A MOSAIC PERSPECTIVE OF THE PSYCHEDELICS LANDSCAPE

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DISCLAIMER

• THIS PRESENTATION REFLECTS THE VIEWS OF THE AUTHOR AND SHOULD NOT BE CONSTRUED TO REPRESENT FDA’S VIEWS OR POLICIES.
OUTLINE

• BACKGROUND
• RESEARCH OVERVIEW
• BEYOND DRUG DEVELOPMENT – POLICY IMPLICATIONS OF THE PSYCHEDELICS RESURGENCE
COMMONLY STUDIED PSYCHEDELIC SUBSTANCES

- HALLUCINOGENS ARE A DIVERSE GROUP OF SUBSTANCES THAT CAN ALTER A PERSON’S CONSCIOUSNESS AND COGNITIVE PROCESS

- THEY FALL INTO TWO BROAD GROUPS:
  1. “CLASSIC” HALLUCINOGENS – WHICH INCLUDE LSD, PSILOCYBIN, IBOGAINE
  2. DISSOCIATIVE TYPES – WHICH CAN INCLUDE PCP, KETAMINE

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BRIEF HISTORY – HUMAN’S QUEST FOR MIND-ALTERING EXPERIENCE FROM PLANTS

• Psychedelics have flourished for thousands of years in indigenous cultures1
• Humanity’s quest for psychoactive mind-altering plants is evidenced in archaeological writings2
• Western/European exploratory ‘research’ began in the late nineteenth to early twentieth century with the identification of mescaline in peyote cactus plants3
• Modern psychedelic research began in 1938 with the work of Albert Hoffman4

Sources:
SELECT NOTABLE MILESTONES IN PSYCHEDELICS
RESEARCH AND DEVELOPMENT

1943
• LSD’s psychoactive effects discovered

1947
• First paper on psychedelic effects of LSD in humans is published

1962
• Marsh Chapel experiment at Harvard

1970
• Controlled Substances Act is signed; psilocybin is classified as schedule I

2000’s
• 2nd wave of psychedelic research

EPI SNAPSHOT: PAST-YEAR USE, 2020 NSDUH

- In 2020, 2.6% of people aged 12+ (or 7.1M people) used hallucinogens in the past year.
- 1.4M people initiated hallucinogen use in the past year, including 251,000 adolescents.

Note: category of hallucinogens includes LSD, PCP, peyote, mescaline, psilocybin, MDMA, ketamine, DMT and Salvia divinorum.
# SUMMARY OF KEY RECENT TRENDS IN PSYCHEDELICS USE

<table>
<thead>
<tr>
<th>Past-year Nonmedical Use, Young Adults: Prevalence and Trend</th>
<th>Data Source(s), Age group, Years</th>
<th>MDMA</th>
<th>Psilocybin</th>
<th>LSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSDUH, 18-25 years, 2015-2020; MTF, 12th graders, 2015-2019</td>
<td>~3%, declining trend</td>
<td>~2%, flat trend</td>
<td>~3%, increasing trend</td>
<td></td>
</tr>
<tr>
<td>Past-year Nonmedical Use, General Population: Prevalence and Trend</td>
<td>NSDUH, 12 years and older, 2015-2020</td>
<td>~1%, slight declining trend</td>
<td>Data not available</td>
<td>~1%, increasing trend</td>
</tr>
</tbody>
</table>

NSDUH: Substance Abuse and Mental Health Services Administration (SAMHSA)'s public online data analysis system (PDAS) Survey: National Survey on Drug Use and Health (NSDUH). Available at [https://pdas.samhsa.gov](https://pdas.samhsa.gov)

MTF: Monitoring the Future (MTF) National Survey Results on Drug Use Volume I, Secondary school students. Available at [http://monitoringthefuture.org/pubs.html#monographs](http://monitoringthefuture.org/pubs.html#monographs)
RESEARCH OVERVIEW
DRUG DEVELOPMENT SNAPSHOT

- 113 CLINICAL TRIALS FOR MDMA
- 99 CLINICAL TRIALS FOR PSILOCYBIN
- 29 CLINICAL TRIALS FOR LYSERGIC ACID DIETHYLAMIDE (LSD)

Source: Clinicaltrials.gov, Accessed 2/16/22; 5/16/22


MDMA TRIALS: CLINICAL DEVELOPMENT

Source: Clinicaltrials.gov, Accessed 5/16/22
MDMA CLINICAL TRIALS: TREATMENT INDICATIONS

Partial list of indications studied from clinicaltrials.gov. Includes “active”, “recruiting”, and “enrolling” studies.

N=28

- PTSD
- Other
- Substance use
- HIV
- Health Volunteer

- Other includes - Depression, interpersonal interaction, and diabetes, among others

Source: Clinicaltrials.gov, Accessed 2/24/22
PSILOCYBIN TRIALS: CLINICAL DEVELOPMENT

Psilocybin; N=99

<table>
<thead>
<tr>
<th>Phase</th>
<th># of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Phase 1</td>
<td>11</td>
</tr>
<tr>
<td>Phase 1</td>
<td>43</td>
</tr>
<tr>
<td>Phase 2</td>
<td>47</td>
</tr>
<tr>
<td>Phase 3</td>
<td>0</td>
</tr>
<tr>
<td>Phase 4</td>
<td>0</td>
</tr>
<tr>
<td>Not Applicable</td>
<td>5</td>
</tr>
</tbody>
</table>

Source: Clinicaltrials.gov, Accessed 5/16/22
PSILOCYBIN CLINICAL TRIALS: TREATMENT INDICATIONS

Partial list from clinicaltrials.gov. Includes studies described as “active”, “recruiting”, and “enrolling”, based on date of extraction

N=36

- Other includes - Opioid use, nicotine dependence, and healthy volunteers, among others

Source: Clinicaltrials.gov, Accessed 2/16/22
LSD TRIALS: CLINICAL DEVELOPMENT

LYSERGIC ACID DIETHYLAMIDE (LSD); N=29

<table>
<thead>
<tr>
<th>Phase</th>
<th># of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Phase 1</td>
<td>6</td>
</tr>
<tr>
<td>Phase 1</td>
<td>15</td>
</tr>
<tr>
<td>Phase 2</td>
<td>4</td>
</tr>
<tr>
<td>Phase 3</td>
<td>0</td>
</tr>
<tr>
<td>Phase 4</td>
<td>1</td>
</tr>
<tr>
<td>Not Applicable</td>
<td>2</td>
</tr>
</tbody>
</table>

Source: Clinicaltrials.gov, Accessed 5/16/22
LSD CLINICAL TRIALS: TREATMENT INDICATIONS

Partial list from clinicaltrials.gov. Includes studies described as “active”, “recruiting”, and “enrolling”, based on date of extraction;

- Healthy Volunteer: 2
- Headache: 1
- Depression: 1
- Substance Use: 1

Source: Clinicaltrials.gov, Accessed 2/24/22
# Drug Development Snapshot: Breakthrough Therapy

<table>
<thead>
<tr>
<th>Year Granted</th>
<th>Sponsor</th>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>Multidisciplinary Association of Psychedelic Studies (MAPS)</td>
<td>MDMA</td>
<td>Post-traumatic stress disorder (PTSD)</td>
</tr>
<tr>
<td>2018</td>
<td>COMPASS Pathfinder Limited</td>
<td>Psilocybin (COMP360)</td>
<td>Treatment-resistant depression (TRD)</td>
</tr>
<tr>
<td>2019</td>
<td>Usona Institute</td>
<td>Psilocybin</td>
<td>Major depressive disorder (MDD)</td>
</tr>
</tbody>
</table>

Sources:
BEYOND DRUG DEVELOPMENT

POLICY IMPLICATIONS OF THE PSYCHEDELICS RESURGENCE
SOCIAL AND ENVIRONMENTAL DRIVERS OF RENEWED INTERESTS

- Research and Development
  - Applications for research and commercial INDs

- States Policy Actions
  - Movement toward decriminalization and legalization gaining momentum

- Private Sector Investments
  - Investments ($$$$)
  - New start-ups

- Pace of Socialization
  - Microdosing
  - Retreats
  - Psychedelics subcultures/ and how they are influencing broader society

- Social Media and other Influences
  - Quest for improved creativity
  - Coverage of psychedelics
  - Therapy promising treatments
LEGALIZATION AND DECRIMINALIZATION STATUTES – OREGON

ACTIVE LEGISLATION – 14 STATES (MA., NY, VT, PA., MD., MI., IA., MS., KS., OK., GA., FL., HI., UT.)

INACTIVE OR FAILED LEGISLATION - 5 STATES (CA., MN., OH., WV., AND VA.)

REDUCED PENALTY - 3 STATES (CO., NJ., WA)

LIMITED JUDICIAL EXCEPTIONS – (NH).

WORKING GROUP TO STUDY PSYCHEDELICS – ONE STATE (TX) + 10 MUNICIPALITIES (INCLUDING SEATTLE, DENVER, DETROIT, AND SANTA CRUZ, ARCATA, AND OAKLAND – IN CA.)

Source: Psilocybin Alpha https://psychodelicalpha.com/data/psychedelic-laws
RECENT STATE ACTIONS FOCUSED ON EXEMPTIONS RELATED TO HEALTH, SOCIAL JUSTICE/EQUITY, AND COGNITIVE LIBERTY JUSTIFICATIONS

- **CONNECTICUT & TEXAS (2021):** LAWS REQUIRING STUDIES ON MEDICAL USE OF PSYCHEDELICS. TEXAS’ PROPOSAL PARTICULARLY HIGHLIGHTS ACCESS FOR VETERANS.

- **CALIFORNIA (CURRENTLY INACTIVE):** BILL WOULD LEGALIZE PERSONAL USE OF CERTAIN PSYCHEDELICS DEFEATED BUT PLANS TO REVISIT IN 2023 WITH POSSIBLE AMENDMENTS.

- **MISSOURI:** BILL WOULD EXPAND STATE’S RIGHT TO TRY LAW TO POSSIBLY INCLUDE PSYCHEDELICS (IBOGAINE, PSILOCYBIN, LSD) ACCESS FOR SERIOUS ILLNESSES.

- **NEW YORK STATE’S BILL A08569:** COULD LEAD TO CREATION OF PSILOCYBIN TREATMENT CENTERS, WITH PRIORITY GIVEN TO WOMEN AND MINORITY OWNED AND ACCESS FOR VETERANS.

Source: Marijuana Moment: https://www.marijuanamoment.net/missouri-patients-could-use-psychedelic-treatments-under-new-gop-right-to-try-bill/#:~:text=A%20Republican%20Missouri%20lawmaker%20on,right%2Dto%2Dtry%2Dtry%2Dtry%20law.
PSYCHEDELICS IN THE NEWS

Public Sector Influence (research funding)

U.S. Government Funds First Therapeutic Psilocybin Research in 50 Years
The National Institutes of Health is helping to fund a Johns Hopkins study looking at whether the psychoactive chemical could help people quit smoking

Private Sector Influence (drug/therapy development)

The next frontier of psychedelic therapy could be your couch
Ketamine therapy pioneer Field Trip is partnering with telehealth company Nue Life to bring psychedelic treatments into the home.

Socialization / Recreational

The Rise of Psychedelic Retreats
Even with cause for concern, retreats in countries like Costa Rica and Jamaica, as well as in the United States, have been popping up for more than a decade.

A Long, Strange Trip: Psychedelics Meet Mainstream Medicine

Grant Supports Development of Training for Psychiatrists in Psychedelic Medicine

More People Are Microdosing for Mental Health. But Does It Work?
Scientists are split over whether the benefits of small microdoses experience are a placebo effect or something more.
RELIGIOUS FREEDOM RESTORATION ACT

• PROHIBITS FEDERAL GOVERNMENT FROM SUBSTANTIALLY BURDENING A PERSON’S EXERCISE OF RELIGION; DEA DISCRETION TO GRANT OR DENY ALL RELIGIOUS EXEMPTIONS

• USE OF THE SUBSTANCE MUST COMPLY WITH ALL OTHER REGULATIONS, INCLUDING THOSE AFFECTING SAFETY

• RECENTLY RELEASED BEST PRACTICES GUIDE FOR SPIRITUAL USE OF PSYCHEDELICS
POLICY CONSIDERATIONS

ETHICAL GUARDRAILS
- All domains

Policy Framework

RESEARCH

DRUG DEVELOPMENT

POST-MARKET SURVEILLANCE

STATES ACTION

SOCIAl/CULTURAL/BEHAVIORAL

TREATMENT SETTINGS

- Risk of amplifying social inequities
- User unmet needs
- Normalized use
- Recreational use

OUTCOME ATTRIBUTION

MONITORING CAPACITY

Monitoring capacity

PATIENT/ACCESS

Monitoring capacity

TREATMENTS WITH PROVIDERS

METHODOLOGY

- Prospecting/Bioactivity
- Comparative effectiveness

Privacy issues

CONFLICT OF INTEREST

VULNERABILITIES

Harm of extractive economies on ICs

ETHICAL INHIBITIONS

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Harm to self, to others

EQUITY ISSUES

INFORMED CONSENT

INTERESTED CONSENSUS

HARM TO SELF, TO OTHERS

PUBLICALLY-DERIVED LINELINES
THANK YOU!

ACKNOWLEDGEMENT

- CSP (VERONICA UZOEBO)
- OSE/DPV
- OND /DP/OMPI
- OMP