

December 4, 2023

Honorable Anne Milgram
Administrator
Drug Enforcement Administration
8701 Morrissette Drive
Springfield, VA 22152

Re: Docket # DEA-1228P, Notice on Proposed Aggregate Production Quotas for Schedule I and II Controlled Substances.

Dear Administrator Milgram:

The National Pain Advocacy Center (NPAC), a 501c3 nonprofit organization that accepts no industry funding and advocates for the health and human rights of people in pain, would like to thank you for the opportunity to provide input on the Drug Enforcement Administration's Docket No. DEA-1228P, Notice on Proposed Aggregate Production Quotas for Schedule I and II Controlled Substances. NPAC is an alliance of clinicians, scientists, public health experts, and people with lived experience of pain, as well as people in recovery from an opioid use disorder. NPAC promotes equitable and effective pain management.

In brief, we are concerned that the DEA is proposing further cuts to the medical supply of opioids at a time when shortages are impeding access to necessary medication and care, risking the health and lives of people with pain. While we applaud the DEA's expressed intention to reconsider its processes in future regulatory actions, until regulatory changes are in place and frontline harms to patients from supply shortages have been explored and explained, the DEA should suspend further production quota reductions in medications presently experiencing shortages.

- 1. Cutting the Medical Supply of Opioids is Not Addressing Overdoses and Risks the Health and Lives of People Who Need Access to Essential Medications*

This is the 8th consecutive year that the DEA has recommended a blanket cut in the medical supply of opioid analgesics. Despite a remarkable nationwide decline in the total prescribing of opioids in the United States, drug overdose deaths continue to rise. In fact, a national study by IQVIA reported that while per capita *prescription* opioid use is down 64% since the peak of prescribing in 2011, opioid overdose deaths have increased by 253% in the same period¹. Opioid prescriptions *per capita* have already fallen dramatically to levels last

¹ <https://www.iqvia.com/insights/industry/2022/09/2022-national-opioid-prescription-trends>

seen in 1992, and prescribed dosage in morphine milligram equivalents (MMEs) has fallen to levels last seen in 2000.²

Per CDC data estimates, the overwhelming majority of opioid overdose deaths are caused by illicit forms of fentanyl and fentanyl-analogues, *not opioid medications* prescribed by providers and dispensed in pharmacies³. This current landscape is a vital point that the DEA must recognize as it promotes further reductions of the medical supply of opioids and other controlled substances. If the proposed cuts go through, the supply of these medications will have been reduced by roughly 70% since 2016.⁴

A. The harms to patients who lose access to essential medications are well documented.

NPAC is gravely concerned that this quota reduction proposal will exacerbate already unconscionable, disparate effects on people with serious pain who require opioid analgesics to manage conditions such as cancer, sickle cell disease, multiple sclerosis, dystonia, and serious injuries. Efforts to reduce opioid prescribing have not only failed to address rising overdose deaths, they have also had devastating effects on pain patients who use opioid analgesics,

² U.S. Food and Drug Administration, "Prescription Opioid Utilization Patterns in the U.S.," October 13, 2021. https://healthpolicy.duke.edu/sites/default/files/2021-10/Opioid_Prescriber_Education_Workshop_Slide_Deck.pdf

³ CDC National Center for Health Statistics. Provisional drug overdose death counts, 2023. Accessed on November 17, 2023. Available from: <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>.

⁴ Anson, Pat, DEA Plans Further Cuts in Rx Opioid Supply in 2024, Pain News Network, November 3, 2023,. Accessed on December 1, 2023. Available from: <https://www.painnewsnetwork.org/stories/2023/11/3/dea-plans-further-cuts-in-rx-opioid-supply-in-2024>.

as is well-documented in the medical literature,^{5 6 7 8 9 10 11 12 13 14 15 16 17 18} a warning from the Food and Drug Administration (FDA),¹⁹ and a clarification from the Centers for Disease Control and Prevention (CDC).²⁰ It is also noteworthy that barriers to both medication and adequate pain management are borne disproportionately by Black and Latinx Americans.²¹

⁵ 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). [Doi: 10.1016/j.jsat.2019.05.001](https://doi.org/10.1016/j.jsat.2019.05.001) Anyone who has taken opioids long-term is likely to develop physical dependence, requiring that opioids be tapered slowly to avoid side effects. Dependence is distinct from addiction, because it lacks the behavioral component that characterizes a use disorder. See e.g., National Institute on Drug Abuse, Media Guide: The Science of Drug Use and Addiction: The Basics, <https://www.drugabuse.gov/publications/media-guide/science-drug-use-addiction-basics>

⁶ 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](https://doi.org/10.1001/jamanetworkopen.2019.2613)

⁷ 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. [Doi: 10.1007/s11606-019-05301-2](https://doi.org/10.1007/s11606-019-05301-2)

⁸ 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](https://doi.org/10.1001/jamanetworkopen.2019.16271)

⁹ 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). [Doi: 10.1007/s11606-019-05227-9](https://doi.org/10.1007/s11606-019-05227-9)

¹⁰ Fenton, J., Agnoli, A., 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](https://doi.org/10.1001/jamanetworkopen.2019.16271)

¹¹ Oliva, E, Bowe, 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: 10.1136/bmj.m283](https://doi.org/10.1136/bmj.m283)

¹² Neprash, H., Gaye, M et al., Abrupt Discontinuation of Long-term Opioid Therapy Among Medicare Beneficiaries, 2012–2017. *J GEN INTERN MED* (2021). [Doi: 10.1007/s11606-020-06402-z](https://doi.org/10.1007/s11606-020-06402-z)

¹³ Agnoli A, Xing, G, et al., Association of Dose Tapering With Overdose or Mental Health Crisis Among Patients Prescribed Long-term Opioids. *JAMA.* 2021;326(5):411–419. doi:10.1001/jama.2021.11013.

¹⁴ Quest Diagnostics. Center for Addiction. Health Trends: Drug Misuse in America. https://mma.prnewswire.com/media/1011170/Quest_Diagnostics_Health_Trends_Report.pdf?p=original. Published 2019. Accessed November 12, 2021 (noting, among other things that 81% of providers are reluctant to care for patients using opioids for pain.)

¹⁵ Lagisetty, P, Macleod, C., Thomas, J, et al. Assessing reasons for decreased primary care access for individuals on prescribed opioids: an audit study, *Pain* 2021; 162 (5):1379-86. Doi: 10.1097/j.pain.0000000000002145.

¹⁶ L` f n i mDL +S` n b q chCl +W m f F +@ m k h @ + l d q m s @ Ed n s m m l I - @ r n b h s n m A d s v d d m N o m l t c S` o d d m f ` n c R t a r d p t d m s G d` l e g B` q l T r d + L d c l b` s n m @ g d q n b d +` n c B g q n t b B n n c s n m B n n s n k JAMA Netw Open. 1/ 12:5' 1(911440/ 0- C n t s d / - 0 / / 0 . i` l ` n d s v n q n o d m 1 / 11-440 / 0

¹⁷ K` q b g d k d L Q + K n c h R + X` m R + B k n s h d q A @ F n k r l h g D R + A n g m d c s @ R A - B n l o` q s t u d D e e b s u d m r r n e N o m l t c S` o d d m f n q @ d q o s C l r b n n s m t ` s n m u r M n C n r ` f d B g ` n f d e n q N o m l t c N u d q n r d n q R t l b t e d e n q O` s d n s Q d b d u m f R s` a l d K n n f , s d q N o m l t c S g d q o x - JAMA Netw Open. 1/ 11:4' 7(91115412- C n t s d / - 0 / / 0 . i` l ` n d s v n q n o d m 1 / 11-15412

¹⁸ Henry, S.G., Fang, SY., Crawford, A.J. et al. Impact of 30-day prescribed opioid dose trajectory on fatal overdose risk: A population-based, statewide cohort study. *J GEN INTERN MED* (2023) Doi: 10.1007/s11606-023-08419-6

¹⁹ FDA identifies harm reported from sudden discontinuation of opioid pain medicines, April 9, 2019. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes>

²⁰ Dowell, D, Haegerich, T, Chou, R, No Shortcuts to Safer Opioid Prescribing, *N Engl. Med* 2019; 380: 2285-87. Doi: 10.1056/NEJMp1904190.

²¹ Hoffman, K, Trawalter, S, Jordan, R, Oliver, M. Racial bias in pain assessment and treatment recommendations, and false beliefs about biological differences between blacks and whites, *Nat Acad. Sci*, 2016: 113(16) 4296-301. Doi: 10.1073/pnags.1516047113; Lee P, Le Saux M, Siegel R, et al.. Racial and ethnic disparities in the management of acute pain in US emergency departments: Meta-analysis and systematic review. *Am J Emerg Med.* 2019 Sep;37(9):1770-1777. Doi: 10.1016/j.ajem.2019.06.014.

- B. NPAC has seen a significant uptick in complaints of barriers to access to opioid medication in 2023, and harms have affected many of its own members

This year, NPAC witnessed a significant uptick in the number of unsolicited emails it receives from patients and providers experiencing barriers to access to opioid medications. We receive such emails every week. Moreover, supply shortages have negatively impacted people within our organization, including members of our Board, our Community Leadership Council of people with lived experience of pain, and our affiliated clinicians.

To illustrate our concerns, we share below a few real-life case examples:

- A retired hospital pharmacist on NPAC's Community Leadership Council gave a news interview about the impact of being unable to fill prescriptions on his life: "I can't do anything, I can't go shopping for food, I can't go to the mall," he told reporters.
- An NPAC Board member who is a wheelchair user with advanced Multiple Sclerosis experienced considerable barriers accessing the medication she uses during occasional flare-ups.
- A Latinx man with quadriplegia who testified on a bill (now law) we put forward in Colorado suffered a heart attack and woke up on a ventilator after his medications were suddenly stopped.
- NPAC-affiliated clinicians reported routinely receiving notices from institutional pharmacies or their patients that prescribed opioids are simply not available. Some working in major tertiary care hospitals have repeatedly been notified that basic medications like oxycodone/acetaminophen 5/325 are down to a "1-day supply" or "not available."

We provide anecdotal examples to complement the data cited herein because they reflect the very peril that people living with pain and clinicians trying to help them are experiencing in America today – under current quotas before the additional cuts the DEA is proposing. Implementing further strict quotas will exacerbate these impediments and cause harm.

II. The Metrics DEA Employs Overreach to Implicate Appropriate Medical Use

We understand the importance of efforts to reduce inappropriate opioid prescribing and diversion. But such efforts must also be targeted and evidence-based. Currently, there is no consistent, evidence-based means of determining when prescription opioids are being used for a legitimate medical reason and when they are not. Some of the metrics that the DEA has used historically, like MMEs, are coming under increased scrutiny by public health

authorities.²² Others, such as number of providers or geographic proximity, have been shown to over-reach to patients with medical needs, such as those managing pain from cancer.²³

Estimates and projections using data from Prescription Drug Monitoring Programs (PDMP) are a flawed measure of medical need. PDMPs capture dispensed medications but contain limited information regarding individual patients. PDMP databases include the medication, dose, and quantity, and only a few patient-level variables that are primarily demographic. There are no clinical and diagnostic data elements that would inform on the *appropriateness* of the prescription and dose for the individual patient. These flaws are amplified when making regulatory decisions at the population level.

The DEA's proposed reductions are based on FDA data and diversion data from PDMPs in the states. But the indicators used as evidence of diversion, specifically the "red flags" from PDMP data, over-reach. The DEA cites three indicators: 1) Number of patients who saw three or more prescribers within 90 days; 2) Number of patients dispensed prescriptions that exceeded 240 morphine milligram equivalents per day; and 3) Number of patients who paid cash for covered controlled substance prescriptions without submitting for insurance reimbursement. We address each in turn.

Regarding the "red flag" for the number of providers, in a study using far more restrictive terms (seeing not 3 but 5 prescribers in 90 days), 20% of the patients who were flagged had cancer.²⁴ Moreover, it is quite common in academic medicine practices for patients to see numerous prescribers.

The blanket use of a preset MME as a proxy for diversion is similarly problematic, especially given individual variability and genomic differences in how people metabolize opioids, as the Centers for Disease Control and Prevention has acknowledged.²⁵ There is also significant variability in MME thresholds depending on critical factors such as the denominator in calculating the prescriptions' days of supply.²⁶

Deciding on the reduction of the medical supply of opioids must be informed by comprehensive evidence that accounts for the medical need of these medications, not simple gross aggregated estimates of volume supplied.

²² FDA. Public Meeting. Morphine Milligram Equivalents: Current Applications and Knowledge Gaps, Research Opportunities, and Future Directions. <https://www.fda.gov/drugs/news-events-human-drugs/morphine-milligram-equivalents-current-applications-and-knowledge-gaps-research-opportunities-and>. Published 2021. Accessed November 14, 2021.

²³Delcher, C, Harris, D, Park, C et al. "Doctor and pharmacy shopping": A fading signal for prescription opioid use monitoring? *Drug Alcohol Depend.*, 2021; 221:108618. Doi: 10.1016/j.drugalcdep.2021.108618.

²⁴ *Id.*

²⁵ See *supra* n. 20.

²⁶ Dasgupta N, Wang Y, Bae J, Kinlaw AC, Chidgey BA, Cooper T, Delcher C. Inches, Centimeters, and Yards: Overlooked Definition Choices Inhibit Interpretation of Morphine Equivalence. *Clin J Pain.* 2021 Aug 1;37(8):565-574. Doi: 10.1097/AJP.0000000000000948.

III. Drug Shortages are Already Causing Documented Harm

Similarly, proposals to reduce production quotas must consider current and clinically meaningful national drug shortages. Drug shortages in the United States are concentrated in pain and anesthesia therapeutic areas.²⁷ As of June of 2023, there are 21 molecules indicated for pain/anesthesia with current shortages. Of these medications, fentanyl and local anesthetics like lidocaine have experienced active shortages since 2017.²⁸

Further decreases in production quotas will exacerbate drug shortages of medications needed to treat pain properly. DEA is considering a fentanyl 2024 proposed quota of 676,062 g – This is a 7.6% reduction from the established quota for fentanyl in 2023.²⁹ Given ongoing and worrisome drug shortages in prescribed fentanyl, the proposed quotas are likely to have unintended consequences for patients needing analgesia for medical procedures.

Shortages in pain medications stand to affect a lot of people, including those with acute pain following surgery or trauma and the 5 to 8 million³⁰ Americans with chronic pain who use opioids to manage it.

Although many factors contribute to shortages and barriers to medication access, drug quotas are undoubtedly one. Shortages are occurring under the 2023 quota – further cuts will exacerbate existing documented barriers and harms.

We applaud the DEA's recent actions to extend prescribing provisions for controlled substances via telehealth and for holding a public hearing that brought together stakeholders from different sectors. We appreciated being able to testify and wish to underscore that our testimony reflected our continued concerns with barriers to medication access. We further applaud the DEA's expressed intention in future regulations to reconsider its processes,

²⁷ See *supra* n. 1.

²⁸ *Id.* L. nq̄nuduq+cq̄ f r gnc̄s̄ f dr g` ud addmq̄lod` sdck̄ q̄lonq̄dc hmCq̄ f Rgnq̄s̄ f d At k̄d̄sm̄ ax sq̄d @ dqb̄` mRnbl̄sx neGnr ois̄ k Og` d ` b̄irs̄ `@SRO` hmb̄k̄ chrf +l nr sq̄bdm̄sx+r gnc̄s̄ f dr hm0(Gxcq̄bnc̄nm̄. b̄ds̄ l hmogdm̄oq̄ct b̄s̄ `2/ MCB eq̄ t k̄ sm̄nr +6 l ` nt ē b̄s̄ q̄lq̄(- Ēl̄r̄ sq̄lonq̄dc nmL ` x 15+1/ 12+` mc̄ t oc` s̄dc Mnudl̄ adq̄2+1/ 12- @ nrf̄ sq̄d 6 l ` nt ē b̄s̄ q̄lq̄+ l nr sb̄nt lc̄ mns̄ dr̄sh̄ ` s̄d c` s̄dr̄ eq̄q̄l̄r̄ t ook̄: 1(Nw̄xbnc̄nm̄ hm̄s̄ n̄sq̄l̄d` r d oq̄ct b̄s̄ `02 MCB eq̄ t k̄ sm̄nr +6 l ` nt ē b̄s̄ q̄lq̄(- Ēl̄r̄ sq̄lonq̄dc nm L ` q̄g 06+1/ 12+` mc̄ t oc` s̄dc Mnudl̄ adq̄8+1/ 12: ` mc̄ 2(Nw̄xbnc̄nm̄. b̄ds̄ l hmogdm̄oq̄ct b̄s̄ `07 MCB eq̄ t k̄ sm̄nr +7 l ` nt ē b̄s̄ q̄lq̄(- Ēl̄r̄ sq̄lonq̄dc l t k̄ 08+1/ 12+` mc̄ t oc` s̄dc Mnudl̄ adq̄6+1/ 12- @b̄drr̄dc nmCdbd̄l̄ adq̄0+1/ 12- @ī k̄ ald̄ eq̄l̄ 9ḡs̄or̄9.v v v -` r go-nq̄ .cq̄ f ,r gnc̄s̄ f dr .bt̄ q̄p̄m̄s̄ r gnc̄s̄ f dr >kn̄f̄ hm̄q̄st̄ q̄m̄f̄ q̄<RRNBḡdbj̄ Nnr̄k̄

²⁹ DEA Established Aggregate Production Quotas for Schedule I and II Controlled Substances and Assessment of Annual Needs for the List I Chemicals Ephedrine, Pseudoephedrine, and Phenylpropanolamine for 2023. Accessed December 1, 2023. Available from: <https://www.federalregister.gov/documents/2022/12/02/2022-26351/established-aggregate-production-quotas-for-schedule-i-and-ii-controlled-substances-and-assessment>

³⁰ Kurt Kroenke, Daniel P Alford, Charles Argoff, Bernard Canlas, Edward Covington, Joseph W Frank, Karl J Haake, Steven Hanling, W Michael Hooten, Stefan G Kertesz, Richard L Kravitz, Erin E Krebs, Steven P Stanos, Mark Sullivan, Challenges with Implementing the Centers for Disease Control and Prevention Opioid Guideline: A Consensus Panel Report, *Pain Medicine*, Volume 20, Issue 4, April 2019, Pages 724–735, [Doi: 10.1093/pm/ply307](https://doi.org/10.1093/pm/ply307).

but we wish to make it eminently clear that patients are suffering from a lack of access to essential medications right now.

IV. Conclusion

Until regulatory changes are in place and frontline harms to patients from supply shortages have been explored and explained, the DEA should cease further production quota reductions in essential medications presently experiencing shortages. Indeed, where shortages risk the health and lives of patients, the DEA should be increasing, not cutting supply. The DEA has already acknowledged shortages of Adderall and other stimulants (commonly used to treat conditions like ADHD) and has proposed a slight increase in the supply of those medications. Similar actions should be considered for opioid analgesic medications.

We thank you again for the opportunity to comment and urge consideration of our concerns.

Respectfully submitted,

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