United States Senate

WASHINGTON, DC 20510

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Lawrence A. Tabak, D.D.S., Ph.D.
Acting Director
National Institutes of Health
9000 Rockville Pike
Rockville, MD 20892

Robert M. Califf, M.D.
Commissioner
U.S. Food and Drug Administration
1093 New Hampshire
Silver Spring, MD 20993

Dear Acting Director Tabak and Commissioner Califf:

We are writing to request information on the latest efforts undertaken by the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) to advance research on psychoactive drugs, and in particular psychedelics, and their potential therapeutic effects. We commend the NIH in taking an important step by hosting its January workshop, "Psychedelics as Therapeutics: Gaps, Challenges and Opportunities," which highlighted existing research and the regulatory challenges and opportunities to advance psychedelic research. We encourage NIH and FDA to further expand their role in identifying research gaps, potentially promising therapeutic uses of psychedelics, and regulatory hurdles in the field of psychedelic research.

The United States previously conducted robust research on psychedelic drugs. In the 20th century, leading researchers in psychiatry and the emerging fields of neuropharmacology and neuropsychopharmacology pursued medical research on psychedelic drugs including LSD, psilocybin, and mescaline.[1] This research was supported by pharmaceutical companies, the National Institute of Mental Health (NIMH), and other government agencies.[2] A U.S. Drug Enforcement Agency (DEA) document reported that from about 1950 to 1965, "research on LSD and hallucinogens generated over 1000 scientific papers, several dozen books, and 6 international conferences, and LSD was prescribed as treatment to over 400,000 patients."[3]

However, in the 1960s, the counterculture movement's embrace of psychedelics and the illicit manufacture and distribution of LSD contributed to its popular cultural rise and its increased non-medical use.[4] This created a backlash resulting in its stigmatization and adverse political repercussions by the latter half of the 1960s.[5] In 1971, some psychedelics were placed in Schedule I of the United Nations Convention on Psychotropic Substances, cementing its status as having no accepted medical use.[6] In addition, in 1970 the *Controlled Substances Act* (CSA) codified harsh penalties for manufacture, possession, and use of many psychedelics, which hindered their research and medicinal development.[7] Pharmaceutical and federal funding for

[1] James J.H. Rucker, Jonathan Iliff, David K. Nutt, "Psychiatry & the psychedelic drugs. Past, present & future," *Neuropharmacology*, 20 Dec. 2017, https://doi.org/10.1016/j.neuropharm.2017.12.040.
[2] Sean J. Belouin, Jack E, Henningfield, "Psychedelics: Where we are now, why we got here, what we must do," *Neuropharmacology*, 21 Feb. 2018, https://doi.org/10.1016/j.neuropharm.2018.02.018.
[3] Ibid.
[4] Belouin, Henningfield, "Psychedelics."
[5] Ibid.
[6] Rucker, Iliff, Nutt, "Psychiatry & the psychedelic drugs."
[7] Belouin, Henningfield, "Psychedelics."

psychedelic research dried up, while CSA licensure requirements made it more difficult to secure regulatory approval for research.[8]

Medication development efforts on psychedelics reignited in the 1990s when researchers rediscovered potential uses of these substances by applying state of the art clinical research development approaches, methods, and procedures.[9] Following these efforts, the Schedule I substance 3,4-methylenedioxymethamphetamine (MDMA), also known as "ecstasy," was granted a Breakthrough Therapy Designation as an MDMA-assisted psychotherapy Investigational New Drug Application for post-traumatic stress disorder (PTSD).[10]

Research on psychedelics still faces significant challenges. Many major pharmaceutical companies have withdrawn or scaled back funding in this field because of the high rate of failure to find medications that are acceptable for FDA approval. Research on psilocybin for severe depression and anxiety-related disorders, as well as MDMA for PTSD, is currently being supported primarily by small organizations that do not have adequate funding to develop medications through expensive safety studies and large-scale phase 3 clinical trials. A key challenge now is to design the optimal clinical trial to demonstrate efficacy, ensure safety and compliance with regulatory authorities, and secure the funding needed to support large-scale trials.

In response to a request for information on research efforts into the use of psychoactive drugs in treating mental illness, NIH and FDA acknowledged some potential therapeutic uses of these substances, as well as the need for additional research.[11] The Biden-Harris Administration recently announced support for expanding research on Schedule I substances to inform and advance evidence-based public policy, and how this research relates to addiction and overdose, chronic pain, and mental health conditions.[12] It is important that federal research agencies continue to assess the efficacy of potential alternatives to drugs with high misuse potential.

NIH has begun to show greater interest in psychedelic research. In April 2021, NIH awarded its first grant dedicated to medicinal psychedelic research, focused on use of neuro-imaging to search for neuronal correlates of clinical change in patients with obsessive-compulsive disorder treated with psilocybin. Further NIH's January 2022 workshop exploring the field of psychedelics as a potential therapeutic for a number of disorders marks another positive step.

As the NIH and FDA consider further methods to expand research of mental health treatments, we request written responses to the following inquiries and questions:

1) Please provide details on current NIH funding of psychedelic research, including a breakout by institute, and a breakout by basic versus clinical research.

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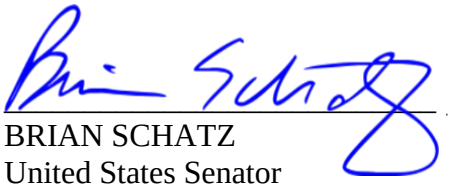
[8] Ibid.
[9] Ibid.
[10] Ibid.
[11] Kyle Jaeger, "Federal Health Agencies Acknowledge Therapeutic Potential Of Psychedelics," *Marijuana Moment*, 19 June 2019, https://www.marijuanamoment.net/federal-health-agencies-acknowledge-therapeutic-potential-of-psychedelics/.
[12] "Biden-Harris Administration Provides Recommendations to Congress on Reducing Illicit Fentanyl-Related Substances, *The White House*, https://www.whitehouse.gov/ondcp/briefing-room/2021/09/02/biden-harris-administration-provides-recommendations-to-congress-on-reducing-illicit-fentanyl-related-substances/.

2) Has NIH conducted a review of the scientific studies on psychedelics funded by NIMH and other federal entities in the period from 1950 to 1965? Was there a focus on the outcomes of those studies and the scientific limitations of those studies, as a means of informing directions of current and future NIH-funded research on psychedelic compounds? If not, would you initiate such a review?
3) What are the gaps in current psychedelic research, including questions about the methods of current clinical trials and other key scientific questions that need to be addressed to further our understanding of psychedelics?
4) What is the current status of collaboration between FDA, NIH, NIH-funded researchers and their academic institutions, and the private sector on research into psychedelics, including on identifying areas of therapeutic impact and potential medications development?
5) What are the regulatory barriers to research on psychedelics?
    a) What, if any, additional regulatory barriers or requirements are there to studying natural or botanical psychedelics, such as psilocybin?

NIH and FDA are critical to ensuring a comprehensive, rigorous, and deliberative science-based approach to the study of psychedelics, including the potential development of medication and therapeutics derived from these substances. Thank you for your attention to this issue, and we look forward to your written response.

Sincerely,



BRIAN SCHATZ
United States Senator

CORY A. BOOKER
United States Senator

cc: Joshua A. Gordon, M.D., Ph.D.
Director
National Institute of Mental Health

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse