REAGAN-UDALL FOUNDATION FOR THE FDA

Advancing Treatments for Post-Traumatic Stress Disorder

Public Hybrid Meeting

Meeting Summary
November 2024

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Funding Disclosure: This activity is one part of a multi-part Foundation project related to substance use disorder. The multi-part project is supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) as part of an overall award of $1,720,109 of federal funds (100% of the project). The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by FDA, HHS, or the U.S. Government. For more information, please visit FDA.gov.

1 Introduction

The Reagan-Udall Foundation for the Food and Drug Administration (FDA) hosted a public meeting titled "Advancing Treatments for Post-Traumatic Stress Disorder," in alignment with the FDA's ongoing efforts to better understand the medical needs surrounding PTSD with a goal of facilitating treatment development.

This hybrid event, offering both virtual and in-person participation, included a panel discussion with federal partners exploring efforts to accelerate treatment development for PTSD, including the potential role of psychedelic drugs. Following the panel, stakeholders were invited to share their perspectives, both in-person and virtually. A diverse range of voices contributed, including individuals with lived PTSD experience (both veterans and non-veterans), their families, patient advocates, researchers, scientists, and drug developers. Stakeholders were also invited to submit written statements.

Overview of PTSD

Dr. Bernard Fischer, Deputy Director for the Division of Psychiatry at the FDA, provided an overview of PTSD, beginning with its history and the evolution of terminology. While PTSD was not formally recognized as a diagnosis until 1980,[1] the associated symptoms have appeared in cultural references throughout history. Greek tragedies and the works of Shakespeare described symptoms consistent with PTSD, such as isolation, physical complaints, and nightmares. In the 1700s, it was called nostalgia and known as "soldier's heart" during the American Civil War, "shell-shock" in World War I, and "battle fatigue" in World War II.

Today, it is widely recognized that PTSD affects both men and women, and it can arise from experiences beyond combat, impacting veterans and non-veterans alike. The National Center for PTSD estimates that around 5% of the U.S. population experiences PTSD in any given year.[2] This condition is a significant public health concern, with symptoms that not only affect the individuals suffering from it but also their families and communities. PTSD can lead to serious consequences such as suicide, housing instability, additional health complications, and premature death.

Currently, only two drugs—sertraline and paroxetine—are FDA-approved for treating PTSD. While these medications can provide symptom relief for some individuals, they are not effective for all, highlighting the need for more safe and effective treatments. Future research should be inclusive of people with PTSD after trauma from single events (e.g., assaults, accidents), as well as those who have experienced repeated trauma (e.g., combat, intimate partner violence).

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[1] Diagnostic and Statistical Manual for Mental Disorders Edition 3

[2] National Center for PTSD. How Common Is PTSD in Adults? U.S. Department of Veteran Affairs. Published February 3, 2023. Accessed October 15, 2024. https://www.ptsd.va.gov/understand/common/common_adults.asp

Additionally, studying brain circuitry, resilience, and biomarkers will be crucial to advancing our understanding and treatment of PTSD.

> *"Despite 150 clinical trials testing over 58 different drugs or drug combinations to treat PTSD in the last 35 years, as we heard earlier, there are still only two FDA-approved drugs that do not show high levels of efficacy, especially in our military population."*
>
> *– Dr. Elyse Katz, U.S. Department of Defense*

Ongoing clinical trials and FDA initiatives, such as Breakthrough Therapy designation, support the advancement of potential new treatments for PTSD. This is evidenced by current research (477 trials registered at www.clinicaltrials.gov) into drugs and devices aimed at treating PTSD symptoms.

2 Federal Panel Discussion

PTSD significantly impacts individuals and communities, highlighting the need for prevention and resilience-building measures. Collaboration is important across government agencies, private industry, and communities to develop additional effective PTSD treatments. Federal agencies that participated in the panel discussion included the Department of Defense (DoD), the Office of the Assistant Secretary for Health-Department of Health and Human Services (OASH/HHS), the U.S. Food and Drug Administration (FDA), the Substance Abuse and Mental Health Services Administration (SAMHSA), and the U.S. Department of Veterans Affairs (VA).

> *"…only by working together we can assure that we are going in the same directions, we have the same goal and the platforms, the innovations that [what] is happening is really aligned and streamlined so we can really get the results that we all want faster."*
>
> *– Dr. Marta Sokolowska, U.S. Food and Drug Administration*

Several key points emerged from the federal panel discussion:

- There are two FDA-approved drugs and a variety of behavioral health treatments indicated for PTSD, which can be effective options for many patients.
- Significant unmet treatment needs persist for patients with PTSD, both in terms of access to existing treatments and availability of additional treatment options that patients find acceptable.
- Multimodal and varied treatment options are needed because PTSD treatment is individualized, and a single approach will not work for everyone.
- Innovative clinical trial designs, with opportunities for veteran and non-veteran enrollment, are critical for development and evaluation of novel treatments.

- Although new treatments and treatment modalities are on the horizon, better coordination among federal agencies and departments can accelerate progress and advance the collective knowledge base.
- Existing federal programs are supporting the development of new treatments for PTSD (e.g., The VA PTSD Psychopharmacology Initiative).

SAMHSA and OASH/HHS have approached PTSD from multiple angles, particularly focusing on social determinants of health and comorbidities like substance use disorder. SAMHSA's core contributions include grants for treatment services, technical assistance, and the promotion of suicide prevention as part of a broader effort to build resilience, especially in children and families affected by trauma. SAMHSA also supports workforce development to improve competency in addressing PTSD.

Federal programs aimed at supporting PTSD treatment include the 988 Crisis Lifeline, mental health block grants, and the ReCAST program, which focuses on building community resilience. Additionally, SAMHSA's collaborations with veterans' services and childhood trauma networks aim to provide comprehensive care for those affected by PTSD, ensuring access to resources regardless of financial status.

The VA has similarly committed to improving PTSD treatment for veterans, with a strong focus on evidence-based therapies. The VA has specialized programs for PTSD care and has invested heavily in research, including innovative studies on psychopharmacology, genetics, and psychedelic-assisted therapy. The VA's Million Veteran Program and the development of platform trials are part of a larger effort to tailor treatments to individual needs, including through biomarker research and precision medicine.

The DoD's PTSD Drug Treatment Program aims to develop effective treatments for PTSD in service members and veterans and has launched the Military and Veterans PTSD Adaptive Platform Clinical Trial (M-PACT), the first platform trial conducted with input from the FDA in the field of psychiatry. This trial allows for more efficient testing of multiple drugs simultaneously, sharing placebo data across treatment arms, and cycling drugs based on evidence of success or failure. The program seeks to advance precision medicine approaches, where drugs will be prescribed based on individual effectiveness.

In its regulatory capacity, the FDA plays a critical role in reviewing new drugs and devices for PTSD symptom treatment, such as the NightWare and Freespira devices. While the agency has encouraged PTSD treatment development, as demonstrated through publicly reported Breakthrough Designations for drugs and devices, continued innovation, research, and collaboration are essential to address the complexities of PTSD and improve care outcomes.

Through all of these steps toward progress—whether moving fully forward, partially forward, or even when progress is slower than expected—we are constantly learning, and that learning advances the work. Panelists spoke about the importance of creativity, partnership, and the ongoing commitment to learning from and working together with federal agencies, the private sector, and individuals. By doing so, we can continue improving the diagnosis, treatment, and prevention of PTSD.

3 Stakeholder Input

Twenty-nine stakeholders, representing a wide range of backgrounds, provided up to three minutes each of public comment either virtually or in-person. Additionally, 335 people provided insights into experiences with trauma and treatment journeys through written statements. The commenters included veterans experiencing PTSD from combat, individuals experiencing PTSD from lived personal trauma, advocacy groups, clinicians who provide treatment for PTSD, and others involved in mental health initiatives and the development of resources.

Key themes and related sentiments were identified from the verbal and written comments regarding advancing treatments for PTSD. Commenters referenced their personal experience to describe PTSD symptoms and how various treatment modalities alleviated symptoms, improved physical and emotional function, and affected quality of life. Self-reported improvements included:

- Better sleep
- Reduced anxiety
- Increased function and ability to engage in everyday tasks
- Decreased suicidal ideation
- Improved relationships
- Improved emotional regulation
- Increased cognitive flexibility
- Improved physical well-being

Key Themes from Public Commenters

Summary of Key Themes from Public Commenters
• A sense of urgency • Concern about PTSD and death by suicide • Criticism of current PTSD treatments • Support for psychedelics and the use of psychedelics in controlled therapeutic settings • Frustration with regulatory delays • Calls for more research

A sense of urgency

Participants emphasized the urgent need for effective PTSD treatments. Words such as "need," "crisis," and "action" reflected the frustration of those waiting for effective treatments. They expressed widespread concern for the time lost (i.e., days, months, and years) as they wait for effective treatments.

There was also a strong sense of urgency to approve psychedelic treatments. Commenters urged the FDA to reconsider its decision regarding midomafetamine (MDMA) and accelerate the approval process for the sake of those living with PTSD.

Concern about PTSD and death by suicide

Participants noted that too many people diagnosed with PTSD are dying by suicide. Stakeholder sentiment emphasized that the more time that passes without additional treatment options, the more lives will be lost.

Criticism of current PTSD Treatments

Numerous comments criticized existing PTSD treatments (e.g., selective serotonin reuptake inhibitors, traditional talk therapies) as being ineffective, inadequate, or poorly tolerated for many. Commenters also noted that innovation in PTSD treatment is lagging, and it has been many years since a new PTSD treatment has been approved. Some participants stated that even a combination of the currently available drugs and treatment modalities do not provide effective relief of symptoms or enable resumption of daily living activities.

Several commenters also discussed stigma associated with mental health treatments, particularly in marginalized communities, and mistrust of medical institutions. Words like "stigma," "betrayal," and "mistrust" stood out in these discussions.

Support for psychedelics and the use of psychedelics in controlled therapeutic settings

Persons with lived experience and health professionals alike highlighted the potential of psychedelic-assisted therapies as innovative treatment options for trauma and PTSD. There was significant support for psychedelics like MDMA, psilocybin, and ketamine as effective treatments for PTSD, often with personal testimonies of how these substances helped individuals where traditional treatments had failed. Words like "life-changing" and "cured" were used.

Commenters voiced support for the use of psychedelics in controlled therapeutic settings and shared experiences describing the benefits of a holistic approach to healing. A common theme was the necessity of combining psychedelics with psychotherapy. Many commenters emphasized that the combination of psychedelic drugs and therapy was essential for healing trauma. The term "psychedelic-assisted therapy" was frequently used.

Many individual respondents shared personal stories of trauma, including childhood abuse, sexual abuse, and institutional betrayal. These personal narratives often advocated for the use of psychedelics in healing complex trauma, describing the relief that traditional therapies had not provided. Personal experiences using psychedelic-based treatments included:

- Relieving a decades-long struggle of living with nightmares
- Reducing anxiety associated with traumatic memories
- Improving functionality and ability to engage in daily tasks
- Crediting MDMA-assisted therapy with saving their life and achieving full remission of symptoms following numerous pharmacological trials that provided little relief and were accompanied by terrible side effects from the drugs
- Sharing how MDMA-assisted therapy helped reduce PTSD symptoms after years of struggling with ineffective treatments

Family members of those suffering from PTSD also spoke about the benefits of psychedelic-assisted therapy. They shared stories of how their loved ones had found healing through these treatments after struggling with conventional mental health care. A family member of a trauma survivor shared how psychedelic therapy saved their spouse's life and transformed their family, reflecting on improvements in both personal and family relationships.

Concerns were also expressed over MDMA treatment discontinuation for those receiving the drug through clinical trials. Without an alternate mechanism to obtain MDMA and continue with MDMA-assisted therapy, study participants were only left with alternatives that were not effective for them.

Frustration with regulatory delays

Many commenters expressed disappointment in the FDA's decision not to approve MDMA-assisted therapy for PTSD. They were disappointed with the pace of research and the time it takes to bring new, potentially life-saving treatments to market. Because of the slow pace of the regulatory system in the U.S., commenters mentioned that people with PTSD often seek treatment overseas in an attempt to find effective treatment and symptom relief. Those who shared their stories of transformation through MDMA-assisted therapy advocated for faster approval of psychedelic treatments.

Commenters criticized the FDA's clinical trial criteria, arguing that the current system is not suited to evaluate therapies like MDMA, which combine drugs with psychotherapy. They called the FDA's criteria outdated and inadequate for this type of treatment. Some critics also argued that the agency failed to provide consistent guidance and necessary context for its external advisors when reviewing MDMA. This inconsistency led to frustration among those supporting the therapy's approval.

Calls for more research

Calls were made for a higher level of scientific rigor in evaluating psychedelics for the treatment of PTSD. Concerns were raised about safety, especially regarding potential long-term effects and the risk of misuse. Commenters emphasized safety and broader accessibility of psychedelic treatments with greater inclusion of underserved communities and populations with complex trauma. One stakeholder noted the prominence of PTSD among Indigenous people and expressed disappointment for the lack of tribal representatives from the American Indian population on the federal panel.

4 SUMMARY

This meeting provided a platform for representatives from federal agencies to share current efforts to accelerate PTSD treatment development and to hear the voices of individuals experiencing PTSD and the broader PTSD community. Federal partners expressed a resounding commitment to improving the delivery of existing treatments for PTSD, as well as to developing additional treatments, while commenters emphasized the urgency of addressing the public health issue of PTSD through their lived experiences. All meeting participants shared the desire for collaboration between public and private partners and continued investment in innovative approaches to research.

5 APPENDICES

A: Meeting Agenda

Advancing Treatments for Post-Traumatic Stress Disorder

Hybrid Public Meeting
Friday, September 6, 1 - 3:30 pm Eastern Time
1333 New Hampshire Avenue NW; Rooftop Meeting Room
Washington, DC, 20036

Agenda

1 pm **Welcome and Opening Remarks**

Speakers:
- Susan C. Winckler, RPh, Esq., Reagan-Udall Foundation for the FDA
- Bernard Fischer, MD, U.S. Food and Drug Administration

1:15 pm **Federal Partner Discussion**

Panelists:
- *Department of Defense*
  - Elyse Katz, PhD
- *Office of the Assistant Secretary for Health, Department of Health and Human Services (HHS)*
  - Leith J. States, MD, MPH, MBA, FACPM
- *U.S. Food and Drug Administration, HHS*
  - Marta Sokolowska, PhD
- *Substance Abuse and Mental Health Services Administration, HHS*
  - Neeraj 'Jim' Gandotra, MD
- *U.S. Department of Veterans Affairs*
  - Paula P. Schnurr, PhD
  - Miriam J. Smyth, PhD

1:55pm **Stakeholder Comment**

3:30 pm **Adjourn**

B: List of Meeting Commenters

(IN PERSON)

Name	Organization	Industry
Karen Dunn	North Suffolk Community Services	Non-Profit/Foundation
Paul Kennedy		Patient
Jonathan Lubecky		Patient
Rogers Masson		Patient
Juliana Mercer	Healing Breakthrough	Non-Profit/Foundation
Vanessa Walker	Depression Bipolar Support Alliance	Non-Profit/Foundation
Aaron Wolfgang	US Army	Government (Federal/State/Local/Tribal Territorial)
Deran Young	Black Therapists Rock	Non-Profit/Foundation

C: List of Meeting Commenters

(VIRTUAL)

First Name	Organization	Industry
Michael Abrams	Public Citizen	Consumer/Consumer Advocate
Mary Armstrong		Patient
Ron Blake	Blake Late Show	Patient
Nese Devenot	Johns Hopkins University	Academic
Jesse Gould	Heroic Hearts Project	Non-Profit/Foundation
Robert Grant	UCSF	Academic
Angela Hargrove	Emmes	Clinical Research
Mo Heidaran	Cory Heidaran Charitable Foundation	Non-Profit/Foundation
David Heldreth Jr.	Panacea Plant Sciences	Clinical Research
Arash Javanbakht	Wayne State University Department of Psychiatry and Behavioral Neurosciences	Academic
Debbie Knight	Harding University	Academic
Matthew Kodrin		Patient
Virna Little		Corporation (not regulated by the FDA)
Raj Mehra	Seelos Therapeutics	Industry
Sonja Patrick		Patient
Debbie Plotnick	Mental Health America	Patient Organization
Jessica Punzo	American Psychological Association Division of Trauma Psychology	Trade Association
Ashley Troxell		Consumer/Consumer Advocate
Barry Walden		Patient
Alan Wiederhold	Neuma Health Corp.	Corporation (Regulated by the FDA)