health				
Thedacare				Pending signed Free agreement
UnityPoint				
UW Health				
Wisconsin Statewide Health Information Network	Y	09/01/2022	3500	

DrFirst Facilities
Alay Health Team
ASSOCIATED MENTAL HEALTH CONSULTANTS
Behavioral Health Svcs of Racine Co.
Door County Memorial Hospital
Dr. Colleen Worth, DNP, APNP
FAMILY PSYCHIATRIC CARE, LLC
Fort Healthcare
GI Associates LLC
Heartland Hospice
Lake Superior Community Health Center
Lifestance Health WI
Marshfield Clinic Health System
Mile Bluff Medical Center
Oak Medical
Oral Surgery Associates of Milwaukee
Orthopedic Hospital of Wisconsin
PAIN MANAGEMENT AND TREATMENT CTR

Richland Hospital
Watertown Rainbow Hospice
Regional Medical Center
Rogers Memorial Hospital
Sauk Prairie Memorial Hospital
Wauwatosa Children's Clinic
Watertown Regional Medical Center

2023 WI PDMP Outreach Calendar

MONTH	EVENT	DESCRIPTION	DATES	NOTES
January	Overdose Fatality Review (OFR) State Advisory Group	DSPS Representative; inter-agency advisory board for OFR participating local sites	1/12/2023	Virtual; Quarterly Meeting
February				
March				
April	Overdose Fatality Review (OFR) State Advisory Group	DSPS Representative; inter-agency advisory board for OFR participating local sites	4/13/2023	Virtual; Quarterly Meeting
May				
June	WI NADDI Conference (National Association of Drug Diversion Investigators)	Presenter; NADDI annual training for WI healthcare professionals and law enforcement agents who focus on drug diversion prevention and detection	6/16/2023	Wauwatosa, WI
July	Overdose Fatality Review (OFR) State Advisory Group	DSPS Representative; inter-agency advisory board for OFR participating local sites	7/13/2023	Virtual; Quarterly Meeting
August	Overdose Fatality Review (OFR) Education Session	Presenter; Tri-county OFR team (Waushara, Green Lake, and Marquette Counties)	8/10/2023	Virtual
September				
October	NASCSA Conference (National Association of State Controlled Substances Authorities)	Participant; annual national meeting for government controlled substances authority, PDMP and healthcare professionals organized by NASCSA	10/23-10/26/2023	Minneapolis, MN
	Overdose Fatality Review (OFR) State Advisory Group	DSPS Representative; inter-agency advisory board for OFR participating local sites	10/12/2023	Virtual; Quarterly Meeting
November				
December				