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Psychedelic Drug Development Takes Center Stage – Do You Have What it Takes to Bring a Psychedelic Drug to Market?

In mid-July, the U.S. Food and Drug Administration (FDA) took additional affirmative steps to advance the development of psychedelic medicines. These steps built upon the Trump administration's Executive Order, Accelerating Medical Treatments for Serious Mental Illness issued in mid-April 2026. The order noted that individuals suffering from major depressive disorder and substance abuse disorder often relapse or do not fully respond to traditional medical and psychiatric therapies, despite massive federal investment and medical research. Therefore, the order continues, innovative research models involving psychedelic drugs, which show potential promise in clinical trials, need accelerated research and "appropriate drug approvals" to help save lives and reverse the mental health illness crisis in America.

The order discusses several key steps to accomplish the objective to bring more psychedelic drugs to market to treat mental illness. First, the order requested the FDA Commissioner to provide Commissioner's National Priority Vouchers to appropriate psychedelic drugs that have received a Breakthrough Therapy designation and otherwise meet the criteria for the voucher. FDA issued three such vouchers in April 2026: psilocybin for treatment-resistant depression, psilocybin for major depressive disorder, and methylone for post-traumatic stress disorder.

The order also requested that FDA work with other federal agencies to facilitate access to research and treatment with psychedelic drugs. First, the FDA and the Drug Enforcement Administration (DEA) were directed to facilitate a pathway for researchers and patients to have greater access to psychedelic drugs for research and treatment, including any applicable waivers under the Controlled Substances Act. Then, FDA and the U.S. Department of Health and Human Services (HHS) were to

allocate $50 million from existing funds to support and partner with State governments to advance psychedelic drugs for serious mental illnesses. The order directed the FDA, HHS, and Veterans Administration (VA) to sign data-sharing memoranda to make psychedelic drug-related information available to FDA. Finally, the order directed the Attorney General, in consultation with HHS, to initiate and complete review of any Schedule I drug that has completed a Phase 3 study to accelerate rescheduling, as appropriate.

The FDA's mid-July initiatives set up a new Psychedelic Drugs Portal, finalized guidance from 2023 on Psychedelic Drug Development, finalized the FDA / HHS / VA Memorandum, and announced a public meeting in September to obtain feedback in collaboration with federal partners on the development of future treatments for mental illness incorporating psychedelic drugs. The memorandum, among other things, described a process for sharing non-public information between the FDA, HHS, and VA to accelerate FDA's action on reviewing and issuing appropriate approvals for new psychedelic therapies to treat mental illness. The public meeting aims to obtain feedback and perspectives on the issues involved in the development of potential psychedelic therapies to be used in supervised and supportive settings. The guidance aims to provide general considerations for sponsors developing psychedelic drugs for the treatment of mental conditions and discusses recommendations for the "unique challenges" for clinical investigations involving psychedelic drugs.

In particular, the FDA noted the unique challenges include the ability for psychedelic drugs to cause perceptual disturbances and alterations in consciousness that can last hours or days. In addition, when used with psychological or behavioral intervention, psychedelic drugs, investigators have hypothesized, may have rapid onset and long-term benefits after only one or a few doses. Below are a few of the additional unique elements addressed in the guidance:

- Some psychedelics may be derived from plants or fungi, fermentation of yeast, bacteria, or plant cells and should be considered under guidance for Botanical Drug Development.
- Some psychedelics have serotonin activity, which has been linked to heart valvulopathy in humans, requiring a thorough microscopic evaluation of the heart and heart valves, as well as a careful evaluation of potential interactions

with concomitant medications.

- Psychedelic drugs typically act on the central nervous system with psychoactive effects (e.g., mood or cognitive changes and hallucinations) that require additional considerations for abuse potential, especially since they are often Schedule I controlled drug substances (high abuse potential with no approved medical use in the U.S.).
- Clinical trial design proposals should be discussed with the review division before initiating a study, including alternatives to traditional placebo studies and additional approaches to minimize bias.
- Investigators have hypothesized that one or few doses of psychedelic drugs may provide a durable response lasting months or years, so double-blind designs incorporating different doses should be considered for illnesses such as post-traumatic stress disorder or major depressive disorders.
- Many psychedelic drug development programs involve psychological or psychotherapy support while experiencing the acute effects of the drug or in a separate session, which may require a factorial design to characterize the separate contributions of any such support versus the drug by itself.
- The FDA expects extra safety monitoring given the fragile patient population including at least two monitors during the duration of the treatment, availability of licensed on-call physicians to reach the site within 15 minutes of a medical emergency, informed consent that explains the potential for extended changes in perception, cognition and judgement as well as all known adverse events (even if observed only with illicit use), extra cardiac and valve monitoring for drugs with serotonin activity as noted above, and risk mitigation in the event of nonmedical use, accidental exposure, or overdose.
- Additional post-approval assessments will likely be required and the potential need for risk evaluation and mitigation strategies should be considered.

Key Takeaways

What is the public challenge?

- The HHS, FDA, DEA, VA, and state government agencies are now aligned to help facilitate the research and development of psychedelic drugs, used alone or in combination with psychotherapy support therapy.

- Various known and new psychedelics are available for such research and development.
- If you are a sponsor of potential psychedelic drug therapies to treat mental conditions, do you have what it takes to apply FDA's most recent guidance and joint initiatives to clinically study and bring psychedelic drugs to market to treat mental conditions?

This blog was drafted by Brian Malkin, a Spencer Fane attorney and co-lead of the FDA Pharmaceutical and Biologics Market Team. For more information, visit spencerfane.com.

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