AMERICAN CLINICAL LABORATORY ASSOCIATION

April 11, 2022

Debra Houry, MD, MPH
National Center for Injury Prevention and Control
Centers for Disease Control and Prevention
4770 Buford Highway NE, Mailstop S106-9
Atlanta, Georgia 30341
Attn: Docket. No. CDC-2022-0024

RE: Proposed 2022 CDC Clinical Practice Guideline for Prescribing Opioids

Dear Dr. Houry,

Please accept the comments of the American Clinical Laboratory Association (ACLA) on the Centers for Disease Control and Prevention (CDC) Proposed 2022 CDC Clinical Practice Guideline for Prescribing Opioids. ACLA is a non-profit association representing the nation's leading clinical and anatomic pathology laboratories, including national, regional specialty, end-stage renal disease, hospital, and nursing home laboratories. Clinical laboratories are at the forefront of personalized medicine, driving diagnostic innovation and contributing more than $100 billion annually to the nation's economy.

Diagnostic drug testing is an essential but underutilized tool for promoting the safe and medically appropriate use of prescribed opioids and other controlled substances and decreasing overdose deaths. ACLA members agree with many of the recommendations in the draft clinical practice guideline, but we believe CDC must go further in clarifying when and how clinicians should utilize clinical toxicology drug testing to ensure the responsible and effective use of prescribed opioids and other controlled medications. Additionally, ACLA believes the final clinical practice guideline should reference the Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for select opioid therapy to ensure that patients receive individualized care.

Following are our comments on portions of the clinical practice guideline relevant to laboratory testing.

A. Toxicology Testing When Prescribing Opioids for Chronic Pain

Line 3421 of the draft clinical practice guideline reads: "When prescribing opioids for subacute or chronic pain, clinicians should consider toxicology testing to assess for prescribed medications as well as other prescribed and non-prescribed controlled substances (recommendation category: B, evidence type: 4)." ACLA strongly recommends that CDC revise this language to indicate that toxicology testing is necessary to assess the use of prescribed medications and other controlled substances. Drug testing plays a valuable role in the initial assessment and ongoing management and treatment of patients prescribed chronic opioid therapy. Drug testing offers an objective way to determine the use of illicit or nonprescribed drugs, as well as a method to identify non-compliance with prescribed controlled medications. Patient self-

reporting is unreliable, and drug abuse, diversion, and medication regimen non-compliance frequently occur without obvious signs or symptoms. Drug testing in chronic opioid therapy is recommended uniformly by applicable medical guidelines, including the American Pain Society (APS), American Academy of Pain Medicine (AAPM), American Society of Interventional Pain Physicians (ASIPP), American Association for Clinical Chemistry (AACC), and the Federation of State Medical Boards (FSMB).

The proposed language in the draft clinical practice guideline should state explicitly that toxicology testing is necessary, rather than something clinicians can "consider". Implying that toxicology testing is optional is not consistent with best practices or standards of care. Providing clinicians the option to consider toxicology testing may lead to inappropriate underutilization and result in at-risk patients not receiving optimal treatment.

B. Baseline and Periodic Toxicology Testing During Opioid Therapy

Line 3429 of the draft clinical practice guideline reads: "Prior to starting opioids and periodically during opioid therapy, clinicians should consider toxicology testing to assess for prescribed opioids as well as other prescription and nonprescription controlled substances that increase risk for overdose when combined with opioids, including nonprescribed and illicit opioids and benzodiazepines." ACLA strongly suggests that the final clinical practice guideline recommend toxicology testing at baseline and periodically thereafter, based on individual patient factors and no less than once annually, rather than suggest that clinicians consider it. ACLA also believes it is important that patients do not feel criminalized as a result of the toxicology testing requirements. The final clinical practice guideline should acknowledge this issue as a struggle patients face and a factor that clinicians must be conscious of when considering using toxicology tests in their clinical management of patients. The guideline should encourage physicians to present testing to their patients as a normal part of pain management and the use of controlled substances, as part of a broader effort to destigmatize it.

Current clinical practice guidelines from the AACC recommend that in addition to baseline drug testing, "random drug testing should be performed at a minimum of one to two times a year for low-risk patients (based on history of past substance abuse/addiction, aberrant behaviors, and opioid risk screening criteria), with increasing frequency for higher-risk patients prescribed controlled substances."[1] The Medicare Local Coverage Determination on Controlled Substance Monitoring and Drugs of Abuse Testing from Palmetto GBA also recognizes the value and medical necessity for those receiving chronic opioid therapy of baseline testing and random testing thereafter.[2] The final clinical practice guideline should give clinicians definitive guidance about the value of baseline and periodic random testing during opioid therapy.

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[1] Langman LJ, Jannetto PJ. Using Clinical Laboratory Tests to Monitor drug Therapy in Pain Management Patients at 7. AACC Academy, Laboratory Practice Guidelines. American Association for Clinical Chemistry, 2018. https://www.aacc.org/media/press-release-archive/2018/01-jan/aacc-releases-practice-guidelines-for-using-laboratory-tests-to-combat-opioid-overdoses.

[2] Palmetto GBA Guidelines. Medicare Local Coverage Determination Policy: Controlled Substance Monitoring and Drugs of Abuse Testing (L35724).

C. Introduction of Cost Considerations into Testing Guidelines

ACLA disagrees vehemently with the inappropriate introduction of cost considerations into the draft clinical practice guideline. Line 3460 reads: "Restricting confirmatory testing to situations and substances for which results can reasonably be expected to affect patient management can reduce costs of toxicology testing." Presumptive testing is a cost-effective screening method to identify possible drug or illicit substance use, but clinicians should not be encouraged to consider cost when deciding whether definitive testing is medically necessary for a patient. Clinicians must not be deterred from requesting definitive testing for patients in this way; as written, the draft guideline would do just that. Concern over cost savings should not take precedence over the need for appropriate individualized care that is critical to patients.

ACLA believes the final clinical practice guideline should recognize the different use cases for presumptive testing and definitive testing. The final clinical practice guideline also should clarify that definitive testing should be utilized when testing for controlled drugs for which presumptive screens are not available, not sufficiently sensitive, or not able to distinguish between drugs in a class (when such distinction is necessary).

ACLA agrees that clinicians should ask patients about the use of prescribed and other drugs and consider whether results of presumptive testing are expected, which may reduce the need for testing (*e.g.*, when a patient stops taking a prescribed opioid because pain has subsided). Presumptive testing can be a cost-effective screening method to identify potential drug or illicit substance use and may be appropriate for some low-risk patients. However, presumptive testing is less sensitive and specific than definitive testing. It screens for drug classes, rather than specific drugs, and a practitioner may not have insight into whether another drug in the class is causing a positive result. Not all prescription medications or synthetic/analog drugs are detectable or have readily-available assays (*e.g.*, Fentanyl and Fentanyl analogs). Additionally, presumptive testing can produce erroneous results due to cross-reactivity with other compounds. Relying entirely on presumptive testing could result in inaccurate conclusions of drug use or nonuse that may diminish the most fundamental aspect of better healthcare: trust between provider and patient.

D. Failure to Include CPIC Guideline in the Draft Clinical Practice Guideline

We are disappointed that the draft clinical practice guideline does not reference the CPIC guidelines for CYP2D6, OPRM1, and COMT genotypes and select opioid therapy.[3] CPIC is recognized as a leading authority regarding gene and drug clinically actionable evidence. The gene in the CPIC guidelines with therapy recommendations is Cytochrome P450 2D6 (CYP2D6), which is associated with metabolization of codeine and tramadol, and genetic variants have a major adverse effect on responses to these therapies. Clinical trials also have shown that CYP2D6-guided opioid therapy improves pain control and reduces opioid use, because patients can be prescribed an effective drug therapy sooner in the course of treatment.[4]

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[3] Kristine R. Crews, et al., Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. Clinical Pharmacology & Therapeutics, 2021.

[4] *See* D. Max Smith, PharmD, et al., CYP2D6-guided opioid therapy improves pain control in CYP2D6 intermediate and poor metabolizers: a pragmatic clinical trial. Genetics in Medicine, 2019. *See also* Cameron D. Thomas, PharmD, A hybrid implementation-effectiveness randomized trial of CYP2D6-guided postoperative pain

It is appropriate for clinicians to consider a patient's genetic makeup when determining whether certain opioid therapies may be effective. ACLA believes that CDC erred in failing to include the CPIC guidelines for select opioid therapy in the draft clinical practice guideline. Its inclusion would direct clinicians to pharmacogenetic testing that may help determine the right treatment for a patient or help determine why a prescribed opioid is not working as expected. The final clinical practice guideline should include the CPIC guideline.

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Thank you for considering ACLA's comments.

Sincerely,

Sharon L. West
Vice President, Regulatory and Legal Affairs
American Clinical Laboratory Association

management. Genetics in medicine, 2021.