

Center for Drug Evaluation and Research

Food and Drug Administration

10903 New Hampshire Ave., Bldg. 22, Rm. 4462

Silver Spring, MD 20993-0002

February 11, 2021

**RE: Docket #FDA-2020-N-1561-0001**

We write this letter on behalf of the National Council on Independent Living (NCIL), a leading national disability rights organization, and the longest-running national cross-disability, grassroots organization run by and for people with disabilities. NCIL represents thousands of individuals with disabilities and organizations including Centers for Independent Living (CILs), Statewide Independent Living Councils (SILCs), and other organizations that advocate for the human and civil rights of people with disabilities throughout the US.

As an organization representing people with disabilities across the country, many who live with chronic pain, NCIL works to protect the rights of people with chronic pain. Our work in this area began as efforts to address the opioid crisis ramped up in the US, and we saw people with chronic pain left out of these efforts and harmed as a result.

Thank you for the opportunity to respond to docket #FDA-2020-N-1561-0001, concerning evaluation of the opioid analgesics REMS program.

The FDA CDER issues paper “Methods for Evaluating the Opioid Analgesic Risk Evaluation and Mitigation Strategy” deftly outlines the difficulty of evaluating continuing medical education (CME) in an environment where prescribing has declined past a 15-year low,[[1]](#footnote-1) with high-dose prescribing down 66%,[[2]](#footnote-2) and over 526 laws and policies have targeted opioid prescribing between 2016 and 2018 alone, with many more since then.

We write primarily to urge the FDA to measure patient outcomes in its evaluation process. In other words, in addition to attempting to tease out the effect of REMS on changing prescriber behavior, we would strongly suggest that CME be evaluated by the outcomes of these behavior changes: What happened to patients *after* their prescribers’ behavior changed? How can CME prevent harms to patients from both prescribing and de-prescribing?

The materials the FDA posted mention patient outcomes, but the presentations and accompanying data provide little to no guidance or detail on whether patient outcomes will indeed be prioritized or how such outcome measures might be effectuated.

Measuring patient outcomes is especially critical in light of emerging reports of serious patient harm. In recent years, evidence has emerged that nationwide reductions in opioid prescribing have resulted in grave harm to people with disabilities, as documented in a letter to the CDC from over 300 health professionals,[[3]](#footnote-3) safety warnings from CDC and HHS,[[4]](#footnote-4) [[5]](#footnote-5) and a clarification by *CDC Guideline* authors in the New England Journal of Medicine.[[6]](#footnote-6) A report by international watchdog Human Rights Watch (HRW) found that while some patients improve after voluntary taper, other patients who were tapered involuntarily report damage to their mental and physical health.[[7]](#footnote-7) This report also concluded that some clinicians were tapering patients out of fear of oversight and against their own better medical judgment, discontinuing medication in patients they believed benefited from opioid therapy. As a result of such tapers, some patients report losing function and the ability to work, suffering financial devastation as a result. Others may resort to the illegal market and even suicide when medication or care is denied.[[8]](#footnote-8) [[9]](#footnote-9) [[10]](#footnote-10) Increasingly, observational studies show that reductions in opioid prescribing have involved unsafe tapering practices with harrowing results.[[11]](#footnote-11) [[12]](#footnote-12) [[13]](#footnote-13) [[14]](#footnote-14) [[15]](#footnote-15) [[16]](#footnote-16) [[17]](#footnote-17) [[18]](#footnote-18) Indeed, the FDA itself has warned of the dangers of such practices in safety communication.[[19]](#footnote-19)

Another outcome of significant concern is the apparent inability of patients who use opioids to manage pain to get access to healthcare at all. According to a recent study of clinics in nine states, more than 50% of clinicians are unwilling to accept patients who regularly use opioids to manage pain, [[20]](#footnote-20) and 81% are reluctant to according to another study. [[21]](#footnote-21) Indeed, the near singular focus on numbers has led to problematic ethical issues that CME should address: “clinicians who are willing to care for patients on higher doses face elevated oversight risk, and this may create an incentive to discard or fail to treat some of the most vulnerable patients.”[[22]](#footnote-22)

New laws and policies almost universally aim for fewer prescriptions and lower dosage as desirable outcomes. Quality metrics rate numerical reduction alone as success, regardless of the functional status of any given patient post-reduction.[[23]](#footnote-23) We believe such metrics fail to capture outcomes important to patients: workforce participation, mobility, participation in activities, avoidance of harms from involuntary opioid taper including incapacitation, overdose and suicide, and ensuring appropriate access to care.

When CME is evaluated for consistency with the 2016 *CDC Guideline for Prescribing Opioids for Chronic Pain*, it is important to keep in mind that the *CDC Guideline* does not endorse hard limits on dosage in MME (morphine milligram equivalent) or duration for opioid prescriptions, as the CDC reiterated in 2019.[[24]](#footnote-24) Neither are appropriate proxies for standards of care. CME that promotes hard limits or medically unnecessary tapering should be considered inconsistent with the *Guideline.* Yet, too often, CME that merely mentions the same numbers as the *Guideline* (e.g. 3 days for acute pain, 50 or 90 MME daily dosage) is rated as “consistent” with the *Guideline*.

If the goal of FDA’s opioid analgesic REMS is to reduce opioid prescribing, a reduction in prescribing has been achieved. Disagreement may exist about the appropriate level of prescribing, which according to the most recent IQVIA data, is roughly at the level of that in the year 2000.[[25]](#footnote-25) We would posit that the near singular focus on aggregate reduction is having an unintended but palpable overreach that poses unacceptable risk to the 8[[26]](#footnote-26) to 13[[27]](#footnote-27) million Americans who use opioids regularly to manage pain, an overreach that cannot continue to be ignored. The REMS program on prescribing patterns, the REMS program (and CME in general) can and should be evaluated for its consistency with consensus recommendations for patient well-being and protection from harm.[[28]](#footnote-28)

We reiterate our comment to FDA from July 2019: Chronic pain varies significantly from one person to another, and no single treatment modality is effective for everyone; rather it is often a combination of treatments that allows individuals to most effectively manage their pain. Because people with chronic pain need access to the full spectrum of available modalities for pain treatment, we support efforts to increase access to non-opioid treatments and therapies and to develop new non-opioid alternatives. At the same time, individualized treatment, as determined by an individual and their physician, *must* be prioritized over across-the-board policies with the sole goal of reducing opioid use. Such narrowly-focused policies disregard physician expertise, diminishing the doctor-patient relationship.

Even a focus on one treatment modality, opioids, misses the bigger picture, in which optimal pain care typically includes different modalities used in combination. This is true even in cases in which opioids are used. Although we understand that this request for comment deals specifically with the opioid analgesic risk mitigation and that coordinated care is undoubtedly beyond the purview of the FDA, reference to the importance of interdisciplinary or multimodal care as part of REMS program is advisable, as some of the presenters mentioned.

Finally, we believe that it is vitally important to include patients in this process. A cornerstone of the disability rights movement is the animating idea of “nothing about us without us,” which refers to the fact that technocratic processes which determine the very lives of disabled people are often conducted without including our input or views. With this in mind, we ask FDA to include patients, people with chronic pain and other disabilities, in the development and evaluation of REMS programs, on advisory boards, and in other decision-making bodies. We at NCIL would be happy to assist and to recommend participants for any workgroup.

We also recommend that FDA committees focused on opioid prescribing continue to include clinicians who care for patients with severe pain on a daily basis, especially those who are willing to take on the complex task of medication management.

We thank you again for the opportunity to comment, and we remain appreciative of FDA’s efforts to include people with disabilities in your work. If you have any questions, please feel free to contact the co-chairs of NCIL’s Chronic Pain/Opioids Task Force, Kate Nicholson at kate@katemnicholson.com or Lindsay Baran at lindsay@ncil.org.

Thank you.

Sincerely,

A close - up of a logo

Description automatically generated with low confidence

Kelly Buckland

1. U.S. Food and Drug Administration, “Quantities of opioid analgesics dispensed from retail pharmacies approach the lowest levels in 15 years,” August 30, 2018. <https://www.fda.gov/about-fda/reports/quantities-opioid-analgesics-dispensed-retail-pharmacies-approach-lowest-levels-15-years> [↑](#footnote-ref-1)
2. CDC National Center for Injury Prevention and Control, 2019 Annual Surveillance Report of Drug-Related Risks and Outcomes — United States Surveillance Special Report. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. November 1, 2019. <https://www.cdc.gov/drugoverdose/pdf/pubs/2019-cdc-drug-surveillance-report.pdf> [↑](#footnote-ref-2)
3. Letter from CDC Director Redfield, at HP3 Health Professionals for Patients in Pain, <https://healthprofessionalsforpatientsinpain.org/press-release> [↑](#footnote-ref-3)
4. “CDC advises against misapplication of the *Guideline for Prescribing Opioids for Chronic Pain,*” April 24, 2019. <https://www.cdc.gov/media/releases/2019/s0424-advises-misapplication-guideline-prescribing-opioids.html> [↑](#footnote-ref-4)
5. US Department of Health and Human Services, “HHS Announces Guide for Appropriate Tapering or Discontinuation of Long-Term Opioid Use,” October 10, 2019. https://www.hhs.gov/opioids/sites/default/files/2019-10/Dosage\_Reduction\_Discontinuation.pdf [↑](#footnote-ref-5)
6. Deborah Dowell, M.D., M.P.H., Tamara Haegerich, Ph.D., and Roger Chou, M.D. “No Shortcuts to Safer Opioid Prescribing,” *New England Journal of Medicine*, April 24, 2019. DOI: 10.1056/NEJMp1904190 [↑](#footnote-ref-6)
7. Human Rights Watch. (2018). *Not Allowed to be Compassionate*. <https://www.hrw.org/report/2018/12/18/not-allowed-be-compassionate/chronic-pain-overdose-crisis-and-unintended-harms-us> [↑](#footnote-ref-7)
8. Morabito, N. (2018). VA reps to discuss impact of opioid reduction on suicides during summit. Retrived from <http://www.wjhl.com/news/va-reps-to-discuss-impact-of-opioid-reduction-on-suicides-during-summit_20180123093420242/934066782> [↑](#footnote-ref-8)
9. Demidenko MI, et al. Suicidal ideation and suicidal self-directed violence following clinician-initiated prescription opioid discontinuation among long-term opioid users, Gen Hosp Psychiatry. 2017 Jul;47:29-35. doi: 10.1016/j.genhosppsych.2017.04.011. Epub 2017 Apr 27. [↑](#footnote-ref-9)
10. Levine, Art. “The Government’s Solution to the Opioid Crisis Feels Like a War to Pain Patients,” Huffington Post, 7/31/2018. <https://www.huffpost.com/entry/government-crackdown-opioid-prescriptions-pain-patients_n_5b51ec57e4b0fd5c73c4a42e> [↑](#footnote-ref-10)
11. Mark, T.L., Parish, W., Opioid Medication Discontinuation and Risk of Adverse Opioid-Related Health Care Events, 103 J. Subst. Abuse Treat. 58-63 (2019). <https://doi.org/10.1016/j.jsat.2019.05.001> [↑](#footnote-ref-11)
12. Oliva Elizabeth M, Bowe Thomas, Manhapra Ajay, Kertesz Stefan, Hah Jennifer M, Henderson Patricia et al. Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation BMJ 2020; 368 :m283 doi: <https://doi.org/10.1136/bmj.m283> [↑](#footnote-ref-12)
13. James, J.R., Scott, J.M., Klein, J.W. et al. Mortality after discontinuation of primary care-based chronic opioid therapy for pain: a retrospective cohort study. J GEN INTERN MED (2019) 34: 2749. <https://doi.org/10.1007/s11606-019-05301-2> [↑](#footnote-ref-13)
14. Glanz JM, Binswanger IA, Shetterly SM, Narwaney KJ, Xu S. Association Between Opioid Dose Variability and Opioid Overdose Among Adults Prescribed Long-term Opioid Therapy. JAMA Netw Open.2019;2(4):e192613. [doi:10.1001/jamanetworkopen.2019.2613](file:///C:\doi\10.1001:jamanetworkopen.2019.2613) [↑](#footnote-ref-14)
15. Perez, H., M. Buonora, C., Cunningham, M. et al., *Opioid Taper Is Associated with Subsequent Termination of Care: A Retrospective Cohort Study*, J Gen Intern Med (Aug 19 2019). <https://doi.org/10.1007/s11606-019-05227-9> [↑](#footnote-ref-15)
16. Demidenko MI, et al. Suicidal ideation and suicidal self-directed violence following clinician-initiated prescription opioid discontinuation among long-term opioid users, Gen Hosp Psychiatry. 2017 Jul;47:29-35. [doi:10.1016/j.genhosppsych.2017.04.011](file:///C:\doi\10.1016:j.genhosppsych.2017.04.011) Epub 2017 Apr 27. [↑](#footnote-ref-16)
17. Fenton, J., Agnoli, A., Xing, G., et al., Trends and Rapidity of Dose Tapering among Patients Prescribed Long-Term Opioid Therapy, 2008-2017. JAMA Netw Open.2019;2(11):e1916271. <https://doi.org/10.1001/jamanetworkopen.2019.16271> [↑](#footnote-ref-17)
18. Neprash, H.T., Gaye, M. & Barnett, M.L. Abrupt Discontinuation of Long-term Opioid Therapy Among Medicare Beneficiaries, 2012–2017. *J GEN INTERN MED* (2021). <https://doi.org/10.1007/s11606-020-06402-z> [↑](#footnote-ref-18)
19. FDA Drug Safety Communication, *FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering* (April 4, 2019), https://www.fda.gov/drugs/drug-safety-and-availability/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes [↑](#footnote-ref-19)
20. # Lagisetty, P.; Macleod, C.; Thomas, J.; Slat, S.; Kehne, A.; Heisler, M; Bohnert, A.; Bohnert, K., *Assessing reasons for decreased* *primary care access* *for individuals on prescribed opioids, an audit study*, PAIN (Nov. 11, 2020), <https://journals.lww.com/pain/Abstract/9000/Assessing_reasons_for_decreased_primary_care.98202.aspx>. *See also* <https://labblog.uofmhealth.org/industry-dx/pain-patients-who-take-opioids-cant-get-door-at-half-of-primary-care-clinics>(Jan. 25, 2021).

    [↑](#footnote-ref-20)
21. Quest Diagnostics and Center for Addiction, HealthTrends, *Drug Misuse in America: Physician Perspectives and Diagnostic Insights on the Evolving Drug Crisis* (2019) <https://questdiagnostics.com/home/physicians/health-trends/trends/pdm-health-trends.html> [↑](#footnote-ref-21)
22. Nicholson, K. and Hellman, D., Opioid Prescribing and the Ethical Duty to *Do No Harm* (May 27, 2020), 46 Am. J.L. & Med., Forthcoming June 2020; Virginia Public Law and Legal Theory Research Paper No. 2020-48. Available at SSRN: <https://ssrn.com/abstract=3611753> [↑](#footnote-ref-22)
23. Kertesz, S; Satel, S; DeMicco, J; Dart, R, & Alford, D., (2019) Opioid discontinuation as an institutional mandate: Questions and answers on why we wrote to the Centers for Disease Control and Prevention, Substance Abuse, DOI: 10.1080/08897077.2019.1613830 [↑](#footnote-ref-23)
24. *supra*, n.5 [↑](#footnote-ref-24)
25. IQVIA Institute Report, *Prescription Opioid Trends in the United States, Measuring and understanding process in the opioid crisis* (Dec. 16, 2020), https://www.iqvia.com/insights/the-iqvia-institute/reports/prescription-opioid-trends-in-the-united-states [↑](#footnote-ref-25)
26. Kroenke, K; Alford, D.; Argoff, C.; Canlas, B., *et al*, *Challenges with Implementing the Centers for Disease Control and Prevention Opioid Guideline: A Consensus Panel Report*, Pain Medicine, Vol. 20, Iss. 4, Pages 724–735 (Apr. 2019). DOI: <https://doi.org/10.1093/pm/pny307> [↑](#footnote-ref-26)
27. Mojtabai R., *National trends in long-term use of prescription opioids,* Pharmacoepidemiol. Drug Saf. 2018 May; 27(5):526-534. doi: 10.1002/pds.4278. Epub: https://pubmed.ncbi.nlm.nih.gov/28879660/ [↑](#footnote-ref-27)
28. Covington, Edward C. et al. “Ensuring Patient Protections When Tapering Opioids: Consensus Panel Recommendations.” Mayo Clinic Proceedings, Volume 95, Issue 10, 2155 – 2171. DOI:<https://doi.org/10.1016/j.mayocp.2020.04.025> [↑](#footnote-ref-28)