DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

National Institutes of Health
Bethesda, Maryland 20892
www.nih.gov

June 15, 2022

The Honorable Brian Schatz
United States Senate
Washington, DC 20510-1105

Dear Senator Schatz:

Thank you for your inquiry to the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) regarding research on the use of psychoactive drugs, and in particular psychedelics, to treat mental illnesses. NIH is responding on behalf of both agencies. Research on psychedelic drugs holds promise for uncovering mechanisms of illness and possible interventions, ultimately leading to novel treatments with fewer side effects and lower potential for misuse. NIH supports a robust portfolio of basic and clinical research for therapeutic discovery and development. Please find responses to your individual questions below.

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

The following table summarizes the currently active NIH-funded projects that focus on studying psychedelic drugs with potential benefit for mental and behavioral health. Please note that this also includes research on non-psychedelic compounds derived from psychedelic drugs. Data are broken out by funding Institute or Center (IC), and by basic versus applied research. In addition to the National Institute of Mental Health (NIMH), other NIH ICs that support research in this area include the National Institute on Drug Abuse (NIDA), the National Institute of General Medical Sciences (NIGMS), the National Institute of Neurological Disorders and Stroke (NINDS), the National Center for Advancing Translational Sciences (NCATS), and the National Center for Complementary and Integrative Health (NCCIH).

NIH IC	Basic Research: Number of Projects	Basic Research: Dollars[1]	Applied Research:[2] Number of Projects	Applied Research: Dollars	Total: Number of Projects	Total: Dollars
NIMH	18	$6,267,616	18	$9,188,174	36	$15,455,790
NIDA	8	$7,735,538	9	$5,284,232	17	$13,019,770
NIGMS	1	$399,666	-	-	1	$399,666
NINDS	-	-	1	$1,697,084	1	$1,697,084
NCATS	-	-	1	$3,601,077	1	$3,601,077
NCCIH	1	$237,750	-	-	1	$237,750
Total	**28**	**$14,640,570**	**29**	**$19,770,567**	**57**	**$34,411,137**

[1] The reported dollar amounts reflect cost for the most recent fiscal year of each active project, not the total cost over the lifetime of each project.
[2] Applied research includes, but is not limited to, clinical studies and trials.

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?**

NIH-supported research in the 1950s and 1960s investigated the potential beneficial effects of psychedelic drugs, especially LSD. These revealed promising effects in mood disorders and addiction, but were conducted prior to the development of modern ethical standards and human subjects protections, adopted by the Department of Health and Human Services in the 1970s.[3,4] More recent psychedelics research studies have also seen the adoption of more rigorous experimental designs; advanced methodologies in non-invasive brain imaging, medicinal chemistry, and other areas; and a more critical approach to measuring outcomes and eliminating potential confounds.[5] In addition to minimizing risks to study participants, these advances in ethics and methodology are enabling current investigators in the psychedelics field to gain a better understanding of both the safety and efficacy of emerging psychedelic therapies.

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?**

To further the understanding of psychedelics and to establish their clinical efficacy, researchers must address several unique methodological challenges. It is difficult to conduct randomized placebo-controlled clinical trials of psychedelic drugs because their effects on perception and consciousness make them easy to distinguish from a placebo. Additionally, a person's subjective experience of a psychedelic drug varies depending on their mental state at the time that the drug is administered and the setting in which they have the experience. These types of confounds make it especially challenging to design clinical trials for psychedelic drugs, and to accurately interpret results.

Further research is needed to examine the efficacy and safety of psychedelic drugs for mental illnesses and substance use disorders, including the effects of repeated exposure and potential interactions with existing treatments. NIH supports an experimental therapeutics approach for the development and testing of therapeutic interventions, including psychedelic drugs, in which the studies not only evaluate the clinical effect of an intervention, but also generate information about the mechanisms underlying a disorder or an intervention response. Understanding the mechanisms of psychedelic drugs is important for identifying new therapeutic targets that could preserve therapeutic effects while minimizing negative side effects.

Additional knowledge gaps in psychedelics research persist due to the lack of participant diversity in clinical trials to date. This includes both racial and ethnic diversity,[6] as well as a lack of participants with diverse medical histories, as most psychedelics trials exclude potential

[3] www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/45-cfr-46/index.html
[4] pubmed.ncbi.nlm.nih.gov/35077687
[5] pubmed.ncbi.nlm.nih.gov/28443617
[6] pubmed.ncbi.nlm.nih.gov/32529966/

participants with a family or personal history of psychosis or suicidal thoughts or behaviors.[7] These specific challenges were discussed during the January 2022 "NIH Workshop on Psychedelics as Therapeutics,"[8] and NIH aims to develop guidance to help the field address the lack of participant diversity.

NIH has several open funding opportunities to encourage research on the development and testing of novel pharmacological interventions (including, but not limited to, use of psychedelic drugs) for mental health and substance use disorders. For instance, NIMH is supporting early-stage testing of pharmacologic interventions with novel mechanisms of action for the treatment of symptoms or domains of altered function in individuals with mental illness (e.g., schizophrenia, depression, autism, obsessive-compulsive disorder, anxiety, bipolar disorder).[9, 10, 11] NIDA is soliciting research to develop and test novel medications for opioid and stimulant use disorders,[12] and currently supports clinical trials investigating whether ketamine can improve outcomes in these disorders.[13,14,15,16] NIDA also supports a trial investigating whether psilocybin-assisted psychotherapy can improve smoking cessation.[17] NCCIH is also interested in supporting research on the therapeutic potential of psilocybin for chronic pain conditions. A key objective of these research efforts is to "de-risk" novel drugs for further clinical development.

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?**

NIH collaborates with researchers in part by hosting public events to inform various, multi-sector stakeholders about challenges, opportunities, and recent advances in psychedelic research. These include the January 2022 "NIH Workshop on Psychedelics as Therapeutics" referenced in your letter, as well as the April-June 2021 "NIH Psilocybin Speaker Series."[18] NIH also partners with the private sector on therapeutic development through the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs.[19]

NIH's role in public health does not stop at supporting research: NIH also collaborates extensively with other federal agencies to ensure that research advances translate into safe, effective treatments that are accessible to the people who need them. One way that NIH does this is through regular engagement with the FDA,[20] to help ensure that NIH-supported researchers are aware of what is needed for a novel therapeutic drug to gain FDA approval.

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[7] pubmed.ncbi.nlm.nih.gov/35301459/
[8] nida.nih.gov/news-events/meetings-events/2022/01/nih-workshop-psychedelics-therapeutics-gaps-challenges-opportunities
[9] grants.nih.gov/grants/guide/pa-files/PAR-21-136.html
[10] grants.nih.gov/grants/guide/pa-files/PAR-21-137.html
[11] grants.nih.gov/grants/guide/pa-files/PAR-21-133.html
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[13] reporter.nih.gov/project-details/9933841
[14] clinicaltrials.gov/ct2/show/NCT03344419
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[16] clinicaltrials.gov/ct2/show/NCT03344419
[17] reporter.nih.gov/project-details/10187739
[18] events.cancer.gov/nci/psilocybinresearch/agenda
[19] seed.nih.gov/
[20] www.fda.gov/science-research/science-and-research-special-topics

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?

As with all human subjects research, clinical research on psychedelic drugs is governed by several statutes and regulations intended to protect the rights and welfare of research participants: NIH does not view these regulatory considerations as barriers, but rather as necessary and beneficial safeguards. For example, NIH has specific requirements for research staff and policies regarding research conduct, safety monitoring, and reporting of information about research progress.[21] In accepting an award that supports human subjects research, the recipient institution assumes responsibility for all research conducted under the award, including protection of human subjects at all participating and consortium sites.[22] All human subjects research must also be reviewed, approved, and monitored by an Institutional Review Board.[23]

Because psychedelic drugs are controlled substances, one additional regulatory consideration for basic and applied research using psychedelic drugs is that these studies must also follow Drug Enforcement Administration (DEA) requirements, including registration, inspection, and certification of the drugs.[24] These requirements apply to all psychedelic drugs, including natural or botanical psychedelics, and NIH is not aware of any additional regulatory considerations unique to natural or botanical psychedelics. NIH has worked closely with the FDA, DEA, and the White House Office of National Drug Control Policy on a proposed framework to facilitate the process of obtaining a DEA registration to conduct research with controlled substances, including psychedelics.[25]

We hope that you find this information helpful, and we greatly appreciate Congress's continued support for NIH to ensure that our Nation remains the global leader in biomedical research and advances in human health. An identical response has been sent to Senator Cory Booker, the co-signer of your letter. Please let us know if you have any additional questions.

Sincerely,

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

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

[21] grants.nih.gov/policy/humansubjects/policies-and-regulations.htm
[22] grants.nih.gov/grants/policy/nihgps/html5/section_4/4.1.15_human_subjects_protections.htm
[23] www.fda.gov/regulatory-information/search-fda-guidance-documents/institutional-review-boards-frequently-asked-questions
[24] grants.nih.gov/grants/policy/nihgps/html5/section_4/4.1.5_controlled_substances.htm
[25] nida.nih.gov/about-nida/legislative-activities/testimony-to-congress/2021/the-overdose-crisis-proposal-to-combat-illicit-fentanyl