STATE OF NEW YORK
OFFICE OF THE ATTORNEY GENERAL

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April 11, 2022

VIA FEDERAL eRULEMAKING PORTAL

Rochelle P. Walensky, MD
Director of the Centers for Disease Control and Prevention
Centers for Disease Control and Prevention
1600 Clifton Road, Atlanta, GA 30329 USA

Re: Comments on Proposed Centers for Disease Control and Prevention ("CDC") Clinical Practice Guideline for Prescribing Opioids–United States, 2022, 87 Fed. Reg. 7838 (Feb. 10, 2022), Docket No. CDC–2022–0024

Dear Director Walensky,

Thank you for your agency's efforts in developing the Proposed CDC Clinical Practice Guideline for Prescribing Opioids–United States, 2022 (the "2022 Guideline").[1] This important voluntary guidance reinforces the CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016 (the "2016 Guideline"),[2] which has been an important tool in addressing the epidemic of prescription opioid abuse that continues to damage individuals and communities across the country. New York has been a leader in fighting this scourge, and I strongly encourage CDC to adopt the Proposed 2022 Guideline, with modifications, as set forth below.

The need to address overprescribing of opioids has never been greater, as opioid overdose deaths continue to rise to heartbreaking levels. Provisional data from the CDC show that in the U.S., overdose deaths from opioids increased to more than 75,000 in the 12-month period ending in April 2021, up from 56,000 the year before.[3] In New York State, CDC provisional data show that, for the 12 months ending in October 2021, more than 4,200 people died from opioid overdoses.[4] During the same period, almost 1,200 New Yorkers died from prescription opioid

[1] https://www.regulations.gov/document/CDC-2022-0024-0002.
[2] https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6501e1.pdf.
[3] CDC, *Drug Overdose Deaths in the U.S. Top 100,000 Annually* (Nov. 17, 2021), https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2021/20211117.htm.
[4] CDC, National Center for Health Statistics, National Vital Statistics System, Provisional Drug Overdose Death Counts, https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm.

overdoses.[5] A preponderance of evidence suggests that the increase in prescription opioid use beginning in the late 1990s served as a gateway to increased heroin use.[6] Fentanyl, a powerful synthetic prescription opioid that is also illicitly manufactured, has been added to heroin to increase its potency, or disguised as heroin.[7]

Every four hours someone dies of a drug overdose in New York City.[8] In 2020 there were 1,745 opioid overdose deaths of which 16% involved prescription opioids, compared with 12% in 2019.[9] 596 opioid overdose deaths were confirmed during the first quarter of 2021 alone.[10] These tragic numbers are at their highest since New York City began tracking opioid deaths in 2000.[11] Black residents have been disproportionately impacted, with more than twice as many dying from prescription opioid overdoses in 2020 than in 2019.[12]

Opioid prescribing in the United States quadrupled from 1999 to 2010, which caused a dramatic rise in opioid overdose deaths.[13] Although opioid prescribing began to decline in approximately 2012,[14] studies indicate that the 2016 Guideline is associated with a reduction in the overprescribing of prescription opioids and mitigation of harms. In particular, a 2021 study of almost 13 million unique patients found that for non-cancer, opioid-naïve, patients high-dose opioid prescribing rates were already decreasing by 2016. That trend continued after the release of the 2016 Guideline, and guideline-concordant care has the potential to improve pain management and reduce opioid-related harms.[15]

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[5] For purposes of certain reports, CDC defines prescription opioids to include natural and semi-synthetic opioids (including methadone) but excludes the synthetic opioids fentanyl and tramadol. https://www.cdc.gov/drugoverdose/deaths/prescription/maps.html.

[6] THE NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE, PAIN MANAGEMENT AND THE OPIOID EPIDEMIC: BALANCING SOCIETAL AND INDIVIDUAL BENEFITS AND RISKS OF PRESCRIPTION OPIOID USE (2017) at 215, https://nap.nationalacademies.org/catalog/24781/pain-management-and-the-opioid-epidemic-balancing-societal-and-individual.

[7] United States Drug Enforcement Administration, Fentanyl, https://www.dea.gov/factsheets/fentanyl.

[8] New York City Department of Health and Mental Hygiene, Unintentional Drug Poisoning (Overdose) Deaths Quarter 1, 2021 (Nov. 2021), https://www1.nyc.gov/assets/doh/downloads/pdf/basas/provisional-overdose-report-first-quarter-2021.pdf.

[9] New York City Department of Health and Mental Hygiene, *Unintentional Drug Poisoning (Overdose) Deaths in New York City in 2020*, NYC Health Epi Data Brief No. 129 (Nov. 2021), https://www1.nyc.gov/assets/doh/downloads/pdf/epi/databrief129.pdf. The totals exclude fentanyl and tramadol.

[10] New York City Department of Health and Mental Hygiene, *Unintentional Drug Poisoning (Overdose) Deaths Quarter 1, 2021, New York City* (Nov. 2021), https://www1.nyc.gov/assets/doh/downloads/pdf/basas/provisional-overdose-report-first-quarter-2021.pdf.

[11] Li Cohen, *New York City opens nation's first supervised injection site to help curb overdose deaths*, CBS NEWS, (Nov. 30, 2021), https://www.cbsnews.com/news/new-york-city-overdose-prevention-centers-injection-sites/.

[12] New York City Department of Health and Mental Hygiene, *Unintentional Drug Poisoning (Overdose) Deaths in New York City in 2020*, NYC Health Epi Data Brief No. 129 (Nov. 2021), https://www1.nyc.gov/assets/doh/downloads/pdf/epi/databrief129.pdf.

[13] Congressional Research Service, *Consumption of Prescription Opioids for Pain: A Comparison of Opioid Use in the United States and Other Countries* (June 2, 2021), https://crsreports.congress.gov/product/pdf/R/R46805.

[14] CDC, *U.S. Opioid Dispensing Rate Maps*, https://www.cdc.gov/drugoverdose/rxrate-maps/index.html.

[15] Jason E. Goldstick, et al., *Changes in Initial Opioid Prescribing Practices After the 2016 Release of the CDC Guideline for Prescribing Opioids for Chronic Pain*. JAMA NETW. OPEN 2021;4(7), https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781924.

A strength of the 2022 Guideline is that its recommendations are consistent with CDC's 2016 Guideline. It is important for the CDC to clarify the misimpression that it has "thrown out" or somehow "reversed" the 2016 Guideline,[16] which is not the case. But the twelve (12) recommendations for prescribers that are contained in Box 1 of the 2022 Guideline (at 208), which will likely be its most frequently reviewed component, should provide more specific guidance. CDC should also make several modifications to the 2022 Guideline, as set forth below.

I. Include numerical thresholds for assessing risks of opioids.

The recommendations contained in Box 1 of the 2022 Guideline should include the evidence-based numerical thresholds that are discussed throughout the 211-page draft. In the 2016 Guideline, Box 1 contained evidence-based numerical thresholds that gave prescribers concrete tools for assessing the risks and benefits of opioid therapy. However, Box 1 in the 2022 Guideline omits all numerical thresholds, despite the fact that the evidence for them is stronger today than in 2016. The numerical thresholds are needed to counter the misleading information regarding risks and benefits that opioid makers have disseminated for decades. For example, a now-defunct advocacy group funded by the pharmaceutical opioid industry promulgated the falsity that opioids have no ceiling dose.[17] In other words, the group duped prescribers into believing that they could increase opioid dosages to dangerous levels without risk of harm to patients. By omitting evidence-based numerical thresholds from Box 1 the 2022 Guideline would likely be of limited utility for prescribers, would be contrary to the scientific evidence, and may result in harm to patients. For example:

- Box 1, Recommendation #4 states that if opioids are continued for subacute or chronic pain, "clinicians should use caution when prescribing opioids at any dosage, should carefully evaluate individual benefits and risks when considering increasing dosage, and should avoid increasing dosage above levels likely to yield diminishing returns in benefits relative to risks to patients." However, the implementation recommendations provide numerical thresholds directly relevant to the recommendation: "*Many patients do not experience benefit in pain or function from increasing opioid dosages to ≥50 MME [morphine equivalent dose]/day but are exposed to progressive increases in risk as dosage increases. Therefore, before increasing total opioid dosage to ≥50 MME/day, clinicians should pause and carefully reassess evidence of individual benefits and risks. If a decision is made to increase dosage, clinicians should use caution and increase dosage by the smallest practical amount.*" (2022 Guideline, at 96.) The implementation recommendations also state that "*Additional dosage increases beyond 50 MME/day are progressively more likely to yield diminishing returns in benefits relative to risks to*

[16] For example, on February 10, 2022, an article by Jan Hoffman in the New York Times bore the headline: "C.D.C. Proposes New Guidelines for Treating Pain, Including Opioid Use: The agency threw out previous recommended limits on doses but encouraged 'nonopioid therapies' wherever possible." https://www.nytimes.com/2022/02/10/health/cdc-opioid-pain-guidelines.html.

[17] *Senate Finance Committee Bipartisan Opioids Report* (Dec. 16, 2020), https://www.finance.senate.gov/imo/media/doc/2020-12-16%20Finance%20Committee%20Bipartisan%20Opioids%20Report.pdf; *see also* J. Fauber, *Painkiller boom fueled by Networking*, MILWAUKEE J. SENTINEL (Feb. 18, 2012), https://archive.jsonline.com/watchdog/watchdogreports/painkiller-boom-fueled-by-networking-dp3p2rn-139609053.html/.

patients as dosage increases further."[18] (2022 Guideline, at 96.) These are important factors for prescribers to consider.

- Box 1, Recommendation #6 states that when opioids are needed for acute pain, "clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids." Yet the implementation considerations specify the sufficient duration of opioid prescribing for acute pain, stating that "*a few days or less are often sufficient, and shorter courses can minimize the need to taper opioids to prevent withdrawal symptoms at the end of a course of opioids.*"[19] (2022 Guideline, at 115.) Again, this is important guidance for prescribers.

- Box 1, Recommendation # 8 states that "[c]linicians should work with patients to incorporate into the management plan strategies to mitigate risk, including offering naloxone when factors that increase risk for opioid overdose are present." Again, the implementation considerations provide a numerical threshold for determining increased risk: "*Clinicians should offer naloxone when prescribing opioids to patients at increased risk for overdose, including patients with a history of overdose, patients with a history of substance use disorder, patients with sleep-disordered breathing, patients taking higher dosages of opioids (e.g., ≥50 MME/day)*[.]*"*[20] (2022 Guideline, at 125.) This threshold, which encourages making available life-saving naloxone, does not inhibit proper opioid prescribing, but rather makes it more likely.

- Box 1, Recommendation #9 states that "clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or combinations that put the patient at high risk for overdose." Yet the implementation considerations provide a specific time frame for PDMP review: "*At a minimum, during long-term opioid therapy, PDMP data should be reviewed before an initial opioid prescription and then every 3 months or more frequently."*[21] (2022 Guideline, at 136.) Again, this consideration is vital for appropriate opioid prescribing.

In sum, eliminating the thresholds from the recommendations risks a return to the dangerous overprescribing practices of the 2000s.

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[18] Box 1, Recommendation #5 in the 2016 Guideline stated: "Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day."

[19] Box 1, Recommendation #6 in the 2016 Guideline stated that when opioids are used for acute pain, "[t]hree days or less will often be sufficient; more than seven days will rarely be needed."

[20] Box 1, Recommendation # 8 in the 2016 Guideline stated: *"*Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present."

[21] Box 1, Recommendation #9 in the 2016 Guideline stated: *"*Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months."

II. Encourage non-opioid therapies for pain.

The scientific evidence shows – and the 2022 Guideline rightly emphasizes in Recommendation #1 – that non-opioid therapies for pain, in particular, non-pharmacological, non-invasive treatments, are effective. Indeed, a 2021 study of more than 22,000 surgical patients found that those who were *not* prescribed opioids after surgery had similar clinical and patient-reported outcomes as patients who *were* prescribed opioids, suggesting that minimizing opioids as part of routine postoperative care is unlikely to adversely affect patients.[22] However, as CDC itself recognizes, lack of health insurance coverage for such treatments has limited access to such modalities. (2022 Guideline, at 66.) It is encouraging that CDC is committing to "work with public and private payers with the aim of improving coverage for nonpharmacologic treatments, increasing access to non-opioid pain medication, supporting patient counseling and coordination of care, increasing access to evidence-based treatments of opioid use disorder, and enhancing availability of multidisciplinary and multimodal care." (2022 Guideline, at 165.) To ensure this happens, CDC should issue a detailed action plan for engaging health insurers and holding them accountable to improve coverage of evidence-based, alternative treatments for pain.

III. Recognize the limited utility of opioids for the treatment of chronic pain.

This need to consider non-opioid treatments is particularly necessary with regards to the treatment of chronic pain. Six years after issuance of the 2016 Guideline, the scientific evidence supporting opioids for chronic pain continues to be very limited. The 2022 Guideline appropriately acknowledges this understanding: "The clinical evidence reviews found that nonopioid therapies are effective for many common types of acute pain and found insufficient evidence to determine long-term (>1 year) benefits of opioid therapy for chronic pain." (2022 Guideline, at 4.) Recommendation 5 states that for patients receiving higher opioid dosages, if risks outweigh benefits, "clinicians should optimize other therapies and work closely with patients to gradually taper to lower dosages or, if warranted based on the individual clinical circumstances of the patient, to appropriately taper and discontinue opioids." The lack of evidence for the effectiveness of opioids for much chronic pain should be explicitly stated in the recommendations contained in Box 1.

IV. Recognize that pain is undertreated and untreated due to clinical bias based on race and gender.

Although the text of the 2022 Guideline properly discusses the need for prescribers to consider disparities in the treatment of pain in women, and Black, Latino, and Asian patients (2022 Guideline, at 7), these considerations should be included in the Box 1 recommendations. It is encouraging that one of the "guiding principles" listed at the end of Box 1 is that "[c]linicians, practices, health systems, and payers should vigilantly attend to health inequities," but this is not sufficient to bring it to front of mind for clinicians. Prescribers should be instructed to address potential biases in clinical decision-making and aim for equity among all patient populations by

[22] Ryan Howard, et al., *The Association of Postoperative Opioid Prescriptions with Patient Outcomes*, ANNALS OF SURGERY (June 4, 2021), https://journals.lww.com/annalsofsurgery/Abstract/9000/The_Association_of_Postoperative_Opioid.93525.aspx.

focusing on the full range of evidence-based therapeutic options for pain management. This principle should be part of the recommendations for determining whether or not to initiate opioids for pain, and to consider and provide alternative treatments for pain.

Lastly, much attention has been given to the practices of some prescribers and health insurance companies in incorrectly applying the 2016 Guideline. The prior Guideline was explicitly directed to "prescribing opioids for chronic pain outside of active cancer, palliative, and end-of-life care" and was intended to be a recommendation. Nevertheless, some health insurance companies and prescribers used the Guideline as an excuse to deny opioid treatment for patients, including people with cancer, causing them needless pain and suffering.[23] To ensure fidelity to the 2022 Guideline, which is limited to "prescribing opioids for outpatients with pain outside of sickle cell disease-related pain management, cancer pain treatment, palliative care, and end-of-life care," CDC should engage in a media campaign to educate the public about the Guideline's recommendations and limitations.

Thank you for the opportunity to comment on the Proposed 2022 Guideline, and for your commitment to appropriate opioid prescribing.

Sincerely,

LETITIA JAMES
New York Attorney General

[23] Letter from the American Society of Hematology, the American Society of Clinical Oncology, and the National Comprehensive Cancer Network to CDC (Feb. 13, 2019), https://www.asco.org/sites/new-www.asco.org/files/content-files/advocacy-and-policy/documents/2019-NCCN-ASCO-ASH-Letter-CDC.pdf.