

Emerging Psychedelic Therapies, Clinical Trials and the Future of Psychedelic Research

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MAPS
Public Benefit
Corporation

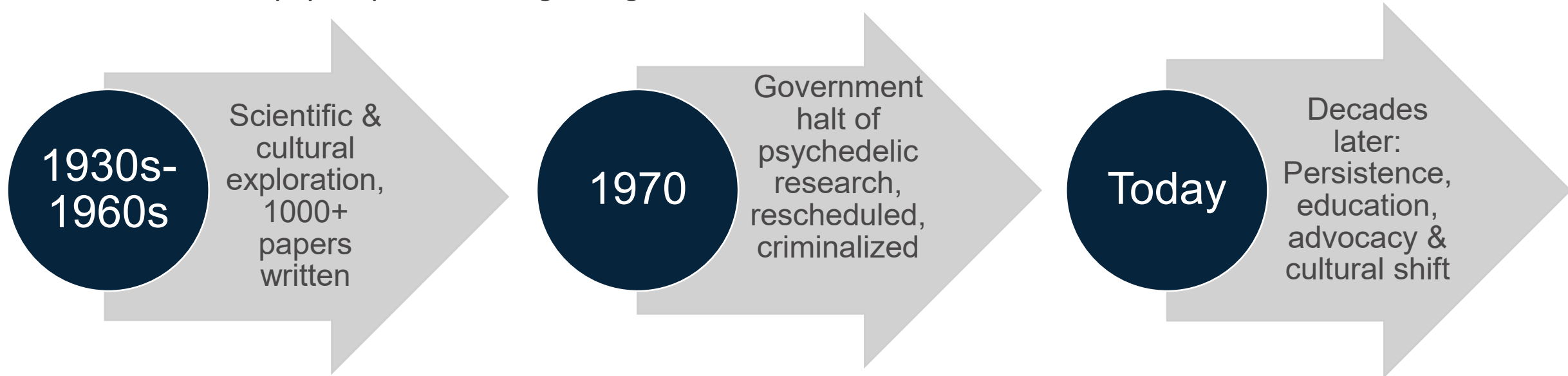


- Nonprofit research and educational organization founded in 1986
- Provided funding for MPBC



- Established in 2014 as a Public Benefit Organization to lead the development of MDMA-AT
- Wholly owned subsidiary of MAPS
- Operates for profit and uses profit to continue research to benefit patients
- Leading the research and development of MDMA-AT. MAPS PBC expects to submit the NDA to the FDA in the third quarter of 2023

- 10,000 BC Psychedelic plants and fungi used in indigenous medicinal traditions for millennia
- Oldest class of psychopharmacological agents known to man



Welcome to the Psychedelic Renaissance

Nichols DE. Psychedelics. *Pharmacol Rev.* 2016 Apr;68(2):264-355. doi: 10.1124/pr.115.011478. Erratum in: *Pharmacol Rev.* 2016 Apr;68(2):356. PMID: 26841800; PMCID: PMC4813425; Doblin RE, Christiansen M, Jerome L, Burge B. The Past and Future of Psychedelic Science: An Introduction to This Issue. *J Psychoactive Drugs.* 2019 Apr-Jun;51(2):93-97. doi:10.1080/02791072.2019.1606472. PMID: 31132970

What compounds are we talking about?

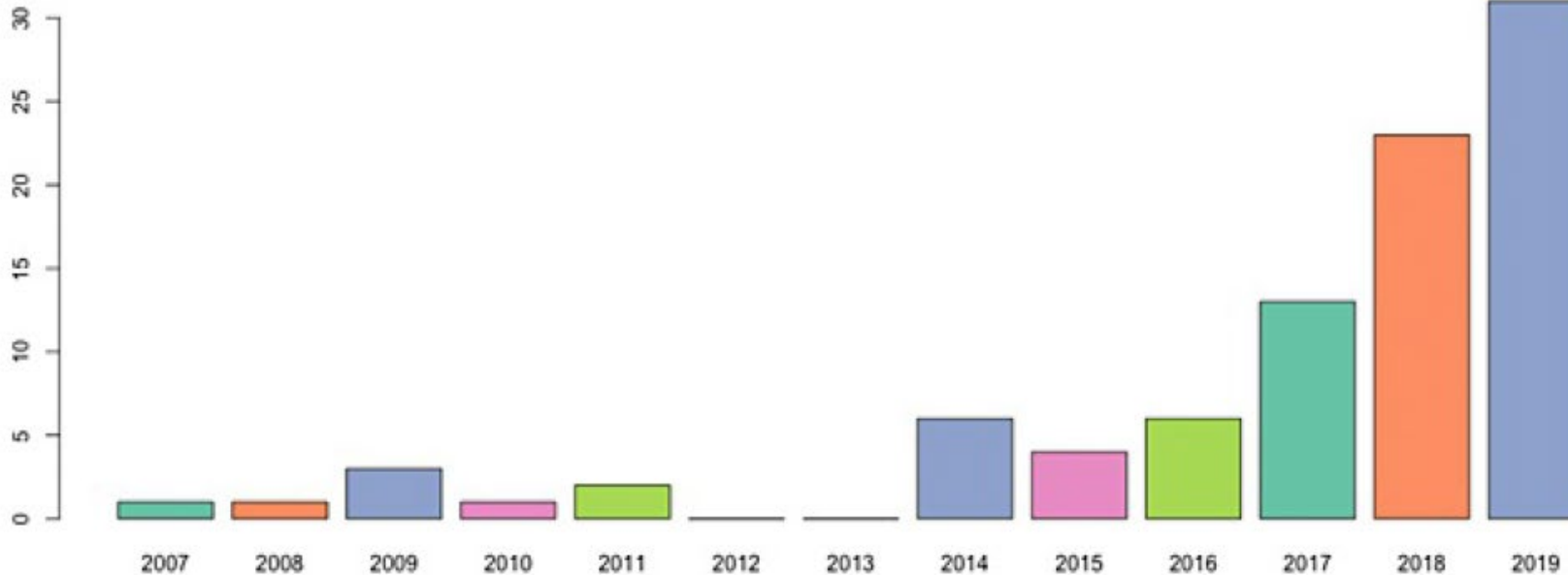
- Psilocybin
- LSD
- DMT
- 5-MeO-DMT
- Mescaline/ Peyote
- Ayahuasca
- MDMA (is an entactogen, not technically a psychedelic)
- Ketamine (not technically a psychedelic)
- Cannabis (not technically a psychedelic)

Nichols DE. Psychedelics. *Pharmacol Rev.* 2016 Apr;68(2):264-355. doi: 10.1124/pr.115.011478. Erratum in: *Pharmacol Rev.* 2016 Apr;68(2):356. PMID: 26841800; PMCID: PMC4813425.

Analysis of currently registered psychedelics studies in the American drug trial registry as of May 1, 2021

N=105 included in final analysis

Newly registered trials over time



- Analysis conducted using the ClinicalTrials.gov Database
- Database search term: “psychedelic” in the “other terms” parameter
- All trials took place from 2007 to 2020, with 77.1% of studies starting in 2017 or later
- US origination=74 (70.5%)
- Majority phase 1 (53.3%) or phase 2 (25.7%)
- No trials were completed:
 - Active=19 (18.1%)
 - Recruiting=63 (60%)
 - Enrolling=1 (1%)
 - Not yet recruiting=22 (21%)

Analysis of currently registered psychedelics studies in the American drug trial registry as of May 1, 2021 by condition

N=105 included in final analysis

Condition or disease	Number of trials	Percentage of all trials
Healthy	35	33%
Substance use disorder	14	13.3%
Alcohol	5	4.8%
Marijuana/cannabis	4	3.8%
Opioids	3	2.9%
Cocaine	1	1.0%
Nicotine	1	1.0%
PTSD	9	8.6%
Depression	8	7.6%
Pain	8	7.6%
Chronic pain	3	2.9%
Post-operative pain	1	1.0%
Neuropathic low back pain	1	1.0%
Inflammatory bowel disease	1	1.0%
Sickle cell disease	1	1.0%

Condition or disease	Number of trials	Percentage of all trials
Cancer	5	4.8%
Degenerative diseases	4	3.8%
Multiple sclerosis	2	1.9%
Alzheimer's disease	1	1.0%
Parkinson's disease	1	1.0%
Headache disorders	4	3.8%
Cluster headache	2	1.9%
Migraine	1	1.0%
Post-traumatic headache	1	1.0%
Multiple conditions or diseases	4	3.8%
Depression, Anxiety, PTSD	1	1.0%
Depression, depressive symptoms, Alzheimer's disease, mild cognitive impairment	1	1.0%

Condition or disease	Number of trials	Percentage of all trials
Distress/grief, depression	1	1.0%
Tourette syndrome, tic disorder	1	1.0%
Psychosis/schizophrenia	3	2.9%
OCD	2	1.9%
Anorexia nervosa	1	1.0%
Anxiety disorders	1	1.0%
Autism spectrum disorder	1	1.0%
Bipolar disorder	1	1.0%
Hepatic impairment	1	1.0%
HIV	1	1.0%
Obstructive sleep apnea	1	1.0%
Tourette syndrome	1	1.0%
Trichotillomania	1	1.0%

Analysis conducted using the ClinicalTrials.gov Database. Database search term: "psychedelic" in the "other terms" parameter.

All trials took place from 2007 to 2020, with 77.1% of studies starting in 2017 or later with 74 (70.5%) originated in the US.

A majority of clinical trials were in phase 1 (53.3%) or phase 2 (25.7%). No trials were completed: 19 (18.1%) were active, 63 (60%) were recruiting, one (1%) was enrolling through invitation, and 22 (21%) were not yet recruiting.

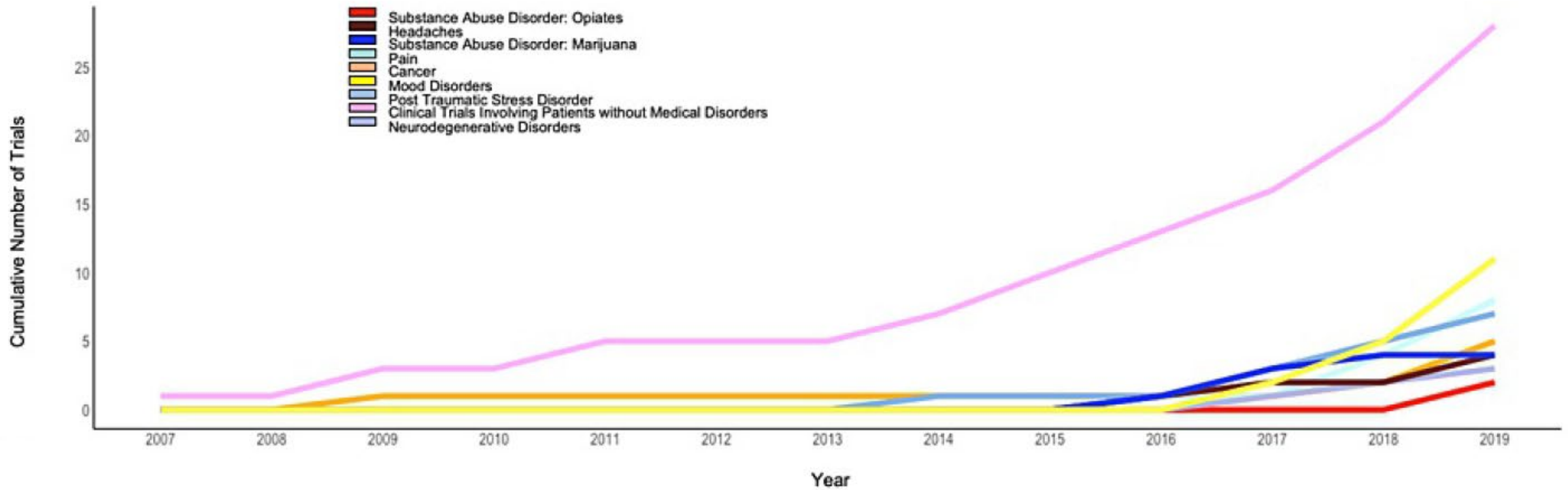
Limitations: only one US database was searched and opinions of patients could not be evaluated.

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Kurtz JS et al. *Cureus*. 2022;14(9):e29167. DOI 10.7759/cureus.29167.

Number of psychedelic clinical trials per treating condition

N=105 included in final analysis



Limitations: only one US database was searched and opinions of patients could not be evaluated.
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Kurtz JS et al. *Cureus*. 2022;14(9):e29167. DOI 10.7759/cureus.29167.

How do these potentially work?



Photo by [David Heslop](#) on [Unsplash](#)



Photo by [Fabrizio Conti](#) on [Unsplash](#)

How are they administered?

- Professionally supervised
 - Regime of Investigational drug with compound specific psychotherapy delivered by specially trained Therapists, w/ DEA schedule 1 License holder
- Can be a single or series of dosing sessions, with focus on preparation and integration
- Often includes set and setting
- Self-healing Intelligence

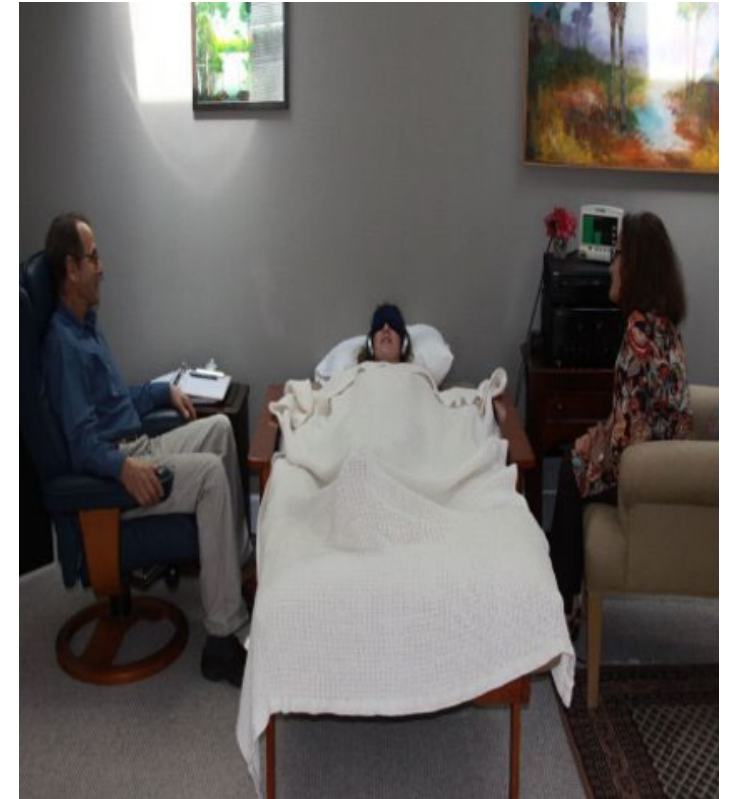


Photo by Hunter McRae, used with permission, Accessed online 21 January, 2023: <https://maps.org/2014/01/27/a-manual-for-mdma-assisted-therapy-in-the-treatment-of-ptsd/>

Thriving clinical investigations after decades of oppression
+

Promising published results ¹
+

FDA breakthrough designation for MDMA/ PTSD (2017) and Psilocybin/ Depression (2018)
+

Attractive financial potential (10.75 billion by 2027) ²
+

100s of pharma and other center/ companies in clinical investigations ³
+

Cultural shifts, drug reform ³

=

An exploding psychedelic industry

➤ Today, there is no current FDA approval of any psychedelic therapies

¹ Nichols DE. Psychedelics. *Pharmacol Rev.* 2016 Apr;68(2):264-355. doi: 10.1124/pr.115.011478. Erratum in: *Pharmacol Rev.* 2016 Apr;68(2):356. PMID: 26841800; PMCID: PMC4813425.; ² Phelps J, Shah RN, Lieberman JA. The Rapid Rise in Investment in Psychedelics—Cart Before the Horse. *JAMA Psychiatry.* 2022;79(3):189–190. doi:10.1001/jamapsychiatry.2021.3972 ³ [Psychedelics 2021: A Year in Review - Psychedelic Alpha](#);

- Continued search for how these compounds work
- How to maximize benefit and limit risk
- Dosing: micro, macro, concurrent meds, drug combinations
- Delivery methods: individual, group, clinic, remote
- Exploration in non-psychiatric populations
- Second generation of psychedelics, shorter acting/ non-hallucinogenic psychoplastogens

- Will there be changes to DEA scheduling?
- Will there be a billable pathway to third party payors?
- How will these therapies be integrated and scalable within healthcare settings, specifically mental healthcare delivery systems?
- How to focus on diversity, access and marginalized communities?



"Psychedelics, used responsibly and with proper caution, would be for psychiatry what the microscope is for biology and medicine or the telescope is for astronomy."

—Stanislav Grof, M.D., Ph.D.

MITIGATING RISKS AND PROTECT SUBJECTS

KELLY M WILLENBERG, DBA, RN, CHRC, CHC, CCRP





PSYCHEDELICS ARE INCREASING

- Research of psychedelic-assisted therapies is at a historical high (1), with 54% of the top-cited 100 psychedelic articles published in the last decade (2).
- (1) Doblin RE, Christiansen M, Jerome L, Burge B. The past and future of psychedelic science: an introduction to this issue. *J Psychoactive Drugs*. (2019) 51:93–7. doi: 10.1080/02791072.2019.1606472
- (2) Hadar A, David J, Shalit N, Roseman L, Gross R, Sessa B, et al. The psychedelic renaissance in clinical research: a bibliometric analysis of three decades of human studies with psychedelics. *J Psychoactive Drugs*. (2022) 10–17. doi: 10.1080/02791072.2021.2022254



INHERENT RISK IN PSYCHEDELICS

- Possible non-compliance with regulatory requirements
- Transparent documentation
- Social perceptions
- High expectations
- Economic issues
- Bias



PSYCHEDELICS MAY BE REPRESENT A PARADIGM SHIFT

- Recognizing that mental health therapies are needed
- Ensuring transparency with patients
- Outlining proper informed consent must be given
- Defining patient safety and comfort as primary goal



ROLE OF PSYCHEDELIC DRUGS IN THE FUTURE

- “Crucial for future practice and research in the field are (1) informed patient referral and co-treatment practices, (2) screening (e. g., choosing the right patients for these therapies), (3) the dosing preparation sessions, (4) the assisted dosing sessions as well as after-care procedures such as (5) psychological integration and (6) supporting the development of structured patient communities.”
- Gründer G, Jungaberle H. The Potential Role of Psychedelic Drugs in Mental Health Care of the Future. *Pharmacopsychiatry*. 2021 Jul;54(4):191-199. doi: 10.1055/a-1486-7386. Epub 2021 May 12. PMID: 33979868.



COMPLIANCE AND RISK TIE TOGETHER FOR ALL TRIALS

1. Risk Assessment
2. Monitoring and Auditing
3. Compliance Work Plans
4. Measuring & Reporting



CONTACT

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COGR

An Association of Research Institutions

Research Using Psychedelics: Legal & Ethical Issues

Kris West, J.D., M.S.
Director, Research Ethics &
Compliance

Overview

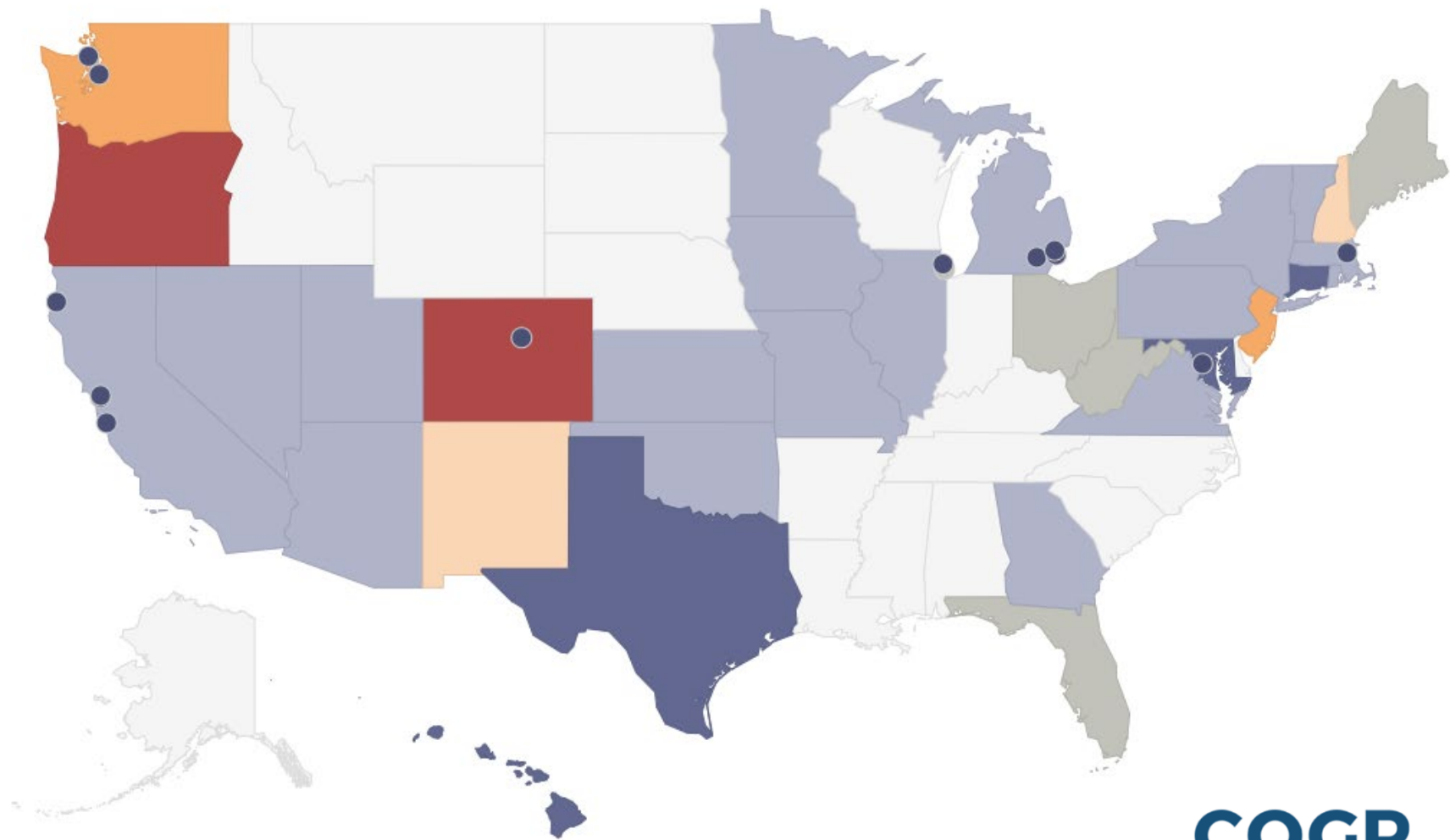
- Types of Drugs
- State v. Federal Laws
- Federal Legislation in the Works
- Current Requirements for Conduct of Research
- Mitigating Risk

Types of Drugs: Dissociative & Hallucinogenic

Drug	Street Name	Research Uses	DEA Schedule
Psilocybin	Magic Mushrooms	Addiction, PTSD, depression, suicide prevention, epilepsy, intractable pain	Schedule I
MDMA	Ecstasy, Molly	Anxiety disorders, PTSD, eating disorders	Schedule I
LSD	Acid	Depression, PTSD, drug dependency, anxiety	Schedule I
Dimethyltryptamine (DMT)	Dimitri	Depression, anxiety, PTSD	Schedule I
Ibogaine	Not use recreationally	Extinguishing addiction	Schedule I
Mescaline	Buttons, Peyote, Cactus	Depression, PTSD, anxiety	Schedule I

Psilocybin

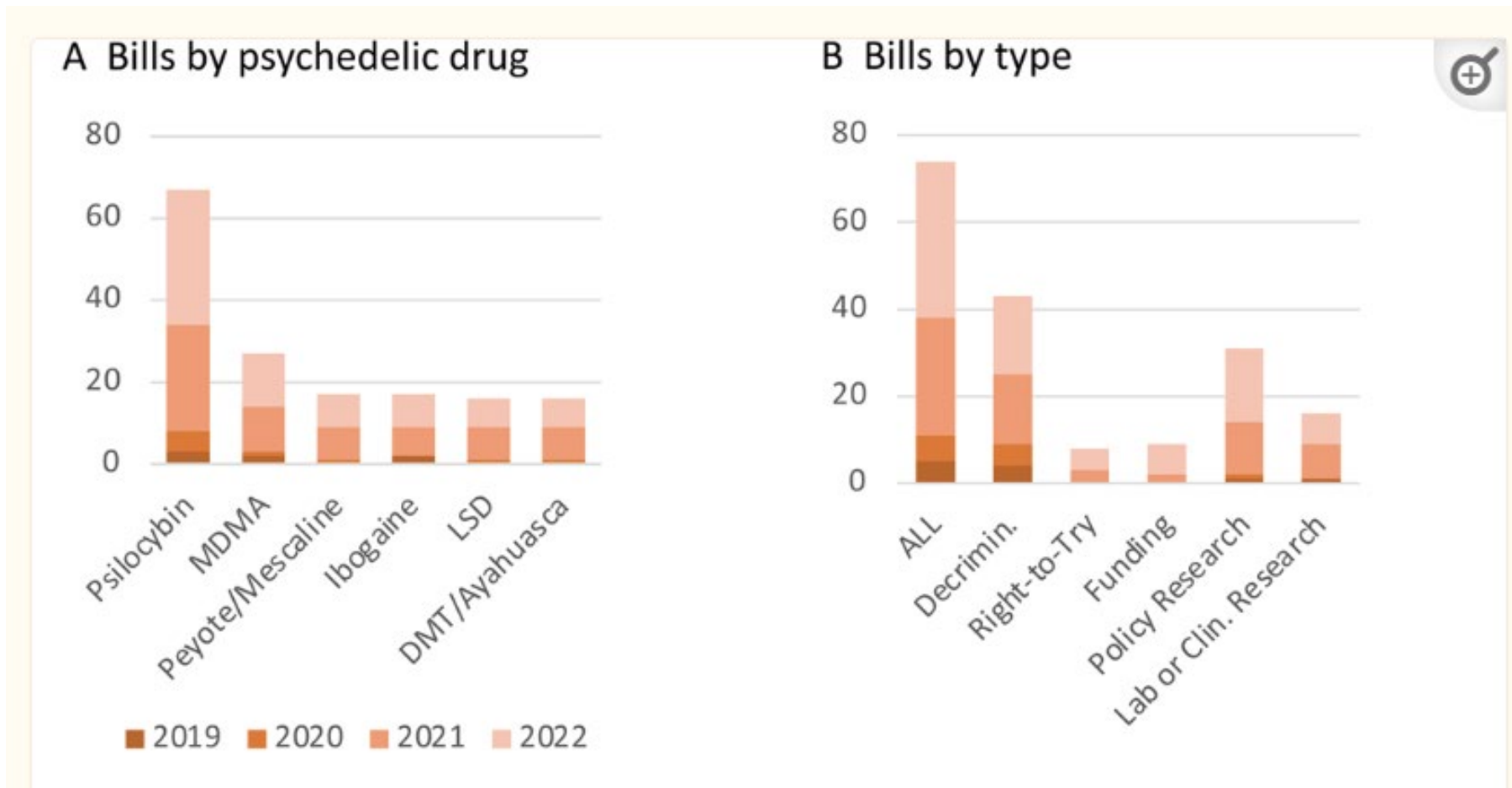
- Legalization & Regulation Statute
- Decriminalization Statute
- Reduced Penalty Statute
- Limited Judicial Exceptions
- Working Group to Study Medical Use
- Active Legislation
- Inactive or Failed Legislation
- Local Government Reforms



And some
municipalities
have separate
laws . . .

- Psilocybin decriminalized in
 - Seattle, WA
 - Ann Arbor, Detroit, & Hazel Park, MI
 - Cambridge, East Hampton, North Hampton & Sommerville, MA

Types of Federal & State Legislation in the Works



Siegel JS, Daily JE, Perry DA, Nicol GE. Psychedelic Drug Legislative Reform and Legalization in the US. JAMA Psychiatry. 2023 Jan 1;80(1):77-83. doi: 10.1001/jamapsychiatry.2022.4101. PMID: 36477830; PMCID: PMC10069558.

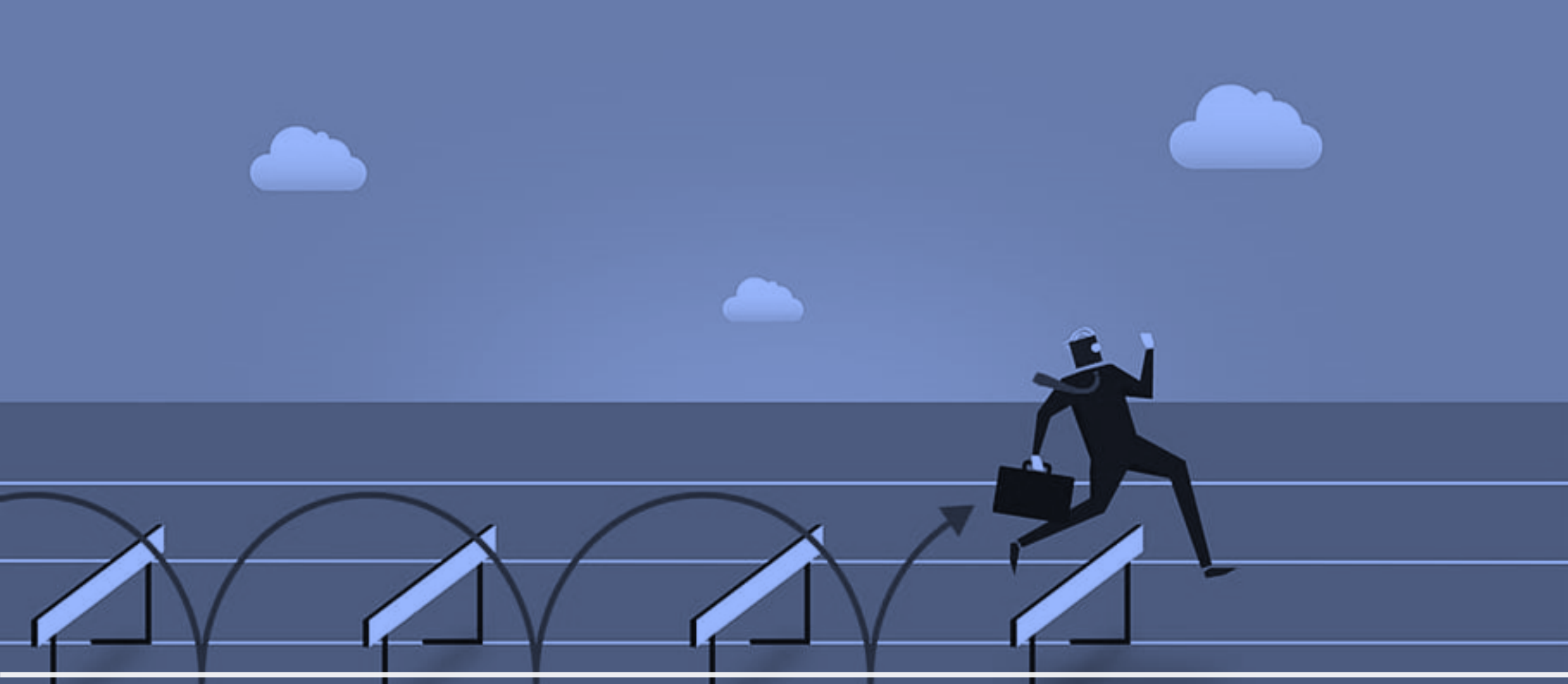
Federal Legislation 2023

Right to Try Clarification Act – Introduced as a bill in the House.

- Terminally ill patients would have access to Schedule I controlled substances that have undergone Phase I studies.

Breakthrough Therapies Act – Introduced as a bill in the House and Senate.

- Expedite reclassification of drugs from Schedule I to Schedule II once they receive breakthrough therapy designation from FDA



Requirements for Conducting Research Using Schedule I Controlled Substance:
So many Hurdles!

Requirements for Conducting Clinical Trials with Schedule I Controlled Substances

FDA

- Compliance with DEA requirements
- IND
 - Chemistry, manufacturing and control information
 - Animal pharmacology & toxicology studies
 - Clinical protocol
 - Investigator information

DEA

- State registration and inspection, if required in state where study is located
- DEA registration
 - Protocol
 - Investigator qualifications
 - Security
 - Inspection

What if your state permits the research?

- Concerns remain for academic research institutions that accept federal funding.
 - Drug Free Schools and Communities Act
 - NIH Grants Policy Statement – clinical trials using controlled substances must comply with all DEA requirements
 - Drug Free Workplace Act

Mitigating Risks



Legal/Ethical Issues to Consider

- Particular vulnerabilities of subjects
 - Under age 21.
 - Past drug use?
 - Persons who have children or may become pregnant?
- Confidentiality
 - Certificates of confidentiality
 - Potential criminal liability
- Impact on employment/school attendance/sports participation
 - Random drug testing
- Institutional concerns
 - Are students being recruited?
- Addressing these issues in the informed consent process