Statement

of

American Society of Addiction Medicine

Kentucky Society of Addiction Medicine

Kentucky's Administrative Regulation Review Subcommittee

Meeting Re: Board of Medical Licensure 201 KAR 009:270. Professional standards for prescribing, dispensing, or administering Buprenorphine-Mono-Product or Buprenorphine-Combined-with-Naloxone. (Amended After Comments)

October 9, 2025

The American Society of Addiction Medicine (ASAM) and the Kentucky Society of Addiction Medicine (KYSAM) respectfully submit this joint statement to urge the Administrative Regulation Review Subcommittee (the "Subcommittee") to find the Kentucky Board of Medical Licensure ("KBML")'s proposed 201 KAR 9:270 deficient and to recommend that KBML amend the proposed regulation to correct its deficiencies. Kentucky has one of the country's highest rates of opioid use disorder (OUD). The language in the proposed 201 KAR 9:270 would restrict access to buprenorphine in a manner that would needlessly perpetuate increased opioid overdose risks and suppress treatment retention throughout the Commonwealth.

Background

On September 4, 2025, ASAM, KYSAM, the American Medical Association, American Academy of Family Physicians, American College of Obstetricians and Gynecologists, American Psychiatric Association, American Academy of Addiction Psychiatry, Kentucky Academy of Family Physicians, Kentucky Psychiatric Medical Association, and Kentucky Section of the American College of Obstetricians and Gynecologists sent a joint statement to KBML, documenting numerous provisions in KBML's proposed regulation that conflict with national medical guidelines and guidance (attached as **Exhibit A**, the "September Joint Statement"). In response, on October 6, 2025, KBML sent a letter to Representative Moser (attached as **Exhibit B**, the "Moser Letter").

ASAM and KYSAM are grateful that KBML agreed in the Moser Letter to correct two drafting errors identified in the September Joint Statement. However, the organizations were deeply disappointed by KBML's remaining response, which does not provide the level of clarity needed to support the current addiction medicine and addiction psychiatry workforce or encourage additional physicians and other healthcare professionals to treat individuals with an opioid use disorder. ASAM and KYSAM acknowledge that KBML has taken additional time to review our concerns, but there is more work to do if Kentucky wants to remove barriers to care for individuals with opioid use disorder. Thankfully, national thought leaders continue to encourage the medical profession to move beyond unproductive philosophical debates about clinical goals for medications for addiction treatment, which unnecessarily pit recovery pathways against one another.[1]

The Deficiencies

Pursuant to KRS 13A.030(2)(a), the Subcommittee should determine that KBML's proposed 201 KAR 9:270 is deficient. More specifically, under KRS 13A.030(2)(c), the Subcommittee should recommend that KBML amend the proposed 201 KAR 9:270 to address the following deficiencies:

- **Section 3(4)(a)1.,2. Prior Medical Records:** In the Moser Letter, KBML states its proposed regulation "requires only documentation of *good faith* efforts when records prove unavailable." This is incorrect. The proposed regulation requires "best efforts," which is a higher legal standard. At a minimum, KBML needs to revise its proposed regulation to reflect "*good faith* efforts," as represented to Representative Moser in the Moser Letter.
- **Section 3(4)(d)1. Behavioral Modification:** In the Moser Letter, KBML clarifies that the proposed regulation "does not mandate cessation if the patient does not immediately engage." Yet, the proposed regulation does not say that. Even if the proposed regulation did say that, such explanation begs the questions: What does "immediately" mean to KBML? What happens when said time expires? To address this deficiency, we suggest that KBML add the following statement, which aligns with SAMHSA's regulations (42 CFR 8.12 (f)(5)(i)) governing opioid treatment programs dispensing methadone: "Patient refusal of objective behavioral modification shall not preclude them from receiving Buprenorphine-Mono-Product or Buprenorphine-Combined-with-Naloxone medication."

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[1] McLellan AT, Volkow ND. Goals for Opioid Use Disorder Medications - Protection, Remission, and Recovery. N Engl J Med. 2025 Oct 2;393(13):1253-1255. doi: 10.1056/NEJMp2505377. Epub 2025 Sep 27. PMID: 41020518.

- **Section 4:** In the Moser letter, KBML acknowledges "exceptions and deviances, too immeasurable to draft into regulation, are allowed and are covered within SAMHSA TIP 63." Indeed, as noted in the September Joint Statement, SAMHSA TIP 63 explicitly states that its guidelines, "should not be considered substitutes for individualized client care and treatment decisions." (ES-12). Since KBML has adopted SAMHSA TIP 63 as the sole acceptable standard for clinical deviations, then that reference surely encompasses the document in its entirety - meaning individualized client care and treatment decisions are permissible under the proposed 201 KAR 9:270 when medically justified in the patient record. If that is KBML's interpretation, then no further national guidelines must be referenced. If it is not, then the following text in Section 4 should be deleted to maintain consistency with the professional respect afforded to Kentucky physicians prescribing Schedule II medications regulated by 201 KAR 9:260: "and in accordance with SAMHSA guidelines as set forth in: Substance Abuse and Mental Health Services Administration, Medications for Opioid Use Disorder, Treatment Improvement Protocol (TIP) Series 63, Publication No. PEP21-01-002, Rockville, MD: Substance Abuse and Mental Health Services Administration, 2021." While we do not understand KBML's criticisms of ASAM's National Practice Guideline (which are relied upon by physicians of all specialties throughout the nation), we believe this solution is a reasonable step forward that will provide appropriate guidance to licensees.

Although KBML's proposed regulation contains other significant shortcomings identified by the September Joint Statement, in the interest of identifying some of the most problematic, we have focused on what we consider reasonable solutions that directly respond to the Moser Letter. ASAM and KYSAM remain willing to work with KBML and the Kentucky Legislature to identify how best to balance increasing access to evidence-based treatment for opioid use disorder with reasonable regulations that ensure the standard of care is met.

ASAM and KYSAM thank you for your time and attention and look forward to your feedback.

Statement

of

American Medical Association

American Academy of Family Physicians

American College of Obstetricians and Gynecologists

American Psychiatric Association

American Society of Addiction Medicine

American Academy of Addiction Psychiatry

Kentucky Academy of Family Physicians

Kentucky Psychiatric Medical Association

Kentucky Section of the American College of Obstetricians and Gynecologists

Kentucky Society of Addiction Medicine

Kentucky's Administrative Regulation Review Subcommittee

Meeting Re: Board of Medical Licensure 201 KAR 009:270. Professional standards for prescribing, dispensing, or administering Buprenorphine-Mono-Product or Buprenorphine-Combined-with-Naloxone. (Amended After Comments)

September 4, 2025

The above-listed medical organizations, representing thousands of physicians nationwide, respectfully submit this statement to urge the Administrative Regulation Review Subcommittee (the "Subcommittee") to find the Kentucky Board of Medical Licensure ("KBML")'s proposed 201 KAR 9:270 deficient and to recommend that KBML either amend the proposed regulation to correct its deficiencies or repeal 201 KAR 9:270 entirely. Kentucky has one of the country's highest rates of opioid use disorder (OUD). We are concerned that current language in the proposed 201 KAR 9:270 would restrict access to buprenorphine in a manner that would needlessly perpetuate increased opioid overdose risks and suppress treatment retention throughout the Commonwealth.

More specifically, pursuant to KRS 13A.030(2)(a), the Subcommittee should determine that KBML's proposed 201 KAR 9:270 is deficient because:

1. Several provisions conflict with nationally recognized, evidence-based, medical guidelines/guidance on prescribing buprenorphine, as detailed in **Exhibit A**. At the same time, the proposed regulation does not provide the clinical flexibility explicitly endorsed by those same guidelines/guidance;
2. KBML's Statement of Consideration Relating to 201 KAR 9:270 contains inaccurate or outdated information; and
3. KBML's proposed 201 KAR 9:270 contains the drafting errors identified below, requiring correction.

Accordingly, under KRS 13A.030(2)(c), the Subcommittee should recommend that KBML amend the proposed 201 KAR 9:270 to address these deficiencies or repeal 201 KAR 9:270 in its entirety.

I. Provisions Conflicting with Nationally Recognized, Evidence-Based, Medical Guidelines/Guidance on Prescribing Buprenorphine and the Proposal's Insufficient Preservation of Necessary Clinical Flexibility

Exhibit A identifies several provisions that conflict with national medical guidelines and guidance. Moreover, unlike 201 KAR 9:260, which governs the prescribing of controlled substances generally, the proposed 201 KAR 9:270 does not permit a physician to document (a) circumstances beyond their control or (b) a professional determination that a specific standard is inappropriate for a patient's diagnosis and treatment, and then proceed with prescribing buprenorphine when clinically justified – that is, unless the prescribing of buprenorphine is also in accordance with SAMHSA Tip 63, ***despite Tip 63's clear statement that its guidelines "should not be considered substitutes for individualized client care and treatment decisions." (ES-12).***

II. Deficiencies in KBML's Statement of Consideration Relating to 201 KAR 9:270

KBML's Statement of Consideration Relating to 201 KAR 9:270 contains the following inaccurate or outdated information:

- **Page 19:** KBML states that 201 KAR 9:270's proposed requirement of buprenorphine prescribers to obtain prior medical records is also required of other controlled substance prescribers in 201 KAR 9:260 for the treatment of pain. This is incorrect. As shown in **Exhibit A**, 201 KAR 9:260 only requires obtaining prior medical records if the prescriber determines such review is necessary to justify long-term prescribing, dispensing, or administering of a controlled substance for the treatment of pain.
- **Pages 23-24**: KBML references guidance on post-initiation buprenorphine doses that ***predate a Food and Drug Administration (FDA)'s December 2024 notice***, in which the FDA recommended changes to the labeling of buprenorphine-containing transmucosal products for the treatment of OUD, to remove a "target dose" and clarify that neither 16 mg/day nor 24 mg/day should be construed as maximum dosages for these medications. (Read more here.)
- **Page 26:** KBML cites selective excerpts from federal guidelines to justify its proposal on objective behavioral modification. However, those same guidelines clearly state that access to buprenorphine for OUD should not be conditioned on participation in such interventions, as further detailed in **Exhibit A**.
- **Pages 30-31:** KBML states that it disagreed with recommendations to allow prescribers to exercise their discretion as long as the discretion complies with American Society of Addiction Medicine (ASAM) guidelines, because ". . . a majority of buprenorphine prescribing for OUD is undertaken by general practitioners" and "ASAM's recommendations are drafted without input from a broader and more diverse prescriber base." This is misleading and incorrect. ASAM represents addiction specialist physicians and primary care clinicians treating addiction, and ASAM guidelines are developed using a rigorous, evidence-informed process.
    - Addiction medicine is a multi-disciplinary medical subspeciality, requiring primary board certification. Addiction medicine specialists are often primary boarded in family medicine or internal medicine.
    - On page 8 of ASAM's National Practice Guideline (NPG) (2020), it states: "This Practice Guideline is primarily intended for clinicians involved in evaluating patients and providing authorization for pharmacological treatments at any level. The intended audience falls into the broad groups of physicians; other healthcare providers (especially those with prescribing authority); medical educators and faculty for other healthcare professionals in training; and clinical care managers, including those offering utilization management services."
    - On page 19 of ASAM's NPG, it states: "These guidelines were developed using the RAND/ UCLA Appropriateness Method (RAM)—a process that

combines scientific evidence and clinical knowledge to determine the appropriateness of a set of clinical procedures . . . . ASAM's Quality Improvement Council (QIC) was the oversight committee for guideline development. The QIC appointed a Guideline Committee to participate throughout the development process, rate treatment scenarios, and assist in writing. . . . The 2015 Guideline Committee was composed of 11 experts and researchers from multiple disciplines, medical specialties, and subspecialties, including academic research, internal medicine, family medicine, addiction medicine, addiction psychiatry, general psychiatry, obstetrics/gynecology, and clinical neurobiology. Physicians with both allopathic and osteopathic training were represented on the Guideline Committee."

- On page 21 of ASAM's NPG, it states: "ASAM sought input from ASAM members, patient and caregiver groups, and other stakeholders including experts from the criminal justice system, government agencies, other professional societies, and hospitals and health systems. ASAM also made the document and a qualitative review guide available to ASAM members and the general public for a 2-week period of review and comment. The final draft Practice Guideline was submitted to the ASAM Board of Directors in April 2015."

III. Drafting Errors

The proposed 201 KAR 9:270 contains the following drafting errors, requiring correction:

- **Prescribing of Buprenorphine-Mono-Product to Patients Transitioning from Full Opioid Agonists:** On page 18 of KBML's Statement of Consideration Relating to 201 KAR 9:270, KBML states that the proposed regulation reflects that physicians may prescribe Buprenorphine-Mono-Product to patients transitioning from full opioid agonists for a period of up to thirty (30) days. This is incorrect. The proposed regulation does not reflect such allowance.
- **Specialty Consultations for Patients Prescribed More Than 16mg every 12 Months:** On page 13 of the proposed regulation, physicians certified by the American Board of Preventive Medicine in addiction medicine are not listed as an acceptable specialty consult though KBML recognizes such physicians as experts in addiction medicine elsewhere in the regulation. This is a clear drafting error.

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
Link to Proposed 201 KAR 9:270.	Link to 201 KAR 9:260	Link to VA Guidelines (2022)	Link to ASAM NPG (2020) and Link to ASAM's Clinical Considerations (CC) (2023).	Link to Tip 63.	Link to OTP Regulations.	See below links.	
In-Office Initiation of Treatment: The licensee shall recommend to the patient an in-office observed initiation. (Section 3(4)(b)1.)			"Both office-based and home-based initiation are considered safe and effective when starting buprenorphine treatment. Clinical judgement should be used to determine the most appropriate setting for a given patient and may include consideration of the patient's past experience with buprenorphine and assessment of their ability to manage initiation at home." (NPG Page 12)	"Induction can occur in the office or at home. Most clinical trials were conducted with office-based induction, and extant guidance recommends this approach. However, office-based induction can be a barrier to treatment initiation. Home induction is increasingly common." (3-63) "Clinical experience indicates that patients suitable			

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
				for home induction: Can describe, understand, and rate withdrawal. Can understand induction dosing instructions. Can and will contact their provider about problems." (3-64)			
With limited exceptions, prohibition on using buprenorphine for pain, unless formulation is approved by the FDA for pain. (Section 3(1)(b))		"For patients receiving daily opioids for the treatment of chronic pain, we suggest the use of buprenorphine instead of full agonist opioids due to lower risk of overdose and misuse." (Page 43)	"Some evidence suggests that patients experiencing substantial pain on high doses of full agonist opioids experience improved pain management when transitioned to buprenorphine. Overall, buprenorphine therapy carries a lower risk of adverse effects, especially overdose, compared to full agonist				

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
			opioids." (NPG Page 55)				
Initiation dose requirements and limit – e.g., Day 1 max 16mg (Section 3(4)(b)3.)			Buprenorphine initiation dosing should be titrated according to withdrawal symptoms; dose should be sufficient to enable patients to discontinue illicit opioid use; doses may exceed 16 mg if clinically indicated. Clinicians using extended-release products should use them as indicated. (NPG Pages 12, 42) "Buprenorphine dose and dosing frequency should be individualized based on patients' treatment needs, the possibility of novel components in the drug supply should be considered	"The guidelines presented should not be considered substitutes for individualized client care and treatment decisions." (ES-12)			Prescriptive dosing standards may result in undertreatment and higher relapse risk. Recommended protocols in 201 KAR 9:270 also does not account for the use of extended-release buprenorphine products.

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
			during OUD treatment . . ." (CC Page 1)				
Mandatory behavioral modification/ Counseling (Section 3(4)(d)1.)			"Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs. However, a patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacotherapy, with appropriate medication	EXHIBIT 2.16. Referring Patients Who Receive OUD Medications to Behavioral Health Therapies: If the patient is unwilling to engage in additional behavioral health therapies, then Offer best advice and ongoing motivational interviewing; revisit offer for	42 CFR 8.12 (f)(5)(i): "Patient refusal of counseling shall not preclude them from receiving MOUD."	May 2023 Dear Colleague Letter: "An often-cited barrier to prescribing buprenorphine for the treatment of OUD is the perception that patients must engage in counseling and other services in order to start or continue receiving the medication. This letter serves to clarify the importance of	Makes MOUD contingent on counseling, directly contradicting federal OTP regulations, national medical guidelines and guidance. It discriminates against underserved patients, creating non-medical barrier to lifesaving addiction medicine.

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
			management." (NPG Page 10)	behavioral health therapies." (2-24)		counseling and other services as part of a comprehensive treatment plan, but to also reiterate that the provision of medication should not be made contingent upon participation in such services."	

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
Rigid visit schedule (Post initiation: within 10 days; Month 2: within 14 days; Then Monthly; After 2 years & compliant: every 3 months) (Section 3(4)(d)3.,4.)			"Patients should be seen frequently at the beginning of their treatment until patients are determined to be stable. The stability of a patient is determined by an individual clinician based on several indicators which may include abstinence from illicit drugs, participation in psychosocial treatment and other recovery-based activities, and productive occupational and social functioning. Stable patients can be seen less frequently." (NPG Page 42)	"The guidelines presented should not be considered substitutes for individualized client care and treatment decisions." (ES-12)			A fixed schedule is not evidence-based, and it may discourage retention. The proposed rigid visit schedule does not appear to account for the use of extended-release buprenorphine products.

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
Mandatory specialist consultation with an addiction specialist physician for certain dosing: Annually, if prescribed more than 16mg of buprenorphine daily and not an addiction specialist physician, then refer patient for a formal consultation with an addiction specialist physician. (Section 3(4)(d)5.c.)						FDA Notice (12/2024): "FDA recommends the following specific changes to the maintenance dosage recommendations in the "Dosage and Administration" section of the most recent approved BTOD labeling: After treatment induction to the recommended dose of [equivalent 16 mg buprenorphine OR equivalent 16 mg/4 mg buprenorphine/naloxone] per day, dosing should be further adjusted based on the individual patient and clinical response. The maintenance dose of [DRUG NAME] is generally in the	Proposal does not appear to account for extended-release buprenorphine products or recent label changes indicating maintenance dose range is generally up to 24mg daily. "In 2019, Kentucky had **almost 160,000** people aged 18–64 years old with OUD—nearly 6 % of the population." (See here.). Yet, based on ABMS' 2022-2023 Certification Report, there are only 113 ABPM-certified addiction medicine physicians in KY, and only 12

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
						range of [equivalent 4 mg buprenorphine OR equivalent 4 mg/1 mg buprenorphine/naloxone] to [equivalent 24 mg buprenorphine OR equivalent 24 mg/6 mg buprenorphine/naloxone] per day. Dosages higher than [equivalent 24 mg buprenorphine OR equivalent 24 mg/6 mg buprenorphine/naloxone] daily have not been investigated in randomized clinical trials but may be appropriate for some patients." Suboxone Label Change (5/2025): "The maintenance dose of SUBOXONE sublingual film is generally in the	ABPN-certified addiction psychiatrists in KY.

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
						range of 4 mg/1 mg to 24 mg/6 mg per day and should be based on clinical response. Dosages higher than 24 mg/6 mg daily have not been investigated in randomized clinical trials but may be appropriate for some patients."	
Mandatory comprehensive evaluation of patient and prescriber obligation to make "best efforts" to obtain prior medical records	"If the licensee determines that the patient has previously received medical treatment for the presenting medical complaint or		"If not completed before initiating treatment, assessments should be completed soon thereafter." (Page 10)		42 CFR 8.12(f)(2)(B): "A patient's refusal to undergo lab testing for co-occurring physical health conditions should not preclude them		Failure to meet rigid evaluation timelines could cause inappropriate discontinuation of buprenorphine, risking patient safety.

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
before (or within 14 days of) initiation (Section 3(4)(a)1.,2.)	related symptoms **and that review of the prior treatment records is necessary to justify long-term prescribing, dispensing, or administering of a controlled substance**, the licensee shall obtain those prior medical records and incorporate the information therein into the evaluation and treatment of the patient." (Section (4)(2)(e))				from access to treatment, provided such refusal does not have potential to negatively impact treatment with medications."		

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
Mandatory specialist consultation with an addiction specialist physician (which can be provider-to-provider) for certain co-prescriptions beyond a period of 3 months. (Section 3(3))			"The use of benzodiazepines and other sedative-hypnotics should not be a reason to withhold or suspend treatment with methadone or buprenorphine. While the combined use of these medications increases the risk of serious side effects, the harm caused by untreated opioid use disorder can outweigh these risks. A risk-benefit analysis should be conducted, and greater support should be provided including careful medication management to reduce risks." (NPG Page 10)	"Co-prescribing benzodiazepines or other sedatives should not preclude or delay treatment with buprenorphine." (Part 3, page 4)		FDA (9/2017): FDA is "advising that the opioid addiction medications buprenorphine and methadone should not be withheld from patients taking benzodiazepines or other drugs that depress the central nervous system (CNS). The combined use of these drugs increases the risk of serious side effects; however, the harm caused by untreated opioid addiction can outweigh these risks. Careful medication management by health care professionals can reduce these risks. We are requiring this information to be added to the	While a specialist consultation may be ideal in this scenario, it's not always practical. Discontinuation of buprenorphine could risk patient safety. "In 2019, Kentucky had **almost 160,000** people aged 18–64 years old with OUD—nearly 6 % of the population." (See here.). Yet, based on ABMS' 2022-2023 Certification Report, there are only 113 ABPM-certified addiction medicine physicians in KY, and only 12 ABPN-certified addiction psychiatrists in Kentucky.

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
						buprenorphine and methadone drug labels along with detailed recommendations for minimizing the use of medication-assisted treatment (MAT) drugs and benzodiazepines together."	
Allowable Deviations from Standards: Must be " . . . in accordance with SAMHSA guidelines as set forth in: Substance Abuse and Mental Health Services Administration, Medications for Opioid Use Disorder, Treatment Improvement Protocol (TIP) Series 63, Publication No. PEP21-01-002, Rockville, MD: Substance Abuse	"If a licensee is unable to conform to professional standards for prescribing, dispensing, or administering controlled substances due to circumstances beyond the licensee's control, or the licensee makes a professional determination that it is not						More clinical flexibility is allowed by 201 KAR 9:260, which covers Schedule II medications, including full opioid agonists.

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
and Mental Health Services Administration, 2021." (Section 4(2))	appropriate to comply with a specific standard, based upon the individual facts applicable to a specific patient's diagnosis and treatment, the licensee shall document those circumstances in the patient's record and only prescribe, dispense, or administer a controlled substance to the patient **if the patient record appropriately justifies the prescribing, dispensing, or administering of a controlled substance under the**						

201 KAR 9:270	201 KAR 9:260	VA Guidelines	ASAM NPG (2020)	SAMHSA Tip 63 (2021)	SAMHSA OTP Regulations/ Guidelines (2024)	FDA/SAMHSA	Comment
	circumstance." (Section 2(2))						

KENTUCKY BOARD OF MEDICAL LICENSURE

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October 6, 2025

Representative Kimberly Poore Moser
Kentucky General Assembly
702 Capital Ave
Annex Room 315
Frankfort, KY 40601

RE: Amendment of 201 KAR 9:270

Dear Representative Moser,

The evidence is unequivocal: 201 KAR 9:270 works. Since implementing this regulation more than ten (10) years ago, data firmly demonstrates that thoughtful regulatory guardrails enhance, rather than impede, safe care and access to treatment:

- Kentucky's overdose death rate is declining. According to the Kentucky Office of Drug Control Policy's 2023 Kentucky Overdose Fatality Report and the Kentucky Harm Reduction Coalition, overdose deaths in Kentucky decreased by more than 5% between 2021 and 2022 and then by another 9.8% between 2022 and 2023. On May 1, 2025, the Kentucky Office of Drug Control Policy released its 2024 Kentucky Overdose Fatality Report, announcing the largest year over year decrease yet: 30.2% decrease in 2024 compared with 2023.

- The number of Kentucky practitioners prescribing buprenorphine is increasing. According to data from the Office of Inspector General, the number of buprenorphine prescribing practitioners increased 15% between 2020 and 2024. Telemedicine has been augmenting access to care since 2018. In addition, since gaining prescriptive authority in 2020, 49 individual physician assistants prescribed buprenorphine in 2024.

- National data confirms that regulations are not a barrier to treatment for those who want treatment. Patient motivation is the primary factor of many complex factors influencing access to treatment. In 2021, a national survey from the Substance Abuse and Mental Health Services Administration ("SAMHSA")

showed that only 22.1% of persons with past-year opioid use disorder ("OUD") received medications for treatment. In the last three (3) years, SAMHSA followed up with those persons who did not get treatment and found that the problem was not "access to treatment" but rather that 95% of that same population "did not want treatment" or "did not feel the need for treatment." Statistically, about 1.1% of patients who desire treatment cannot access it for any number of reasons (including financial or logistical).[1]

In short, thoughtful regulatory guardrails enhance, rather than impede, safe care and access to treatment.

On behalf of the members of the Kentucky Board of Medical Licensure ("the Board"), thank you for inviting members of the Board (William Craig Denham M.D.) and its executive staff (Michael Rodman, Executive Director, and Leanne Diakov, General Counsel) to your office for a meeting with representatives from the Kentucky Society of Addiction Medicine ("KYSAM") (Colleen Ryan, M.D. and Oliver Benes, M.D.) on Friday, August 29, 2025. Although I was not present at that meeting, it was relayed to me to be a very thoughtful and productive meeting. As agreed at that meeting, the Board has received and considered additional comments to the long-pending proposed amendments to 201 KAR 9:270, the Board's regulation setting forth acceptable and prevailing medical practices in regard to the prescribing and dispensing of buprenorphine medications. I write to address the recent opposition to our proposed amendments and to provide the legislative oversight committee with the complete factual record necessary for informed decision-making.

I. CLEAR MANDATE, COMPELLING NECESSITY

The Board operates under unambiguous legislative authority. KRS 311.565 and 311.601 explicitly empower the Board to promulgate regulations establishing acceptable and prevailing medical practices and ensuring professional competency among licensees. 201 KAR 9:270 fulfills precisely that mandate.

The necessity for such regulation emerged from Kentucky's own painful experience. In 2012, in response to the Commonwealth's devastating opioid "pill mill" crisis, the Legislature specifically criticized the Board for insufficient proactivity in establishing and enforcing controlled substance prescribing standards. The Legislature then passed comprehensive laws requiring the Board to promulgate regulations defining stricter prescribing standards.

The pattern has repeated itself with buprenorphine. Shortly after the Legislature addressed "pill mills," similar problematic practice models emerged in clinics focusing on buprenorphine prescribing for opioid use disorder (OUD). The federal Drug Enforcement Administration

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[1] https://www.samhsa.gov/data/sites/default/files/reports/rpt42731/2022-nsduh-annual-national-web-110923/2022-nsduh-nnr.htm#:~:text=Among%20the%201.8%20million%20adolescents,think%20they%20should%20get%20it

("DEA") confirms that buprenorphine diversion, trafficking, and misuse became increasingly common following its Schedule III classification.[2] Kentucky's buprenorphine prescription rate per capita is presently 5 times the national average (22.4 vs 4.7/100 patients).[3] Also, Kentucky's high prevalence of OUD and low social support systems place it into a much higher level of hazard than nearly all other areas of the country. The Board looks to balance benefit and risk with harm reduction in exercising caution in its targeted interventions of monitoring and support systems in the amended regulation.

The clinical evidence demands attention. Kentucky resides within the nation's "cardiac belt," with exceptionally high rates of underlying cardiac conditions (much undiagnosed) among our patient population. Buprenorphine carries specific cardiac risks, including QTc interval prolongation, as well as, dangerous interactions with benzodiazepines - combinations that have resulted in deaths.[4] The specific benzodiazepine-opioids combination is a leading cause of overdose deaths in the United States, significantly increasing the overdose risk by up to 10-fold.[5]

Patients with opioid use disorder also face heightened risk for developing concurrent substance use disorders, particularly involving benzodiazepines. It is not uncommon to observe patients in OUD clinic request treatment with other high-risk substances with addiction risk. This cross-susceptibility appears to stem from genetic, neurobiological, and behavioral factors that transcend specific substances.[6] The Board maintains that such at-risk patients work with their health provider to have Addiction Medicine oversight when high-risk drugs of dependency are presented to high-risk patients with a substance use disorder.

II. UNPRECEDENTED STAKEHOLDER ENGAGEMENT

Critics suggesting inadequate stakeholder consultation fundamentally misrepresent our process. It bears setting forth for the record that there have now been effectively four (4) comment periods over nearly two (2) years on the proposed amendments to 201 KAR 9:270:

- **Informal Period** (June-November 2024): Proactive outreach to key stakeholders including KYSAM, Kentucky Academy of Family Physicians, Kentucky Chapter of the American College of Obstetricians and Gynecologists, Kentucky Psychiatric

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[2] DEA Diversion Control Division, Drug and Chemical Evaluation Section, "Buprenorphine," March 2025.

[3] Benzodiazepines and Opioids, National Institute on Drug Abuse. https://nida.nih.gov/research-topics/opioids/benzodiazepines-opioids.

[4] Poliwoda S, Noor N, Jenkins JS, Stark CW, Steib M, Hasoon J, Varrassi G, Urits I, Viswanath O, Kaye AM, Kaye AD. Buprenorphine and its formulations: a comprehensive review. *Health Psychol Res.* 2022 Aug 20;10(3):37517. doi: 10.52965/001c.37517. PMID: 35999975; PMCID: PMC9392838; DEA Diversion Control Division, Drug and Chemical Evaluation Section, "Buprenorphine," March 2025.

[5] National Institute on Drug Abuse. Co-Occurring Disorders and Health Conditions (October 2024). https://nida.nih.gov/research-topics/co-occurring-disorders-health-conditions; Lofwall MR, Walsh SL. A review of buprenorphine diversion and misuse: the current evidence base and experiences from around the world. *J Addict Med.* 2014 Sep-Oct;8(5):315-26.

[6] Robins, L. N. *The Vietnam drug user returns: Final report, September 1973.* Washington, DC: US Government Printing Office (1974).

Medical Association, Kentucky Medical Association, medical schools, and public health agencies

- **Initial Formal Period** (January-March 2025): Written comments from these organizations and national affiliates, including ASAM
- **Refiled Period** (April-June 2025): Additional written comments and public hearing on June 27, 2025
- **Post-Filing Period** (August 2025-present): Additional consultation following your August 29 meeting

A public hearing in March 2025 was cancelled and rescheduled only because of unprecedented numbers of persons requested to testify - a testament to the thoroughness of our outreach, not its inadequacy. We subsequently accommodated public testimony in June and continue engaging stakeholders through this correspondence.

III. ADDRESSING THE OBJECTIONS

A. The Regulation is Not "Deficient"

Many of the comments offered by ASAM and the co-signing organizations after the August 29 meeting are repetitive of comments shared between March 2024 and June 2025. The Board having declined to repeal the regulation, these organizations now urge the legislators to find the regulation deficient but cite no discernable reason for deficiency under KRS Chapter 13A. They simply disagree with the existence of the regulation. Many of the provisions they argue are "deficient" are not new regulatory requirements. These were not grounds for the regulation to be deemed "deficient" when the regulation was first promulgated in 2015 or when it was amended in 2016, 2017, 2020 or 2021, and these are not grounds to find this proposed amended regulation "deficient" now. The Board declines to belabor the point further and instead relies on its previous response on this matter in the Statement of Consideration.

B. Prior Medical Records Requirements Are Standard Practice

Critics mischaracterize the requirement for obtaining prior medical records as burdensome. This is, and always has been, a standard medical practice across all specialties and all patient care architectures. 201 KAR 9:270 allows records to be obtained "within two weeks of initiating treatment" and requires only documentation of good faith efforts when records prove unavailable. No prudent physician should continue long-term controlled substance treatment without understanding the patient's medical history and previous treatment responses. Prescribers of controlled substances – whether for treatment of pain or treatment of OUD - cannot simply rely on the course of treatment established by a previous provider (as relayed by KASPER or by the patient's word-of-mouth) to continue along the same course. Each clinician is responsible for an inquiry into whether the initial diagnosis was correct and whether the course of treatment was appropriate (or accurately relayed to the new prescriber by the patient), in order to make an independent clinical judgment in the course of treatment.

C. Behavioral Modification Components Are Evidence-Based

Since its initial promulgation in 2015, 201 KAR 9:270 has required that objective behavioral modification be part of the OUD treatment plan. The regulation does not mandate cessation if the patient does not immediately engage (which would not be unusual until further stabilized in recovery) and it does not mandate the format of a behavioral modification program (only suggesting that it may include programs such as counseling or a twelve (12) step facilitation). Treatment of OUD requires more than the prescribing of medications for acute symptom management and an effective treatment plan must include an expectation of objective behavioral modification by the patient. Opposition to requiring behavioral modification components reveals a profound misunderstanding of addiction treatment.

The field's most successful, long-term addiction treatment program in existence is that experienced by Alcoholics Anonymous, a behavioral-based treatment program. The seminal L.N. Robins' 1974 Vietnam veteran longitudinal study demonstrated that *85% of service veterans* with opioid exposure *recovered without requiring indefinite pharmaceutical maintenance*, utilizing a structured environmental support proving critical to success.[7] A key insight of the Robins' study was the critical role that behavioral health and social environment play in the successful healing of patients stricken with OUD. These crucially important factors are ones ignored by a medication-only approach and factors to be considered in Kentucky's unique population, where compromised support systems are often the rule rather than the exception.

Notably, the Board recognizes that there has been insufficient investment in well-designed studies measuring the objective influence of behavioral health and counseling for OUD, likely because there is no economic incentive to fund research that might demonstrate non-pharmaceutical treatment superiority. The lack of such studies should not excuse the Board from requiring evidence-based comprehensive care that addresses the psychological and social dimensions of addiction recovery.

This component of treatment is not unique to OUD: Behavioral modification is also required in the Board's regulation, 201 KAR 9:016 setting forth acceptable and prevailing medical practices for use of amphetamine and amphetamine-like anorectic controlled substances. Objective behavioral modification provides patients the fortitude and tools necessary to prevent or decrease the risk of fatal overdose if the patient relapses outside of treatment. During the previous comment periods, persons in long term recovery attributed their ongoing recovery to the importance of non-pharmacological approaches coupled with pharmacological components of their treatment. One commentor stated, "I owe it all to my group counseling and the use of saboxen [sic]." Another

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[7] Robins, L. N. *The Vietnam drug user returns: Final report, September 1973*. Washington, DC: US Government Printing Office (1974).

noted that successful treatment "is not a mater [sic] of just stopping opioids" but also requires treatment of the mind.

D. ASAM Guideline Deference Is Inappropriate

ASAM urges the Legislature to find the Board's regulation deficient because it does not defer to ASAM guidelines instead of SAHMSA TIP 63. ASAM has not cited to any meaningful variances between its "guidelines" and the SAMHSA TIP 63 referenced in Section 6 of the regulation. During the August 29 meeting with you, Representative Moser, KYSAM representatives stated that ASAM objects to having its guidelines promulgated into regulations or statutes, so much so that ASAM may repeal/withdraw its guidelines altogether in order to avoid their incorporation into law.

Regardless, the Board declines to participate in the "turf battle" of a single membership-driven professional association. The Board regulates *all* physicians, any of whom may prescribe buprenorphine and not all of whom are members of ASAM. The Board reviewed the ASAM guidelines and found a document so riddled with vague discretionary terminology as to be entirely meaningless to enforce from a regulatory standpoint; such language would never pass muster of the legislative review commission. The Board studied a variety of resources – not only from ASAM - to ensure that the proposed amendments correspond with the consensus of acceptable and prevailing medical practices for a broad range of practitioners. Since 2015, the regulation has been broadly drafted primarily based upon accepted federal standards set forth in SAMHSA TIP 63; exceptions and deviances, too immeasurable to draft into regulation, are allowed and are covered within SAMHSA TIP 63. For these reasons, it is sensical to defer to SAMHSA TIP 63 if circumstances require deviation from other parts of the regulation.

E. Sixteen (16) Milligrams/Daily Is The Acceptable and Prevailing Induction/Target Dose

Before 201 KAR 9:270, Kentucky's average buprenorphine dose approached 32 milligrams daily - far exceeding therapeutic necessity. Current evidence demonstrates that 97% of patients achieve successful outcomes on 16 milligrams or less daily. Only 3% require higher maintenance doses. Sound regulatory policy cannot be constructed around statistical outliers while ignoring the 97% majority.

Critics mischaracterize recent FDA recommended labeling changes regarding *maintenance* dosing. The FDA has not modified its induction and target dosing recommendations and continues to recommend 16 milligrams as the appropriate target dose. The FDA's statement speaks for itself and is attached herewith. (**Attachment A**).[8]

[8] It may also be reviewed at https://www.federalregister.gov/d/2024-30776/p-32

201 KAR 9:270, Section 4, provides mechanisms for the exceptional 3% of patients who may initially require higher doses, ensuring individualized clinical judgment while protecting the vast majority from unnecessary over-medication.

IV. THE RECOVERY VS. MAINTENANCE PARADIGM

This debate transcends regulatory technicalities and reaches fundamental treatment philosophy. Market forces favor lifelong medication for patients in OUD treatment — a financially lucrative, intellectually lazy, yet potentially destructive approach. Kentucky has witnessed how unregulated medication-only approaches can lead to new forms of dependency disguised as treatment. International experience confirms these concerns: France, despite a decade of comprehensive primary care support model and nationalized cost coverage, experienced 20% diversion rates of prescribed buprenorphine when unregulated.[9]

The Legislature must understand that it is the nature and design of buprenorphine to create a clinical withdrawal syndrome if the medication is suddenly discontinued or decreased — this is the same chemical mechanism, a physiologic dependency, that forwarded Kentucky the original opioid crisis. This pharmacological characteristic makes patient discontinuation without medical supervision challenging and contributes to long-term dependency, underscoring the need for regulatory oversight to ensure treatment focuses on recovery rather than perpetual pharmaceutical reliance.

Many healthcare providers utilizing buprenorphine for OUD treatment work in capacities where they have minimal education, experience, or background in providing care to this complex and at-risk patient population. This regulation provides the **minimum guardrails** for providers entering this specialized field in order to assure safety to the public. Experience demonstrates that clinicians provide better care and patients receive safer treatment when acceptable and prevailing medical practices are clearly established and enforced. This regulation provides essential guidance to clinicians seeking clarity for clinical work with this high-risk population. This regulation ensures buprenorphine functions as intended: **a bridge to recovery, not a lifelong destination.**

V. FLEXIBILITY AND IMPROVEMENT

Critics portraying the Board as inflexible ignore our demonstrated responsiveness. The Board, over its nearly two-year review and revision process, has instilled many science and practice-based changes throughout the regulation that will both ease provider and patient burdens. To that same end, the Board reviewed and concurs with the specific "drafting errors," ASAM and

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[9] Lofwall MR, Walsh SL. A review of buprenorphine diversion and misuse: the current evidence base and experiences from around the world. *J Addict Med.* 2014 Sep-Oct;8(5):315-26. doi: 10.1097/ADM.0000000000000045. PMID: 25221984; PMCID: PMC4177012; see also French field experience with buprenorphine, *Am J Addict* 2004:13 Suppl 1:S17-28.

co-signing organizations outlined in their September 4 Joint Statement: (1) that the proposed amendments to the regulation do not reflect that physicians may prescribe Buprenorphine-Mono-Product to patients transitioning from full opioid agonists for a period of up to thirty (30) days and (2) that physicians certified by the American Board of Preventive Medicine in addiction medicine be included among those qualified to provide specialty consult for patients prescribed more than 16mgs every 12 months, because they are recognized as qualified for specialty consults in other parts of the regulation.

Accordingly, an amendment will be filed at Page 5, Line 22, to read:

> "(d) To a patient transitioning from a full opioid agonist [~~methadone~~] to buprenorphine, limited to a period of no longer than thirty (30) days [~~one week~~]."

In addition, an amendment will be filed at Page 13, Line 2, to read:

> "... the American Board of Addiction Medicine, the American Board of Preventative Medicine in addiction medicine, the American Board of ....."

VI. CONCLUSION

The Board respectfully requests the legislative oversight committee recognize that the proposed amendments to 201 KAR 9:270 serve Kentucky's public health interests. The Board has demonstrated unprecedented stakeholder engagement, regulatory flexibility, and commitment to continuous improvement based on emerging evidence. The Board's statutorily-delegated mission remains unchanged: preventing empiricism and protecting the health and safety of the public. The proposed amendments to this regulation advance that mission by outlining comprehensive and evidence-based buprenorphine prescribing standards and ensuring appropriate safeguards against diversion while maintaining robust access to care.

Respectfully submitted,

William C. Thornbury, Jr., M.D., FAAFP
President, Kentucky Board of Medical Licensure

Reviewed and approved by the Board, 10/3/2025.

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or other forms of information technology. Consideration will be given to comments and suggestions submitted within 60 days of this publication.

Authority: 6 U.S.C. 279; 8 U.S.C. 1232; 45 CFR 410; 45 CFR 411.

Mary C. Jones,
ACF/OPRE Certifying Officer.

[FR Doc. 2024-30851 Filed 12-26-24; 8:45 am]
BILLING CODE 4184-45-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2024-N-5381]

Modifications to Labeling of Buprenorphine-Containing Transmucosal Products for the Treatment of Opioid Dependence

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is announcing that we have concluded that certain statements set forth in the FDA-approved labeling for buprenorphine-containing transmucosal products for the treatment of opioid dependence (BTODs) related to the recommended maintenance dosage and dosage adjustments during pregnancy can be modified. We believe that certain statements in BTOD labeling can be modified because the labeling for these products may be misinterpreted by some as establishing a maximum dosage when none exists. FDA is concerned that misinterpretation of these labeling statements may be adversely impacting patients' access to BTODs. We encourage sponsors of approved applications for BTODs to submit supplemental new drug applications (NDAs) (labeling supplements) to modify these labeling statements as described in this notice.

FOR FURTHER INFORMATION CONTACT: Kimberly Compton, Center for Drug Evaluation and Research (HFD-170), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 3168, Silver Spring, MD 20993, 301-796-1191, *kimberly.compton@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

A. FDA-Approved BTODs

Buprenorphine is a mu-opioid receptor partial agonist and a kappa-opioid receptor antagonist. BUPRENEX (buprenorphine hydrochloride (HCl)) injection (under NDA 018401) is a schedule III controlled substance under the Controlled Substances Act (CSA) and was the first buprenorphine product to be approved in the United States (approved in 1981) for management of moderate to severe pain. Other buprenorphine products were subsequently approved for the treatment of opioid use disorder (OUD) [1] and are also controlled under schedule III of the CSA.[2] BTODs have been approved by FDA since 2002. BTODs are available both as products containing buprenorphine alone and as fixed combination drug products containing buprenorphine and naloxone. BTODs include ZUBSOLV (buprenorphine HCl and naloxone HCl) sublingual tablets; SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual film (for sublingual or buccal use); Buprenorphine and Naloxone Sublingual Film; and Buprenorphine and Naloxone Sublingual Tablets.

The first BTODs approved were SUBUTEX (buprenorphine HCl) sublingual tablets (NDA 020732)and SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets (NDA 020733).[3] Approval of these products was based, in part, on clinical studies of Buprenorphine Sublingual Tablets with and without Naloxone Sublingual Tablets, and on studies of sublingual administration of a more bioavailable ethanolic solution of buprenorphine (Ref. 1). Dosing recommendations were based on data from one trial of both buprenorphine products and two trials of the ethanolic solutions. In a double-blind, parallel-group, 16-week study, 731 subjects were randomized to receive 1 of 4 dosages of buprenorphine ethanolic solution: 1 milligram (mg), 4 mg, 8 mg, and 16 mg. For comparison purposes 1 mg of solution would be equivalent to less than 2 mg of buprenorphine in sublingual tablets; 4 mg, 8 mg, and 16 mg of buprenorphine in the solution would be roughly equivalent to 6 mg, 12 mg, and 24 mg of buprenorphine in sublingual tablets, respectively. Buprenorphine (administered once daily) was titrated to a maintenance dosage over 1 to 4 days and continued for 16 weeks. Based on retention in treatment and the percentage of thrice-weekly urine samples negative for non-study opioids, the three highest tested dosages of the ethanolic solution (*i.e.*, 4 mg, 8 mg, and 16 mg once daily dosages) were superior to the 1 mg once daily dosage. This study and the additional information submitted to support the approval of SUBUTEX and SUBOXONE demonstrated Buprenorphine Sublingual Tablets are effective from 4 mg to 24 mg once daily. The "Dosage and Administration" section of the original labeling for these products in describing the appropriate maintenance dosage read, in part:

The dosage of SUBOXONE should be progressively adjusted in increments/decrements of 2 mg or 4 mg to a level that holds the patient in treatment and suppresses opioid withdrawal effects. This is likely to be in the range of 4 mg to 24 mg per day depending on the individual [Ref. 1].

In 2011, the Agency took several actions including the approval of two additional strengths, updates to the labeling, and modifications to the risk evaluation and mitigation strategy (REMS) for SUBUTEX and SUBOXONE sublingual tablets (Refs. 2, 3, 4, 5). The goals of the REMS for SUBUTEX and SUBOXONE were to mitigate the risks of accidental overdose, particularly in the pediatric population, and to mitigate the risks of misuse and abuse, as well as to inform patients of the serious risks associated with use of these products (Refs. 2, 4). It was at this time and within the context of addressing these concerns that the application holder for SUBUTEX and SUBOXONE proposed changes to the "Dosage and Administration" section of the approved labeling. For SUBOXONE, FDA approved the following language related to the maintenance dosage in the "Dosage and Administration" section of the labeling (SUBUTEX shares similar language in its labeling (Ref. 5)):

- SUBOXONE sublingual tablet is indicated for maintenance treatment.
- The recommended target dosage of SUBOXONE sublingual tablet is 16 mg/4 mg buprenorphine/naloxone/day as a single daily dose.
- The dosage of SUBOXONE sublingual tablet should be progressively adjusted in increments/decrements of 2 mg/0.5 mg or 4 mg/1 mg buprenorphine/naloxone to a level that holds the patient in treatment and suppresses opioid withdrawal signs and symptoms.
- The maintenance dose of SUBOXONE sublingual tablet is generally in the range of 4 mg/1 mg buprenorphine/naloxone to 24 mg/6 mg buprenorphine/naloxone per day depending on the individual patient. Dosages higher than this have not been

[1] For the purposes of this notice, the terms *opioid dependence* and *opioid use disorder* are used interchangeably.

[2] 21 CFR 1308.13(e).

[3] Approvals of Subutex and Suboxone sublingual tablets were withdrawn on September 15, 2022 (87 FR 50337, August 16, 2022).

demonstrated to provide any clinical advantage.

Relevant to this notice is the inclusion of the statement, "Dosages higher than [24 mg/6 mg buprenorphine/naloxone per day] have not been demonstrated to provide any clinical advantage" in the BTOD labeling (Ref. 5). This language is consistent with 21 CFR 201.57(c)(3)(i)(B) and conveys, in part, that clinical trial data support the safety and effectiveness of buprenorphine dosages up to 24 mg once daily. Although clinical trial data support the effectiveness of buprenorphine dosages ranging from 4 mg to 24 mg once daily for maintenance treatment, this statement may be misconstrued by some as imposing a maximum dosage beyond which buprenorphine may not be prescribed. Further, although the labeling for SUBUTEX and SUBOXONE has always referred to the 16 mg buprenorphine dosage and 16 mg/4 mg buprenorphine and naloxone dosage, respectively, as the "target" dosage, we understand that this too may be misinterpreted as a maximum dosage.

The labeling for these products has changed since the inclusion of the 2011 statement, but the maintenance dosage recommendations in the "Dosage and Administration" section of the SUBUTEX and SUBOXONE labeling have largely remained the same (Refs. 6, 7). Additionally, labeling for other BTODs includes similar language as the labeling for SUBUTEX and SUBOXONE regarding maintenance dosage and treatment (Refs. 8, 9).

B. Perceived Dosage Maximums for BTODs

In recent years, a number of interested parties have raised concerns that the labeling for BTODs, in particular the maintenance dosage recommendations in the "Dosage and Administration" section, may be adversely impacting patient access to this OUD treatment. In August 2022, FDA received a citizen petition submitted by the Colorado Society of Addiction Medicine, in which the petitioner raised concerns that the current labeling for BTODs may be perceived as a barrier to prescribing buprenorphine dosages higher than 24 mg once daily[4] for certain patients, and even dosages higher than 16 mg once daily, and that the language in the labeling may have other implications, such as being used to limit insurance coverage for higher dosages (Ref. 10).[5] The citizen petition specifically cited the maintenance dosage recommendations in the "Dosage and Administration" section of the SUBOXONE labeling and asserted that these recommendations do not recognize the needs of certain patients for buprenorphine dosages higher than 24 mg once daily (Ref. 10). In May 2023, the Reagan-Udall Foundation hosted a 2-day public meeting with FDA and the Substance Abuse and Mental Health Services Administration (SAMHSA), entitled "Considerations for Buprenorphine Initiation and Maintenance Care" (Ref. 11). Some interested parties attending the public meeting expressed concerns similar to those raised in the citizen petition about perceived buprenorphine maximum dosages (Refs. 12, 13). Additionally, on December 11, 2023, SAMHSA, FDA, and the National Institute on Drug Abuse, hosted a listening session to discuss the medical need, emerging data, and barriers to accessing higher doses of buprenorphine in the context of high potency synthetic opioid exposure and concerns were raised about a perceived dosage "cap at 24 mg/day" that is "set to the FDA label" for BTODs (Ref. 14).

The reported reluctance of some healthcare practitioners to prescribe buprenorphine daily dosages of 24 mg or higher, and even 16 mg in some instances, may be based on a misinterpretation of the labeling that 16 mg or 24 mg once daily dosages are a required "dosage limit." Some publications have incorrectly interpreted BTOD labeling as imposing "dosage limits" or "dose limits" of 16 mg or 24 mg once daily (Ref. 15). Moreover, the Agency is aware that some States' Medicaid plans require prior authorization as a condition of reimbursement, to include such requirements as documentation of medical necessity for buprenorphine daily dosages of 16 mg or 24 mg and higher, before buprenorphine is dispensed to the patient (Ref. 16). Additionally, we understand that some States impose additional requirements on healthcare practitioners who prescribe buprenorphine dosages higher than 16 mg/day.[6] States have authority to regulate the activities of doctors and pharmacists within their jurisdictions. However, we want to minimize the possibility that the approved labeling for BTODs is misinterpreted in a way that results in stakeholders believing that such labeling recommendations reflect dosage limitations. The labeling, which states that dosages higher than 24 mg daily "have not been demonstrated to provide any clinical advantage," or that 16 mg/day is the "recommended target dose," are not buprenorphine dosage caps.

The inclusion of a buprenorphine "target" dosage in BTOD labeling reflects the need to move quickly from the very low dosages recommended for treatment initiation (to reduce the risk of precipitation of opioid withdrawal) to dosages that are effective for the treatment of opioid dependence. BTOD labeling recommends a "target" buprenorphine daily dosage of 16 mg, which is not a maximum dosage. The labeling for these products recommends that the buprenorphine dosage should be progressively adjusted in increments or decrements to a level that holds the patient in treatment and suppresses opioid withdrawal. The labeling further provides a general range of daily maintenance buprenorphine dosages of 4 mg to 24 mg per day, depending on the individual patient and clinical response.

The labeling also includes the statement "Dosages higher than 24 mg/day have not been demonstrated to provide a clinical advantage." This statement informs healthcare practitioners regarding the limitations of data available at the time of approval of the application from adequate and well-controlled studies evaluating safety and efficacy beyond a buprenorphine dosage of 24 mg/day. In other words, higher daily dosages have not been subjected to evaluation in randomized trials; it does not mean that daily dosages higher than 24 mg have been shown to be ineffective or that 24 mg/day is a maximum dosage. The labeling does not include any recommended maximum daily buprenorphine dosage.

II. Proposed Revisions to the Labeling for BTODs

A. Ways in Which Labeling May Be Revised

Labeling, including the Prescribing Information (PI), must be updated when new information becomes available that causes the labeling to become inaccurate, false, or misleading (21 CFR 201.56(a)(2)). An applicant may, on its own initiative, submit a supplemental NDA (labeling supplement) to propose

[4] The dosages of buprenorphine listed herein are based on the bioavailability of SUBUTEX and SUBOXONE sublingual tablets. Some fixed combination products containing buprenorphine and naloxone may provide equivalent buprenorphine exposure at alternate dosages due to differences in formulation. Refer to the product labeling for these products, as appropriate, for equivalent dosing to SUBOXONE.

[5] Issues concerning insurance coverage and reimbursement are outside FDA's regulatory purview.

[6] See Tennessee Code Annotated section 53-11-311 (d) (requiring the healthcare provider to document rationale for prescribing higher than 16 mg/day); Ohio Administrative Code 4731-33-03 (same).

changes to the PI based on new information to satisfy this requirement. FDA may also ask applicants to voluntarily update the PI with information, such as safety information or how to safely use the medication, by sending applicants a letter requesting them to submit a labeling supplement. FDA can also require applicants make safety labeling changes if FDA becomes aware of new safety information or information related to reduced effectiveness (pursuant to section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(o)(4))) that it determines should be included in the labeling of the drug. Less commonly, FDA has encouraged application holders to submit labeling supplements to modify the approved labeling of drug products by announcing recommended changes to the labeling through a **Federal Register** notice.[7] We are issuing this notice today because we believe that the recommended clarifications to BTOD labeling would benefit the public health by providing clearer dosage and administration recommendations for these important OUD treatments.

B. Recommended Changes to the Maintenance Dosage Recommendations in the "Dosage and Administration" Section of the Labeling

The "Dosage and Administration" section of the most recently approved labeling for BTODs contains the following: (1) "Dosages higher than 24 mg daily have not been demonstrated to provide a clinical advantage;" and (2) reference to dosage of 16 mg as a "target" dosage.

As stated previously, the statement "Dosages higher than 24 mg daily have not been demonstrated to provide a clinical advantage" was added to the labeling to convey, in part, that clinical trial data support the safety and effectiveness of buprenorphine daily dosages up to 24 mg. However, this statement should not be construed as a buprenorphine maximum dosage, and its inclusion is not a recommendation against healthcare practitioners prescribing buprenorphine daily dosages higher than 24 mg.

Regarding the reference in the labeling to a buprenorphine daily dosage of 16 mg as a "target" dosage, the "target" dosage is to emphasize the need to move quickly from the very low dosages recommended for treatment initiation (to reduce the risk of precipitation of opioid withdrawal) to the dosages that are effective for the treatment of opioid dependence. For example, patients generally begin at a low buprenorphine dosage and titrate upward, which allows the healthcare practitioner to monitor for effectiveness and adverse reactions, such as precipitated opioid withdrawal. During this time of titration, the "target" buprenorphine dosage provides healthcare practitioners with a dosage to aim for because most patients can be stabilized at around 16 mg/day, while also recognizing that further upward titration may be necessary. Due to patient variability in response, daily dosages higher or lower than 16 mg/day may be needed, and each patient should be dosed to clinical effect. The "target" dosage is not a maximum daily maintenance dosage.

Accordingly, we are announcing that the statements in the labeling that dosages higher than 24 mg daily have not been demonstrated to provide a clinical advantage and the reference to the dosage of 16 mg as a "target" dosage can be modified. FDA recommends the following specific changes to the maintenance dosage recommendations in the "Dosage and Administration" section of the most recent approved BTOD labeling: [8]

> After treatment induction to the recommended dose of [equivalent 16 mg buprenorphine OR equivalent 16 mg/4 mg buprenorphine/naloxone] per day, dosing should be further adjusted based on the individual patient and clinical response. The maintenance dose of [DRUG NAME] is generally in the range of [equivalent 4 mg buprenorphine OR equivalent 4 mg/1 mg buprenorphine/naloxone] to [equivalent 24 mg buprenorphine OR equivalent 24 mg/6 mg buprenorphine/naloxone] per day. Dosages higher than [equivalent 24 mg buprenorphine OR equivalent 24 mg/6 mg buprenorphine/naloxone] daily have not been investigated in randomized clinical trials but may be appropriate for some patients.

C. Recommended Changes to the "Pregnancy" Subsection of the "Use in Specific Populations" Section of the Labeling

The "Pregnancy" subsection of the "Use in Specific Populations" section of the most recently approved BTOD labeling contains the statements "Dosage adjustments of buprenorphine may be required during pregnancy, even if the patient was maintained on a stable dose prior to pregnancy. Withdrawal signs and symptoms should be monitored closely, and the dose adjusted as necessary" (Refs. 6, 7). To better align with the changes that the Agency is recommending for the maintenance dosage recommendations in the "Dosage and Administration" section of BTOD labeling, the Agency further recommends that "dosage adjustments" be revised in the "Pregnancy" subsection of BTOD labeling to qualify that the adjustment is most often a dosage increase. For example, the labeling would read, "Dosage adjustments of buprenorphine, such as using higher doses, may be required . . . ."

FDA recommends these changes given the concerns raised regarding the maintenance dosage recommendations in the "Dosage and Administration" section of BTOD labeling. Specifically, it may not be clear from the most recent approved labeling that certain populations, including pregnant females,[9] may need a higher dosage of buprenorphine. For example, the "Pregnancy" subsection of the "Use in Specific Populations" section of the labeling discusses the possible need for "dosage adjustments" for pregnant females but does not specifically highlight the potential need for higher dosages (Refs. 17, 18, 19, 20). We believe it is important that the labeling clearly communicate that this population may require a higher dosage.

Further, these changes are consistent with the data submitted to support the initial inclusion of the "dosage adjustment" statement to the "Pregnancy" subsection of BTOD labeling (Ref. 21). When the statement on "dosage adjustments" for pregnant females was first added to BTOD labeling, FDA reviewed data showing that this population may need higher

[7] See 78 FR 19716 (April 2, 2013), 66 FR 55679 (November 2, 2001).

[8] Some BTOD products contain buprenorphine only and others are fixed combination products containing buprenorphine and naloxone. Further, as discussed in footnote 2, some products containing buprenorphine may provide equivalent buprenorphine exposure at alternate doses (*e.g.*, equivalent to 16 mg or equivalent to 24 mg buprenorphine in SUBUTEX and SUBOXONE) due to differences in formulation. Accordingly, where this notice recommends changes to the labeling, application holders of these BTOD products should update the labeling with appropriate product-specific information, including the appropriate dose(s) specific to their products.

[9] For purposes of this notice, "sex" is a biological construct based on anatomical, physiological, hormonal, and genetic (chromosomal) traits, and is generally assigned based on anatomy at birth typically categorized as male or female, but variations occur. Variations of sex refers to differences in sex development or intersex traits. See Measuring Sex, Gender Identity, and Sexual Orientation (2022). National Academies of Science, Engineering, and Medicine. Washington, DC: The National Academies Press. FDA recognizes that sex and gender are distinct terms, with sex defined as a biological construct and gender as a social construct. For more information, see the guidance for industry Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs (November 2020) available at: *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enhancing-diversity-clinical-trial-populations-eligibility-criteria-enrollment-practices-and-trial.*

dosages. This labeling statement was supported, in part, by a retrospective case review of buprenorphine dosage adjustments for 45 adult females maintained on buprenorphine during pregnancy, in which 89 percent of all patients required an increase of buprenorphine dosage during pregnancy (Ref. 17). Pharmacokinetic data submitted at the time the "dosage adjustment" statement was added to the "Pregnancy" subsection is also consistent with the changes that are being proposed in this notice. A study of nine pregnant females, where pharmacokinetic data were collected on three subjects, reported a trend suggesting a lower buprenorphine and norbuprenorphine (major metabolite) maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve ($AUC_{0-24hrs}$) over the last 24-hour dosing interval during the third trimester of pregnancy than after delivery (Ref. 22). The magnitude of this exposure reduction was highly variable; however, the study authors found that lower C_{max} and $AUC_{0-24hrs}$ suggest "pregnant opioid-dependent women may require increased [buprenorphine] dose during gestation and decreased dose postpartum" (Ref. 22).

Accordingly, we are announcing that the statement in BTOD labeling regarding the potential need for dosage adjustments during pregnancy can be modified as described below. FDA recommends the following specific change under the "Dose Adjustment during Pregnancy and the Postpartum Period" subheading under the "Clinical Considerations" heading in the "Pregnancy" subsection of the "Use in Specific Populations" section in BTOD labeling:

Dosage adjustments of buprenorphine, such as using higher doses, may be required during pregnancy, even if the patient was maintained on a stable dose prior to pregnancy. Dosing should be based on individual response, and withdrawal signs and symptoms should be monitored closely and the dose adjusted as necessary.

D. Summary of Proposed Labeling Revisions

To clarify that the recommendations in the current BTOD labeling do not reflect a maximum buprenorphine dosage of 16 mg or 24 mg once daily, FDA recommends changes to the maintenance dosage recommendations in the "Dosage and Administration" section of BTOD labeling as noted in table 1.

TABLE 1—RECOMMENDED CHANGES TO MAINTENANCE DOSAGE RECOMMENDATIONS IN THE "DOSAGE AND ADMINISTRATION" SECTION OF BTOD LABELING

Most recently approved labeling	Proposed labeling
2 DOSAGE AND ADMINISTRATION . . . After treatment induction and stabilization, the maintenance dose of [DRUG NAME] is generally in the range of [equivalent 4 mg buprenorphine OR equivalent 4 mg/1 mg buprenorphine/naloxone] to [equivalent 24 mg buprenorphine OR equivalent 24 mg/6 mg buprenorphine/naloxone] per day depending on the individual patient. The recommended target dosage of [DRUG NAME] is [equivalent 16 mg buprenorphine OR equivalent 16 mg/4 mg buprenorphine/naloxone] as a single daily dose. Dosages higher than [equivalent 24 mg buprenorphine OR 24 mg/6 mg buprenorphine/naloxone] have not been demonstrated to provide any clinical advantage.	2 DOSAGE AND ADMINISTRATION . . . After treatment induction to the recommended dose of [equivalent 16 mg buprenorphine OR equivalent 16 mg/4 mg buprenorphine/naloxone] per day, dosing should be further adjusted based on the individual patient and clinical response. The maintenance dose of [DRUG NAME] is generally in the range of [equivalent 4 mg buprenorphine OR 4 mg/1 mg buprenorphine/naloxone] to [equivalent 24 mg buprenorphine OR equivalent 24 mg/6 mg buprenorphine/naloxone] per day. Dosages higher than [equivalent 24 mg buprenorphine OR equivalent 24 mg/6 mg buprenorphine/naloxone] mg daily have not been investigated in randomized clinical trials but may be appropriate for some patients.

Additionally, to align with the changes that the Agency is recommending for the maintenance information in the "Dosage and Administration" section of BTOD labeling, FDA recommends changes to the "Dose Adjustment during Pregnancy and the Postpartum Period" subheading under the "Clinical Considerations" heading in the "Pregnancy" subsection of the "Use in Specific Populations" section of BTOD labeling as noted in table 2.

TABLE 2—RECOMMENDED CHANGES TO THE "PREGNANCY" SUBSECTION OF THE "USE IN SPECIAL POPULATIONS" SECTION OF BTOD LABELING

Most recently approved labeling	Proposed labeling
8 USE IN SPECIFIC POPULATIONS 8.1 Pregnancy Clinical Considerations . . . *Dose Adjustment during Pregnancy and the Postpartum Period.* Dosage adjustments of buprenorphine may be required during pregnancy, even if the patient was maintained on a stable dose prior to pregnancy. Withdrawal signs and symptoms should be monitored closely and the dose adjusted as necessary.	8 USE IN SPECIFIC POPULATIONS 8.1 Pregnancy Clinical Considerations . . . *Dose Adjustment during Pregnancy and the Postpartum Period.* Dosage adjustments of buprenorphine, such as using higher doses, may be required during pregnancy, even if the patient was maintained on a stable dose prior to pregnancy. Dosing should be based on individual response, and withdrawal signs and symptoms should be monitored closely and the dose adjusted as necessary.

We have determined that these labeling revisions may be addressed through a supplement submitted under 21 CFR 314.70(c)(6). Any labeling revisions submitted pursuant to this notice should reflect changes to all of

the relevant sections of the labeling identified in this notice, which include the "Dosage and Administration" and "Use in Specific Populations" sections of BTOD labeling.

III. Electronic Submissions

Submit any draft labeling as a prior approval supplement to your NDA. Any labeling supplement must be submitted in the electronic common technical document (eCTD) standard format. The eCTD is the standard format for electronic regulatory submissions to FDA's Center for Drug Evaluation and Research. The FDA Electronic Submissions Gateway (available at: *https://www.fda.gov/industry/electronic-submissions-gateway*) is the central transmission point for sending information electronically to FDA and enables the secure submission of regulatory information for review.

IV. References

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

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2. * Supplement Approval for SUBUTEX (buprenorphine HCl) sublingual tablets (NDA 020732), Dec. 22, 2011, available at: *https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2011/020732s006,s007ltr.pdf.*
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9. * BUNAVAIL (buprenorphine HCl and naloxone HCl) buccal film (NDA 205637), June 17, 2022, available at: *https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/205637s023s024lbl.pdf.*
10. * Citizen petition submitted by the Colorado Society of Addiction Medicine (FDA–2022–P–1863), posted Aug. 10, 2022, available at: *https://www.regulations.gov/docket/FDA-2022-P-1863.*
11. Reagan-Udall Foundation, virtual public meeting entitled "Considerations for Buprenorphine Initiation and Maintenance Care," May 10–11, 2023, meeting materials and transcripts available at: *https://reaganudall.org/news-and-events/events/considerations-buprenorphine-initiation-and-maintenance-care.*
12. Reagan-Udall Foundation, Meeting Transcript, "Considerations for Buprenorphine Initiation and Maintenance Care—Day One," May 10, 2023, available at: *https://reaganudall.org/sites/default/files/2023-07/Transcript%20-%20Buprenorphine%20Initiation%20-%20Day%201%20-%20REVISED%20FINAL.pdf.*
13. Reagan-Udall Foundation, Meeting Transcript, "Considerations for Buprenorphine Initiation and Maintenance Care—Day Two," May 11, 2023, available at: *https://reaganudall.org/sites/default/files/2023-05/Transcript%20-%20Buprenorphine%20Initiation%20-%20Day%202%20-%20final.pdf.*
14. * SAMHSA, Meeting Summary, "Listening Session: Use of High Dose Buprenorphine for the Treatment of Opioid Use Disorder," December 11, 2023, available at: *https://store.samhsa.gov/sites/default/files/high-dose-buprenorphine-report-pep24-02-013.pdf.*
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20. * Substance Abuse and Mental Health Services Administration (SAMHSA) Advisory, "Evidence-Based, Whole-Person Care for Pregnant People Who Have Opioid Use Disorder," March 2024, available at: *https://store.samhsa.gov/sites/default/files/whole-person-care-pregnant-people-oud-pep23-02-01-002.pdf.*
21. * Supplement Approval for SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual film (NDA 022410), Feb. 13, 2017, available at: *https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2017/022410Orig1s023ltr.pdf.*
22. Concheiro, M, HE Jones, RE Johnson, et al., 2011, "Preliminary Buprenorphine Sublingual Tablet Pharmacokinetic Data in Plasma, Oral Fluid and Sweat During Treatment of Opioid-Dependent Pregnant Women," *The Drug Monit*, 33(5):619–626.

Dated: December 18, 2024.

P. Ritu Nalubola,

Associate Commissioner for Policy.

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BILLING CODE 4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Indian Health Service

Request for Public Comment: 60-Day Notice for Extension of the Indian Health Service Loan Repayment Program

AGENCY: Indian Health Service, HHS.

ACTION: Notice and request for comments; request for extension of approval.

SUMMARY: In compliance with the Paperwork Reduction Act of 1995, the Indian Health Service (IHS) invites the general public to take this opportunity to comment on the information collection Office of Management and Budget (OMB) Control Number 0917-