

September 28, 2022

President Joseph R. Biden
The White House
1600 Pennsylvania Avenue, NW
Washington, DC 20500

Dear President Biden,

We respectfully write regarding a temporary policy known as class-wide scheduling of fentanyl analogues. This policy categorically places fentanyl-related substances (FRS) — both real and hypothetical — into Schedule 1 based solely on chemical structure, without first evaluating data related to their pharmacological effects and epidemiological studies.¹ We write in support of a recent Congressional request to the heads of the Department of Justice (DOJ), Health and Human Services (HHS), and the Drug Enforcement Administration (DEA) concerning the administration's plan to make permanent this temporary classwide scheduling of FRS. We are scientists and public health professionals in the laboratory and on the frontlines of the fight to end the overdose crisis, exploring new therapies and providing care and treatment to people who use drugs. By making permanent the temporary classwide scheduling of FRS, Congress may inadvertently criminalize therapeutic medications similar to naloxone² and other life-saving medications at a time when the U.S. is facing record number of overdose deaths.³

Fentanyl itself is a Schedule 2 substance with approved medical use, and other analogues of fentanyl likewise have already – and historically – demonstrated medical and therapeutic value. For example, remifentanyl was developed from fentanyl and approved in 1996 to be an ultra-short-acting pain and sedation medication, with significant safety benefits when compared to other drugs, and allows for quicker post-operative recovery periods. Sufentanil, an opioid drug derived from fentanyl back in 1974, is valuable to this day in anesthesia, where it is used for short-term pain relief and sedation. Notably, the U.S. Department of Defense developed a sublingual formulation of sufentanil that was approved in 2018 for treatment of battlefield injuries that are inadequately treated by other options. Even the higher potency carfentanil is an approved and established veterinary medicine, because its increased potency helps with medicating large animals. When used properly, these and other analogues of fentanyl can have important benefits.

It is not uncommon for structurally related substances to have complementary therapeutic values. For example, naloxone is an opium derivative similar in chemical structure to many Schedule 1 and 2 opium derivatives, but it functions pharmacologically as an opioid receptor antagonist, counteracting the effects of opioid drugs. Likewise, there is evidence (see below) that FRS may

¹ Letter from Cory A. Booker et. al to Merrick Garland, Attorney General, U.S. Dept of Justice (Jun. 28, 2022), https://www.booker.senate.gov/imo/media/doc/frs_information_request_doj_hhs_dea.pdf.

² *Naloxone DrugFacts*, National Institute of Drug Abuse (Jan. 11, 2022), <https://nida.nih.gov/publications/drugfacts/naloxone>.

³ *Drug Overdose Deaths in the U.S. Top 100,000 Annually*, CDC (Nov. 17, 2021), https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2021/20211117.htm.

hold the key to better life-saving treatments for fentanyl abuse and overdose. However, research on Schedule 1 substances is prohibitively difficult for most researchers. Placing substances into Schedule 1 has the effect of severely limiting further research and development, which in this case could preclude the development of life-saving therapies.

Permanent classification of FRS on Schedule 1, without first studying the pharmacological effects and epidemiological data of the individual substances, would set a dangerous precedent in U.S. drug scheduling. Since 1970, the federal government has conducted a scientific evaluation of all controlled substances in order to understand if or where on the drug schedule a particular substance should be classified. In order for a substance to be placed on Schedule 1, the DEA must determine it has potential for abuse and no medical value.⁴ Further, the Attorney General must request a scheduling recommendation from the Secretary of HHS based on an eight-factor medical and scientific analysis.⁵

Yet, here, the federal government is advocating for making permanent the temporary classwide scheduling of FRS without conducting individual testing of each uniquely identified chemical compound or novel substance, despite acknowledging that not all substances are similar and harmful.⁶ In a December 2021 House hearing, the Food and Drug Administration (FDA) testified that it had identified 44 FRS and studied 25, reporting that some of the substances in the FRS class were inert, and at least one of the substances was not psychoactive and behaved like naloxone, meaning it could potentially help reverse the effects of an opioid overdose.⁷ Policymakers, the scientific community, and the public still do not know what the FDA studies revealed about each of the substances nor if any efforts have been made to deschedule or reschedule the substances pursuant to the FDA's findings.

Moreover, it is distressing for the federal government to advocate for making permanent the temporary classwide scheduling of FRS when it knows that not all FRS are harmful. In fact, HHS has previously undertaken a review of the FRS class, but it could not provide findings because of the vast number of hypothetical FRS and more importantly, because it had identified examples of substances in the class that acted as opioid antagonists.⁸ This means that people will be deterred from FRS research and/or may potentially be incarcerated for FRS activities related to benign or even beneficial substances. This would be a devastating and consequential outcome for our patients and communities.

⁴ *Drugs of Abuse, A DEA Resource Guide (2020 Edition)*, Drug Enforcement Administration, U.S. Department of Justice (2020), https://www.dea.gov/sites/default/files/2020-04/Drugs%20of%20Abuse%202020-Web%20Version-508%20compliant-4-24-20_0.pdf.

⁵ 21 U.S.C. § 811(b)

⁶ *The Overdose Crisis: Interagency Proposal to Combat Illicit Fentanyl-Related Substances: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 117th Cong. 4 (2021) at <https://www.c-span.org/video/?c4994371/user-clip-fda>.

⁷ See *The Overdose Crisis: Interagency Proposal to Combat Illicit Fentanyl-Related Substances: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*.

⁸ Testimony of Sandra D. Comer, Ph.D., Pub. Policy Officer, Coll. on Problems & Drug Dependence, Before the Subcomm. on Crime, Terrorism & Homeland Sec., H. Comm. on the Judiciary at 3 (Jan. 28, 2020), <https://docs.house.gov/meetings/JU/JU08/20200128/110392/HHRG-116-JU08-Wstate-ComerS-20200128.pdf>.

It is misguided for the federal government to restrict research and study of FRS at a time when approximately 300 people die of a preventable overdose each day.⁹ The federal government should support research and health services. This includes studying FRS for potential treatment options and ensuring people can receive the best treatments imaginable. We need the federal government to support our efforts to help save as many lives as possible. Ensuring that federal agencies and the research community can study emerging substances for potential therapeutic value, including FRS, is a critically important component of these efforts.

We implore the Administration to reconsider making permanent the temporary classwide scheduling of FRS on Schedule 1 until data related to the pharmacological effect and epidemiological data of FRS is publicly reported, and ultimately to reconsider scheduling of substances based solely on chemical structure, when in fact it is the pharmacological effects of specific substances that are the true points of concern. Thank you for reading this letter. For any questions or to discuss this issue further, please contact Prof. Gregory Dudley, Ph.D. and Dr. Ryan Marino, M.D.

Sincerely,

A Aguilar
A. Van Doren, MD MPH
Adam Viera
Alex Duello
Allison Daurio, MS
Amber King, RN
Ashish Thakrar, MD
Audrey Collins
Benjamin Hayes, MD, MPH
Bethany Medley, MSW
Bianca Rivera
Bill J. Baker
Brenice Duroseau, MSN, FNP-C, AAHVIS
Brian McCrystal
Brian V. Popp
Cheyenne Gratale
Claire Heaney
Claire Zagorski, MSc, LP
Daliah Heller, PhD MPH
David Michael Coletta, PA-C
Derek Johnson
Diana Victoria Zeigler
Dr. Liseli Mulala
Dr. Nabarun Dasgupta
Dr. Nisha Beharie

⁹ *Breaking the Stigma That Exacerbates the U.S. Overdose Crisis*, Vital Strategies (August 30, 2022) <https://www.vitalstrategies.org/breaking-the-stigma-that-exacerbates-the-u-s-overdose-crisis/>.

Dr. Ryan Marino, M.D
Dr. Sarah Clingan
Dr. Wayne C. Guida
Elizabeth E Hinkle
Elodie C Warren
Emile Legault
Eric Struth
Erin Bray Gibson
Erin Tracy
Gabriel Quaglia, CHW
Grant Lawrence
Grant Patch
Gretchen Bergman
Griffin Epstein, PhD
Jacob W. Cohen, PhD
James Leahy
Jamie Favaro
Jasmine Myrick
Jeffrey Bratberg, PharmD, FAPhA
Jennifer Muggeo, MPH
Jeremiah Escajeda MD
Jess Morrow
Jessica L. Moreno, PharmD
Jessica Morrow
John Knebel PharmD, BCCCP
Joy D Scheidell, PhD MPH
Ju Nyeong Park, Ph.D.
Judith Feinberg, MD
Katherine Kahn
Katie Lynch, PA-C
Kendall Darfler, MS
Kimberly Bliss Fields, Ph.D.
Kimberly Sue, MD, PhD
Krystyna Northeim, MSN, APRN, FNP-C
Lauren E. Walker
Lauren Hendricks
Leslie L Wood, MA
Lindsey J. Loera, PharmD
Lisa McElwee-White, Ph.D.
Liza Vance, FNP-C
Logan Neitzke-Spruill, MA
Marisela Sanchez
Mariya Masyukova, MD MS
Mark Plassmeyer, Ph.D. MSW
Matthew H Loxton
Matthew Westling, PharmD, MPA

Max C. Thompson
Maya Doe-Simkins
Miles Hoffman
Mr. Christopher Daniel Jennings
Nancy Curran AGNP-C
Nao Sakurai
Nicole Silvestri
Noa Krawczyk, PhD
Olivia Flemmer
Patricia Fortunato
Paul Tammaro NREMT-P
Peter J. O'Brien, Ph. D.
Prof. Donald A. Watson
Prof. Gregory Dudley, Ph.D.
R. Nick Gorton, MD
Rachel Russell
Ricky N. Bluthenthal, PhD
Ronald K. Castellano, Ph.D.
Sarah Mackin
Scott Coon
Scott E. Denmark
Seth Trueger, MD, MPH, FACEP
Shannon E. O'Malley, MS
Shannon L Roberts
Sharon F
Shelby TaylorGoalby
Stefan G. Kertesz, MD, MSc
Susan Miller
Trevor Harris
Victoria Jent, MAS
Victoria Oberzil
Virginia Cheatham, RN
Zac M

cc:

Merrick Garland
Attorney General
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530

Xavier Becerra
Secretary
U.S. Department of Health & Human Services

200 Independence Avenue, SW
Washington, DC 20201

Anne Milgram
Administrator
Drug Enforcement Administration
Department of Justice
8701 Morrisette Drive Springfield, VA 22152

Senate Majority Leader Charles Schumer
322 Hart S.O.B.
Washington, DC 20510

Senate Minority Leader Mitch McConnell
317 Russell S.O.B.
Washington, DC 20510

Speaker Nancy Pelosi
1236 Longworth H.O.B
Washington, DC 20515

House Majority Leader Steny Hoyer
H-107, The Capitol
Washington, DC 20515

House Minority Leader Kevin McCarthy
2468 Rayburn H.O.B.
Washington, DC 20515