NATIONAL PAIN ADVOCACY CENTER

Kate Nicholson
President and Founder
kate@nationalpain.org
nationalpain.org

February 11, 2021

Re: Opioid Analgesics Risk Evaluation and Mitigation Strategy (OA REMS)

Kate Nicholson, JD
President and Founder

To members of the FDA:

We are a new alliance of scientists and clinicians, civil rights advocates and people with lived experience of pain. Our mission is to advance the health and human rights of people living with pain. We envision a world in which pain is treated equitably and effectively so that all people in pain have the opportunity to live full and productive lives.

We appreciate the opportunity to provide these comments on methods for evaluation of the opioid analgesics REMS program, docket #FDA-2020-N-1561-0001. We write to voice our concern that pain patients are increasingly being left without access to necessary medication and, in some cases, without healthcare altogether. In light of this harm, we believe that any evaluation of the OA REMS must include meaningful measures to document patient outcomes. We would also urge the FDA to solicit the input of patients as part of its evaluative process.

We fully endorse the expanded statement submitted by the National Council on Independent Living (NCIL). We write separately to highlight that, while the NCIL letter focuses on the common ground of disability—given that people in serious pain as well as those in recovery from addition are covered by the Americans with Disabilities Act and associated civil rights laws—important health equity concerns extend to other disadvantaged groups as well.

COVID19 has revealed in stark, life or death, terms that Black, Indigenous and Latinx people, people with disabilities and older Americans have been disparately affected by a virus to which we are all vulnerable. Social determinants of health and disparities in treatment are reflected in pain and pain care also. Numerous studies demonstrate, for example, that Black or Brown Americans are far more likely to have their pain rated lower by a provider[1] on the diagnostic side, and, on the treatment side, are less likely to

H

[1] Hoffman KM, Trawalter S, Axt JR, Oliver MN. *Racial bias in pain assessment and treatment recommendations, and false beliefs about biological differences between blacks and whites*, Proc. Natl. Acad. Sci. U S A. (April 2016)113(16):4296-301. doi: 10.1073/pnas.1516047113.

P.O. Box 4172
Boulder, CO 80302

info@nationalpain.org
(303) 909-3175

Kate Nicholson
President and Founder
kate@nationalpain.org
nationalpain.org

receive pain medication.[2] [3] [4] It is important to keep in mind, then, that the harms which we outline are likely to fall especially hard on historically disadvantaged groups. Indeed, at least one study has shown that people of color are more likely to be subjected to opioid tapering.[5] In our plea that the FDA incorporate the views of patients in its evaluation process, we would urge that the full diversity of patients likely to be affected be represented.

In short, we highlight the following concerns with respect to treatment of all patients living with pain:

- In addition to evaluating the effect of REMS on changing prescriber behavior, **we would strongly suggest that CME be evaluated by the outcomes of prescriber 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 FDA materials and presentation mention outcomes, but provide little elaboration or guidance.

- **Measuring patient outcomes is especially critical in light of emerging reports of patient harm**, as documented in warnings from the CDC and HHS,[6] [7] a clarification by *CDC Guideline* authors in the New England Journal of Medicine,[8] a report by international

---

[2] Meghani SH, Byun E, Gallagher RM. *Time to take stock: a meta-analysis and systematic review of analgesic treatment disparities for pain in the United States,* Pain Med. (Feb 2012)13(2):150-74. doi: 10.1111/j.1526-4637.2011.01310.x.

[3] Lee P, Le Saux M, Siegel R, Goyal M, Chen C, Ma Y, Meltzer AC. *Racial and ethnic disparities in the management of acute pain in US emergency departments: Meta-analysis and systematic review*, Am J Emerg Med. (Sep. 2019) 37(9):1770-1777. doi: 10.1016/j.ajem.2019.06.014.

[4] Sabin JA, Greenwald AG. *The influence of implicit bias on treatment recommendations for 4 common pediatric conditions: pain, urinary tract infection, attention deficit hyperactivity disorder, and asthma*, Am J Public Health (May 2012) 102(5):988-95. doi: 10.2105/AJPH.2011.300621.

[5] 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. doi:10.1001/jamanetworkopen.2019.16271.

[6] "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

[7] 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

[8] Dowell, D., Haegerich, T, and Chou, R., *No Shortcuts to Safer Opioid Prescribing*, , April 24, 2019. DOI: 10.1056/NEJMp1904190

NPAC
NATIONAL PAIN ADVOCACY CENTER

Kate Nicholson
President and Founder
kate@nationalpain.org
nationalpain.org

watchdog, Human Rights Watch,[9] and a safety communication from the FDA, itself.[10]

- **Harms which especially concern us are the inability of patients to access necessary medication and healthcare**. In addition to facing barriers at the pharmacy,[11] patients who use opioids regularly to manage pain are facing difficulty finding care for any reason, not just for pain. According to a recent study of clinics in nine states, for example, more than 50% of clinicians are unwilling to accept a prospective who regularly uses opioids to manage pain, [12] and 81% are reluctant to according to another study. [13] This cannot be an acceptable outcome of provider education or public health policy.

- **We are also concerned by increasing reports of forced or abrupt opioid cessation or reduction.** While we recognize that voluntary tapering benefits some patients, observational studies show that

---

[9] Human Rights Watch. Report, *Not Allowed to be Compassionate* (Dec. 2018), https://www.hrw.org/report/2018/12/18/not-allowed-be-compassionate/chronic-pain-overdose-crisis-and-unintended-harms-us

[10] 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

[11] *See, e.g.,* Brown, J., Torres, H., *et al, Cancer Patients' Perceived Difficulties Filling Opioid Prescriptions After Receiving Outpatient Supportive Care,* J Pain Sympt. Mgmt. (Nov. 2020) 60 (5): 915-922 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7305512/.

[12] 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. 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).

[13] 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

P.O. Box 4172
Boulder, CO 80302

info@nationalpain.org
(303) 909-3175

Kate Nicholson
President and Founder
kate@nationalpain.org
nationalpain.org

tapering is happening in dangerous and unethical ways,[14] [15] [16] [17] [18] [19] [20] [21] as the FDA itself has acknowledged.[22] Resulting harms are serious, as they include heightened risk of death by suicide and drug overdose.[23] [24] [25] Some patients appropriately use opioids long term to manage pain, and some appropriately require higher doses.

- **For these reasons, we believe that quality metrics should not focus only on aggregate reductions in opioid prescribing absent evaluation of patient outcomes.** Considerations like workforce participation, engagement in life and family activities, access to healthcare, and the avoidance of serious harm like drug overdose and suicide, ought also to figure into measures of quality and success.

---

[14] 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

[15] Oliva, E., Bowe, T., Manhapra, A., Kertesz, St., Hah, J., Henderson, P. *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

[16] James, J., Scott, J., Klein, J. *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

[17] Glanz J., Binswanger I., Shetterly S., Narwaney K., 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

[18] 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

[19] 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.

[20] 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

[21] Neprash, H., Gaye, M. & Barnett, M., *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

[22] *See supra* note 10.

[23] Morabito, N. VA reps to discuss impact of opioid reduction on suicides during summit (2018). Retrieved from http://www.wjhl.com/news/va-reps-to-discuss-impact-of-opioid-reduction-on-suicides-during-summit_20180123093420242/934066782

[24] 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. (Jul 2019) 47:29-35. doi: 10.1016/j.genhosppsych.2017.04.011. Epub 2017 Apr 27.

[25] 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

NATIONAL PAIN ADVOCACY CENTER

Kate Nicholson
President and Founder
kate@nationalpain.org
nationalpain.org

In sum, we believe that reasonable measures should be taken to protect the health and safety of the nearly 8[26] to 13 [27]million Americans who currently use opioids long term to manage pain, and of those who may require this therapy in the future.

We note in reviewing specifics of the OA REMS that long-term use is not always a sign of misuse. In addition, while we recognize that this evaluation is specifically about opioid prescribing, we applaud mention in the presentations of the importance of access to multimodal, interdisciplinary and multidisciplinary care, since optimal treatment of pain, even where opioids are used, often involves employing multiple modalities in combination. We stress the importance in any curriculum of patient-centered care, given that pain is such an enormous umbrella category that includes a host of drivers and underlying conditions.

Finally, we appreciate efforts to promote clinician education given evidence that education about pain and pain treatment is generally poor.[28] [29] Nevertheless, we are concerned by the near singular focus on opioid reduction, where there is evidence that such a focus is, in some cases, overreaching and causing real and palpable harm.

In closing, we urge the FDA to measure patient outcomes in evaluating the success of its OA REMs, and to incorporate the views and experiences of patients in this process.

Thank you. If you have any questions you may reach Kate Nicholson at kate@katemnicholson.com.

Sincerely,

Kate

Kate M. Nicholson

---

[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

[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/

[28] *See, e.g.,* Shipton, E., Bate, F., Visser E. *et al*, *Systematic Review of Pain Medicine Content, Teaching, and Assessment in Medical School Curricula Internationally,* Pain Ther. 7(2): 139-161 (Dec. 2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6251835/

[29] Mezei L., Murinson, B., Johns Hopkins Pain Curriculum Development Team, *Pain Education in North American Medical Schools*, Pain vol. 12, Iss. 12: 1199-1208 (Dec. 2011) DOI: https://doi.org/10.1016/j.pain.2011.06.006

P.O. Box 4172
Boulder, CO 80302

info@nationalpain.org
(303) 909-3175

NPAC
NATIONAL PAIN ADVOCACY CENTER

Kate Nicholson
President and Founder
kate@nationalpain.org
nationalpain.org

P.O. Box 4172
Boulder, CO 80302

info@nationalpain.org
(303) 909-3175