

Altered Stakes: Identifying Gaps in the Psychedelic-Assisted Therapy Research
Informed Consent Process
by

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Program in Bioethics and Science Policy
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Date: June 20, 2022

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Thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Arts in the Program in Bioethics and Science Policy in the Graduate School
of Duke University

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ABSTRACT

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Abstract

Nearly 60% of the US population experiencing posttraumatic stress disorder have not received a meaningful clinical response from traditional interventions (Akiki & Abdallah, 2018). Early research using psychedelics in tandem with psychotherapy may offer a more effective option (Feduccia et al., 2019) and has been shown to provide or contribute to long-term relief or remission from PTSD symptoms (in small samples). Funding for psychedelic-assisted therapy (P-AT) clinical trials has increased to hundreds of billions of dollars since 2018 (Phelps et al., 2022) (Rivlin & Sharpe, 2021) and while the research is propitious, it is far from complete. Concerns about safety and generalizability have begun to surface (Love, 2022), including recent allegations of abuse (Goldhill, 2020). Though abuse is a serious issue within all clinical practice, the risk is amplified by the altered states of consciousness experienced in high-dose P-AT trials. In the US, treatment models using mind-altering substances are shaped by the requirements of FDA-approved clinical research trials, which in turn define ethical practices and standards of care. By examining how existing regulations inform governance for the informed consent (IC) process and reviewing publicly available documents from P-AT trials, I aim to: 1) illuminate how risk and accountability are currently communicated to P-AT participants; and 2) suggest how existing research policy might be updated to

make working with trauma patients under altered states of consciousness safer and more ethically robust.

Dedication

There is no page long enough to express my gratitude so this will be kept short. Thank you to my advisor Misha Angrist and committee member Thomas Williams for your continued support and belief in my abilities, and to committee member Sarah Rispin for your guidance. Thank you also to all at Duke's Initiative for Science and Society with an extra thank you to Buz Waitzkin and Esko Brummel for helping coordinate this process. Finally, I am grateful to all my loved ones for patiently loving me while in this writing tunnel.

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Disclosures

During this thesis process, the author accepted a position at the University of Ottawa's Experimental Psychology PhD program under the tutelage of Dr. Monnica Williams; there are pieces of her research cited here. The author has been contracted by Synaptic Training Institute to organize and teach sections of the ethics curriculum in their Entheogenic Medicine Training Program, a program currently undergoing review by the Oregon Health Authority to train psilocybin facilitators who will offer psilocybin services made legal under Oregon Measure 109 beginning in January 2023. The author holds a Master's degree in Marriage, Couple, and Family Therapy from Lewis and Clark Graduate School of Counseling, whose program is rooted in social justice and equity principles and is a Marriage and Family Therapy Associate (#R7376) under the Board of Licensed Professional Counselors and Therapists in the State of Oregon. She is actively practicing as a part-time therapist as part of her virtual teletherapy private practice Retune Space, LLC. The author, though not actively practicing, is also a licensed massage therapist and maintains a license through the Oregon Board of Massage Therapy (#13861).

1. Introduction

Psychedelic-assisted therapy (P-AT) research trials for the treatment of varying psychiatric diagnoses have entered mainstream media consciousness with narratives espousing this treatment as offering new hope for mitigating the mental health care crisis (Piore, 2021). While psychedelic research has a history in Western medical science since the 1940s, the recent research resurgence has seen an unprecedented amount of funding and media attention; widespread use of psychedelic-assisted therapy in clinical practice appears to be imminent.

The last five years have been particularly fruitful in the way of scientific research advances, increased public interest, regulatory changes, and funding (Aday et al., 2019). Special issues on psychedelics have been published in prestigious journals like *Neuropsychopharmacology*; the National Institute of Mental Health in cooperation with the National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism hosted a two-day workshop on “Psychedelics as Therapeutics” (2022); entrepreneur Tim Ferris publicly committed to investment in the world’s first psychedelic research center at Imperial College London (Brodwin, 2019) (Aday et al., 2019); and the NIH funded its first psychedelic research study in fifty years to Johns Hopkins University (Martinez, 2021). Prior to the NIH grant, private funding (between 2018 – 2019) saw around \$60 million in investment in psychedelic-focused companies;

that figure grew ten-fold by 2020 and investment in psychedelic research is soon expected to exceed \$2 billion globally (Rivlin & Sharpe, 2021).

Meanwhile, regulatory approaches to P-AT have been happening concurrently as evidenced by FDA granting breakthrough therapy designation for MDMA-assisted psychotherapy to treat PTSD in 2017 (Feduccia et al., 2019) and psilocybin-assisted therapy for treatment-resistant depression in 2018 (Aday et al., 2019). Both MDMA and psilocybin are drugs that remain classified as Schedule I by the U.S. Drug Enforcement Administration (DEA), i.e., as substances defined as having “no currently accepted medical use and a high potential for abuse” (dea.gov), which has been proven to be an inaccurate characterization of both drugs (Nichols, 2016) (Marks, 2021). In any case, the reality on the ground is overtaking that of the DEA: various state laws targeting the decriminalization of psychedelics are on the ballot or already approved (Aday et al., 2019), while in 2020 the state of Oregon voted both to decriminalize psychedelics and legalize “psilocybin services” under Oregon Ballot Measure 109, thereby allowing for legal access to experiencing psilocybin in an approved “service center” by a trained “psilocybin facilitator” (*Oregon Psilocybin Services Act*, 2019).

Since Michael Pollan’s book *How to Change Your Mind: What the New Science of Psychedelics Teaches us About Consciousness, Dying, Addiction, Depression and Transcendence* was published in 2018, major media outlets have continued making claims like *Time*

Magazine's "This will change your mind about psychedelic drugs" (Oaklander, 2018), *Newsweek's* "Magic Mushrooms May Be the Biggest Advance in Treating Depression Since Prozac" (Piore, 2021), and the *New York Times's* "The Psychedelic Revolution is Coming. Psychiatry May Never Be the Same" (Jacobs, 2021). Less publicized are the ethical and scientific concerns around implementing a truly double-blind study, suggestibility in altered states of consciousness and the potential for bad outcomes, risks of abuse, and lack of ethnoracial representation that might limit the generalizability of findings (Grau et al., 2022). Though the US has long had regulations for the protection of human subjects that many regard as overly stringent (Schneider, 2015) (Klitzman, 2015), not all P-AT clinical trial participants have been immune from harm. Allegations of therapist abuse of power have been reported both in underground (community-regulated) and above-ground (conventional clinical trials) settings that use psychedelics for the treatment of trauma (Psymposia, 2022). While harmful abuses of power in the therapeutic relationship between patient and therapist have occurred within all treatment disciplines, the altered states of consciousness experienced in high-dose P-AT trials amplify risk by placing already-traumatized patients in an even more vulnerable position.

In the US, FDA-approved clinical research trials shape treatment models, guide the ethical practice and standards of care, and set precedents for the ways risk is

communicated and accountability is implemented. The first P-AT treatment close to becoming approved by FDA (in Phase III as of June 2022) is the use of 3,4-methylenedioxyamphetamine (MDMA) as a catalyst alongside psychotherapy for post-traumatic stress disorder (PTSD), which is a common manifestation of sexual abuse (Scott et al., 2017) and a diagnosis that has a disproportionate impact on people of color (Roberts et al., 2010) and LGBTQIA2S+ communities (Livingston et al., 2020). PTSD's connection to sexual abuse makes the safety of P-AT trials even more fraught while the lack of representation diminishes the prospect of generalizability.

Further, racial trauma (or race-based traumatic stress [RBTS]), an unrecognized diagnosis in *The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [DSM-V]*) is often comorbid in c-PTSD¹ and PTSD participant populations in the BIPOC community who have experienced prolonged racism (Williams et al., 2021). The concerning lack of ethnoracial representation in psychedelic-assisted therapy PTSD clinical trials (Smith et al., 2022) impairs mental health practitioners' ability to offer culturally sensitive, evidence-based P-AT PTSD treatment and inhibits the detection of cross-cultural differences in treatment response (Fogg et al., 2021). In a methodological

¹ c-PTSD, abbreviation for complex PTSD. c-PTSD is characterized by experiencing chronic trauma that continues to repeat for months to years at a time. Consideration of the characteristics of c-PTSD as a new diagnosis was suggested by Dr. Judith Herman of Harvard with many others concurring that the traditional PTSD diagnosis does not fully capture the severity of psychological harm and associated symptoms including behavioral, emotional, cognitive, interpersonal, difficulties and somatization. (ptsd.va.gov)

search of psychedelic studies from 1993 - 2017 entitled "Inclusion of people of color in psychedelic-assisted psychotherapy: a review of the literature," Michaels et. al. found that in the 18 studies meeting their criteria (n = 282 participants), 82.3% of participants were non-Hispanic White (Michaels et al., 2018); the remaining breakdown included 2.5% African American, 2.1% of Latino origin, 1.8% Asian origin, 4.6% Indigenous origin, 4.6% mixed race, 1.8% identifying as "other," and 8.2% of participants were of unknown ethnicity (Michaels et al., 2018).

Alongside the growing resurgence of psychedelic medicine for the treatment of mental health disorders is growing distress around repeating and perpetuating harmful practices within research and clinical practice. If researchers are to begin explicitly including larger numbers of participants in P-AT trials, particularly non-White and other marginalized participants, the trialists themselves must be equally diligent in ensuring the emotional and physical safety of those populations whose experience of safety is influenced by anticipatory stigma and other threats to psychological well-being (Kruk & Matsick, 2021). To create safe environments for those who experience a devalued social identity in the U.S., it must be acknowledged that participants in those populations are at higher risk of harms like discrimination (Diop et al., 2021) than their

White² counterparts (whom are most widely represented in scientific research).

Meanwhile, issues like discrimination remain largely unaddressed in the informed consent (IC) process (Gehlert & Mozersky, 2018).

The answer to ensuring safety within clinical trials involving human beings is often believed to lie within the process of IRB (institutional review board) approval and detailed informed consent documents for participants. No research using humans can be done legally in the U.S. without being monitored and approved by the IRB (Schneider, 2015). Each institution or organization appoints its own IRB from its own faculty, clinicians, and staff as well as the local community. IRBs are required to have more than four members, at least one may not be an employee of the institution, at least one's primary area of expertise must be scientific, and one must be nonscientific (Schneider, 2015). Members of IRB committees should have enough expertise related to the investigation carried out by the trial to consider the breadth of unique ethical considerations related to it. Though "more consent" in principle may seem wise,

² There are several arguments for/against the formatting choice to capitalize or not capitalize racial categories. After deliberation, I chose to follow a statement made by two nonwhite staff members at the Center for the Study of Social Policy, in a statement by two non-white staff members announcing that it would follow the American Psychological Association's style rules further stating "To not name 'White' as a race is, in fact, an anti-Black act which frames Whiteness as both neutral and the standard ... We believe that it is important to call attention to White as a race as a way to understand and give voice to how Whiteness functions in our social and political institutions and our communities. Moreover, the detachment of 'White' as a proper noun allows White people to sit out of conversations about race and removes accountability from White people's and White institutions' involvement in racism." (Appiah, 2021) (Nguyễn & Pendleton, 2021)

mounting evidence suggests that there is a great distance between the ideal of consent and its actual practice (Henderson, 2011). One possible contributor to this distance is that individual autonomy and personal control have been the cornerstone of American bioethics, yet these principles are often disconnected from the reality of human decision-making (Held, 2007).

Our regulations in the U.S. for human subjects research were not created by those thinking about studies of consciousness-altering substances and the power dynamics that underscore therapeutic relationships and their corresponding clinical interventions. The altered states of consciousness associated with P-AT create increased vulnerability in participants that enter a trial already psychologically vulnerable from their existing symptoms. Therapists like myself, and I know I'm not alone, feel an ethical responsibility to protect our clients/patients from ethical violations, a protection that must be extended when working as a clinician in a research setting. We do not yet have consensus around standards of care and best practice in P-AT research, leaving researchers and associated clinicians working in P-AT trials continually concerned about the psychological safety of participants and which ethical and policy standards are governing our clinical practices as therapists working with psychedelics. With no current unified ethical guidelines or independent ethical review of research practices beyond traditional IRB structures (again, which were not designed with P-AT in mind),

the initial review for research protocols involving P-AT and the associated accountability processes for ethical violations continue to be ambiguous (Zohny, 2021).

Calls to consider more relational frameworks, like care ethics, as part of human subjects research and clinical practice have been emerging in conversations related to P-AT practice, which may in turn positively influence the consent process. Care ethics views humans as moral agents not solely in terms of independence, equality of power, and unrestricted freedom to enter and dissolve contracts, but as agents who are mutually interconnected, vulnerable, and dependent, often in asymmetric ways (Pettersen, 2011). Care ethics values our relationships and relational systems as fundamental to reckoning with bioethical problems (Lindemann et al., 2009). Further, care ethics acknowledges that almost all medical care is *necessary* care. Many who enter P-AT trials have had unsuccessful results with traditional treatments; thus, they view their participation as not just a matter of contentment or flourishing, but of necessity and survival. Additionally, care ethics recognizes the inherent power imbalance that exists between providers/researchers and care receivers and requires that attention be paid to the moral contours of the therapy process (Lindemann et al., 2009). It is through the ethics of care, and trauma-informed, culturally responsive clinical practice models that the consent process may be improved to increase trust and safety for future trial

participants. Care ethics provides a useful framework for reforming existing governance and conduct of P-AT research and clinical practice.

The egregious amount of exploitation and abuse that one finds in psychedelic research's history up to now and the associated safety issues (despite having established codes for the protection of human participants) are what prompted this review looking at informed consent (IC) documents to understand how P-AT trials are reckoning with the characteristics unique to using high-dose psychedelics in a therapeutic setting and are considering ethical issues risks of harm involving things like therapeutic touch, altered states of consciousness, patient vulnerability, and potential for sexual misconduct. Most recently, allegations of sexual abuse against practitioners involved in the Phase II methylenedioxymethamphetamine (MDMA)-assisted therapy trials sponsored by the Multidisciplinary Association of Psychedelic Studies (MAPS) (Goldhill, 2020) have amplified concerns across the P-AT research community (*Addressing abuse and repair: An open letter to the psychedelic community*, 2022) and further demonstrate the importance of continual review and examination of psychedelic research protocols and the specifics of the informed consent process.

2. Historical Abuse in Psychedelic Research

The history of vulnerable populations being harmed in psychedelic research is as old as such research itself; many of these past transgressions remain hidden in current narratives (Belser, 2020). Some researchers suggest that ethnicity, cultural norms, and stigmatization around psychedelics have hindered self-disclosure and help-seeking by those afflicted (Belouin & Henningfield, 2018) and believe it may be possible that more abuse is out there than has been reported. We must bring awareness to past abuse in order to recognize and prevent future abuse, create accountability frameworks in the event of abuse, and maximize support for participants who experience abuse during clinical trials.

2.1 First Wave

Though plants and plant-derived substances that produce psychedelic effects (including psilocybin³, cannabis⁴, and ayahuasca⁵) have been used in ceremonial healing and for pleasure for millennia (Hoffman, 1980; Multidisciplinary Association for Psychedelic Studies, 2007; Nichols, 2004; Strassman, 1995), the modern era of

³ Hallucinogenic chemical that may be obtained from certain types of fresh and dried mushrooms. Street names: magic mushrooms, shrooms, mushrooms. (dea.gov)

⁴ Mind-altering (psychoactive) drug derived from the plant *Cannabis sativa*, THC (delta-9-tetrahydrocannabinol) is believed to be the main component producing psychoactive effects. Street names: marijuana, bud, pot, ash, weed, ganja) (dea.gov)

⁵ Tea made from DMT (N, N-dimethyltryptamine) found naturally in some Amazonian plants known to alter awareness, thoughts, and feelings. (nih.gov)

psychedelic research was launched by Albert Hoffman's⁶ discovery of lysergic acid diethyl amide (LSD) in 1938. It was not until Hoffman self-experimented with the substance in 1943 that LSD's potential to alter mood and cognition was realized and prompted research into its potential effects for treatment of mental and behavioral disorders, and as a possible tool for espionage and warfare (Belouin & Henningfield, 2018). During this first wave of psychedelic research in the US between 1943 and 1980, over 1000 scientific articles were published on psychedelic medicine and several international conferences were held (Strauss et al., 2021), yet many first-wave investigations have been found to include accounts of questionable research methods, abuses against research participants, and covert Central Intelligence Agency financial involvement (Strauss et al., 2021). These research abuses were ultimately not what halted psychedelic research trials; rather, it was the Controlled Substances Act of 1970, which effectively criminalized them. As a result, psychedelic clinical research did not fully re-emerge until the 1990s (Strauss et al., 2021).

2.1.1 Ethical Violations and the Emergence of Regulation

The covert CIA project code-named MKUltra (formally established in 1953) recruited 1600 German physicians and scientists to develop technologies for use against

⁶ Albert Hoffman worked as a chemist for Sandoz pharmaceutical company. The Federal Food, Drug, and Cosmetic Act (Federal FD&C Act) of 1938 permitted Sandoz to distribute LSD samples for investigational research under the name "Delysid." (Belouin & Henningfield, 2018)

the Soviets in the Cold War; MKUltra included projects focused on mind-control, 'brainwashing,' and the use of LSD as a 'truth serum' for interrogating spies (Strauss et al., 2021). Part of this team included fifteen dedicated Nazis, six of whom had stood trial at Nuremberg in 1946-1947 for conducting medical experiments on thousands of concentration camp prisoners without their consent (Kelley, 2014) (Strauss et al., 2021). In response to the human rights violations uncovered in the Nuremberg trials, the *Nuremberg Code* was established in 1947, which stated that "[T]he voluntary consent of the human subject is absolutely essential" (Shuster, 1997) (Steneck, 2004), thus making consent an explicit and fundamental moral principle without which human subjects research could not ethically proceed. Prior to *Nuremberg*, the implementation of ethical research practices and accountability structures in the United States was the responsibility of the principal investigator to create; no mandates to obtain participant consent prior were in existence (Barrow et al., 2021). However, there is research that indicates that ethical issues and informed consent in guidelines for human experimentation were recognized as early as the nineteenth century (Vollmann & Winau, 1996). Yet *Nuremberg* remains regarded as the first international document to advocate for voluntary participation and informed consent, though it was not a policy carrying any force of law and did not prevent the abuse endured by the participants

exploited in the MKUltra trials (to say nothing of dozens of other post-War experiments) (Beecher, 1966).

Many early psychedelic research studies (including those funded by the MKUltra program) disregarded ethical guidelines agreed on by the US government after *Nuremberg* (Strauss et al., 2021). In a study published in *Social History of Medicine* (Campbell & Stark, 2015), scholars examined recent archival documents that included public testimony, interviews, and oral histories from participants in the early LSD studies at the U.S. NIMH's Addiction Research Center and the NIH Clinical Center (NIHCC); at the addiction center it was found that Black prisoners with substance use issues were "routinely harmfully exploited in these LSD studies" (Strauss et al., 2021). Strauss et. al. reviewed available empirical research publications to understand how variables like race and ethnicity of participants, population vulnerability, drug administration conditions, informed consent (or lack thereof), and undue influence impacted people of color and other vulnerable populations in psychedelic research and found that many of the first-wave psychedelic studies would not have passed ethical review today. Ethical violations included problematic dosing, questionable scientific

merit, unsafe set and setting⁷ for participants, and lack of informed consent given by participants (Strauss et al., 2021).

MKUltra's status as a CIA-sponsored research program was not revealed to the public until 1977 by Admiral Stansfield Turner (the CIA director at the time) in a hearing held by the U.S. Senate Select Committee on Intelligence. Later investigation revealed that over 80 institutions (including universities and hospitals) were provided with MKUltra CIA funds (some unknowingly)⁸ to conduct this experimental research with LSD on civilians, prisoners, and patients (Strauss et al., 2021). Many records were destroyed by Richard Helms (CIA director from 1966-1973)⁹, but enough remained for examination in multiple hearings by the Senate (Strauss et al., 2021).

These egregious ethical violations were not only perpetrated post-*Nuremberg*, but also after the adoption of *The Declaration of Helsinki* by the World Medical Association in 1964. The conduct of biomedical research involving human subjects was further addressed by *Helsinki*, which established recommendations to guide clinical research in

⁷ Set and setting is terminology used commonly in the psychedelic community to convey that the internal conditions or the "Set" of the participant (e.g., intentions, personality, preparedness) and external conditions or "Setting" (physical and social environment), may influence the outcome of the participant's experience. (Strauss et. al. 2021) This concept is well established by Indigenous cultures practicing psychedelic healing. (Neitzke-Spruill, 2019)

⁸ Stated in the 1977 Committee on Intelligence hearing; "Second, there are two boxes of miscellaneous MKUltra papers including audit reports and financial statements from "cut-out" (i.e., intermediary) funding mechanisms used to conceal CIA's sponsorship of various research projects." (*Project MKULTRA, The Cia's Program of Research in Behavioral Modification*, 1977)

⁹ Richard Helms served as Director of Central Intelligence from 1966 – 1973.

particular. This declaration provided foundational material for best clinical practices, including the notions that informed consent is essential; that individuals must be capable of giving informed consent; and that they must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, anticipated benefits, potential risks and discomforts, right of refusal, and that “special attention should be given to the specific information needs of individual potential subjects as well as to the methods to deliver the information” (*World Medical Association Declaration of Helsinki*, 2013). *Helsinki* additionally states explicitly that research goals should never take precedence over the well-being of research participants; subsequent revisions stated that protection must be offered to those who are vulnerable and that those groups must benefit from the resulting knowledge and interventions flowing from the research itself (Strauss et al., 2021).

Nuremberg and *Helsinki* may have provided protective guidelines for clinical trial participants, but as mentioned, these seminal documents did not provide actionable governance to prevent the events of MKUltra, nor did they prevent other research scandals and abuses. Most egregiously, the 40-year Tuskegee Syphilis Study¹⁰ shocked

¹⁰ The Tuskegee Syphilis Study, beginning in 1932, monitored 600 low-income African American males, 400 of whom had syphilis, without their consent. Subjects of Tuskegee were given free medical exams, but their health status was withheld, and treatment was denied them even after the availability of curative penicillin in the 1940s (Alsan & Wanamaker, 2017). Further, when some participants were diagnosed with syphilis by

the American conscience. Only after the publicity and political embarrassment around Tuskegee was the study stopped (in 1973) by the U.S. Department of Health, Education, and Welfare (Alsan & Wanamaker, 2017) and processes to create federal policy for and strict governance of the protection of human research subjects in the US were initiated. The National Research Act (1974) led to the creation of the Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Steneck, 2004). The goal of the commission was to identify the basic ethical principles and guidelines that should govern research; its deliberations resulted in *The Belmont Report* (1979)¹¹ (Steneck, 2004). *Belmont* has provided the philosophical backbone of clinical research governance in the US since its publication (Barrow et al., 2021); it identified respect for persons, beneficence, and justice as the three key ethical principles and outlined their corresponding applications. Informed consent lies underneath the principle of respect for persons, i.e., the idea that individuals should be treated as autonomous agents and that persons with diminished autonomy are entitled to protection (*The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, 1979). In theory, informed consent ensures that participants, to the degree that they are capable,

other physicians, researchers intervened to prevent their treatment. Participants were monitored and subjected to these crimes for 40 years, more than 100 subjects died,

¹¹ *The Belmont Report* was issued in 1978 but not published in the federal register until 1979.

will be given the opportunity to choose whether to participate in consideration of the information they are given about risks and benefits of the research at hand. *Belmont* also mandates three elements in the consent process: information, comprehension, and voluntariness, along with the nature and scope of risks and benefits to be assessed in a systematic manner (*The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, 1978).

Other first-wave ethical violations included the use of psychedelic substances to “correct” the behaviors of the LGBTQIA2S+ community. Lead investigators in the first-wave psychedelic movement perpetuated profoundly harmful homophobic narratives (Belser, 2020). Timothy Leary infamously said, “The fact is that LSD is a specific cure to homosexuality,” while Ram Dass¹² claimed that LSD treatments helped a “homosexual” patient remain in a long-term heterosexual relationship (Belser, 2020). For historical context, “homosexuality” was considered a disordered pathology until it was removed from the *DSM* (Diagnostic Statistical Manual of Mental Disorders) in 1973. In the 1960s some were using psychedelics as part of “conversion therapy” to “treat lesbian gay, bisexual, transgender, and queer people to become cisgender heterosexuals” (Belser, 2020). Conversion therapy today has been condemned by multiple professional

¹² Former Harvard Professor under former name Richard Alpert and colleague of Timothy Leary; both men performed research examining LSD. Alpert is the author of *Be Here Now* (As Ram Dass, 1971), an influential publication centered around spirituality, yoga and meditation.

organizations, including the American Psychological Association, the American Medical Association, the National Association of Social Workers, and the American College of Physicians (Belser, 2020). Conversion therapy is highly unethical, causing psychiatric harms, high risk of suicidality, social withdrawal, and substance use disorders among many other symptoms for those who undergo “treatment.” The psychedelic research community has engaged in little discourse around this problematic past, which could be used as a meaningful steppingstone to examine how problematic heteronormative discourses present themselves in the current research paradigm (Belser, 2020).

Understanding research injustice during the first wave of psychedelic research requires understanding the position of that research within a historical context (Strauss et al., 2021). Research abuse in the first wave, like many of the abuses of Tuskegee, occurred contemporaneously with or after *Nuremberg* (1947) and *Helsinki* (1964); however, it must be noted that public awareness regarding mental health and ethical standards of research did not look the same as they do today. Further, many of these studies occurred prior to the civil rights movement in the US, with many taking place in the White majority South where equal rights for people of color were continually threatened (Strauss et al., 2021). It wasn’t until *Belmont* in 1979 that the concept of ‘vulnerable’ populations (largely inspired by the civil rights movement) was even brought forth (Strauss et al., 2021). Without the language and understanding of

vulnerable populations, researchers did not prioritize protection of such populations. Though *Belmont* was an upgrade by providing a framework outlining what constitutes ethical research, its basic approach to ethical conduct and approval of investigational drugs was also, as famously stated by Carol Levine, “born in scandal and reared in protectionism” (Levine, 1988). *Belmont*, being a product of its time, may no longer be sufficiently responsive to the ethical demands of the research enterprise (Schupmann & Moreno, 2020), especially as it relates to clinical P-AT trials.

2.2 Second Wave

The revival of research for the therapeutic use of psychedelics was largely spearheaded by MAPS, which was founded in 1986. As mentioned, the lull in research between the 1970s and 1980s was a result of the Controlled Substances Act, which sorted substances into a five-tiered list according to their perceived potential for abuse and was signed into law by President Richard Nixon in 1970 (Marks, 2021). Nixon further proclaimed Timothy Leary to be “the most dangerous man in America.” This characterization of Leary by Nixon and the illegalization of psychedelics were thought to be motivated by their role in the widespread cultural upheavals of the 1960s deemed undesirable by Nixon and his allies (Bell et al., 2017). Nixon’s “War on Drugs” campaign (1971) was meant in part to stigmatize anti-Vietnam war protesters and left-leaning young people (especially) minorities, by conflating them and their activities with newly

designated illegal drugs (Smith et al., 2022). In 2016, John Ehrlichman, former White House counsel and Chief Domestic Advisor under Nixon admitted, “We knew we couldn’t make it illegal to be either against the war or Black, but by getting the public to associate hippies with marijuana and Blacks with heroin, and then criminalizing both heavily, we could disrupt those communities... Did we know we were lying about the drugs? Of course, we did” (Baum, 2016) (Smith et al., 2022). The repercussions of the Nixon administration’s federal drug policy led to disproportionate arrests and incarceration of Black and Latino men for the transgression of experimenting with psychedelics and other potentially healing substances (Smith et al., 2022). As schedule I drugs psychedelics were deemed to have “no currently accepted medical use,” “a lack of accepted safety” for supervised use, and a “high potential for abuse” (dea.gov) (Marks, 2021). Consequently, P-AT research has had a five-decade uphill climb to legitimacy (Marks, 2021).

Psychedelic research is now a high-profile media staple, with many referring to this second wave as the “psychedelic renaissance” (Lu, 2021). While recent data have not been released, an exploratory analysis by Aday et. al. investigated public interest in the term “psychedelics” using Google Trends; the study reported significant usage increases between 2004 and 2018 with the most significant increase between 2017 and 2018. This increase coincides with the publication of *How to Change Your Mind* by Michael Pollan,

and the concomitant increase in the number of research publications coming out of major institutions (beginning with Johns Hopkins University circa 2007). In order to build and sustain this momentum in the second phase of psychedelic investigations, researchers and clinicians were (and are) also hoping to avoid the past abuses of the first wave.

The second wave, however, has already had its own ethical lapses. In the early 1980s two therapists, Rick Ingrasci and Francesco DiLeo, were sued resulting in DiLeo losing his license and Ingrasci's license resignation after administering MDMA to their patients, ostensibly to support them in overcoming "therapeutic blockages" (Passie, 2018). In the process, Ingrasci and DiLeo initiated intimate body contact, sexual touch, and intercourse during their MDMA sessions (Passie, 2018). How did this happen? In the case of Ingrasci, several accusations came forward including statements that Ingrasci had administered MDMA or ketamine to female patients and had assaulted them through inserting his hand in their vaginas (Hausfeld, 2021). One woman who began counseling with Ingrasci after learning of her cancer diagnosis was told that sexual contact could help heal her ailments, and another was reported by Boston Globe journalist Alison Brass to have attempted suicide after terminating sessions with Ingrasci. Two other women reported to Brass that they were emotionally devastated by their experiences with Ingrasci (Hausfeld, 2021). In the case of one of DiLeo's patients, "a

therapeutic impasse” had been reached, and the patient was “unable to verbalize feelings she had for her therapist.” DiLeo, in response, asked the patient if she felt an MDMA session would be beneficial (Passie, 2018). It was reported that DiLeo initiated the session and that they “lay down on a mat together, and [DiLeo] began caressing and fondling her” (Passie, 2018). It wasn’t until the third MDMA session that DiLeo initiated sexual intercourse, after which the patient immediately terminated “treatment,” escaping from further sexual assault and rape (Passie, 2018). Following the assault by DiLeo, the patient was diagnosed with PTSD and anxiety neuroses by her physician. The patient suffered from panic attacks and impairment to her overall functioning. DiLeo’s “treatment” was found to be “totally unacceptable, counter-therapeutic, and forbidden by the American Psychiatric Association.” The patient was awarded \$200,000 for medical expenses and \$500,000 for other damages (Court of Special Appeals of Maryland, 1991) (Passie 2018).

The most recent high-profile allegations of sexual assault have surfaced from former participant Meaghan Buisson against the husband-and-wife practitioner team of Richard Yensen and Donna Dryer, who were involved in the MAPS MDMA PTSD clinical research trials in Phase II; Buisson was referred to the trial in 2013 (Goldhill, 2020). According to a civil court claim in British Columbia, Canada, Yensen allegedly committed “sexual assaults constituting battery” (*Notice of Civil Claim*, 2018) with a

participant enrolled in the study under his therapeutic treatment. Video evidence from one of Buisson's MDMA sessions during the MAPS trial depicts her being spooned and physically restrained in the room (Busby, 2022). Buisson also recalled being coaxed to relive her sexual assaults, to spread her legs; at several points Yensen and Dryer lie down on top of her while holding her wrists, later comforting her by stroking her face and climbing into bed with her; there are also periods of time when Yensen is in constant physical contact with Buisson (Rosin, 2022). Beyond the sexual assault and battery charges, Yensen was accused of negligence and breach of contract for failing to provide appropriate therapy and maintain a professional relationship (Goldhill, 2020). Buisson filed additional complaints asserting that MAPS: 1) failed to adequately protect subjects from abuse; and 2) did not warn FDA or study participants of the risk until after the allegations became public (Goldhill, 2020). Also noteworthy is that the MAPS protocol only requires one practitioner providing psychotherapy during trials to be licensed, including during the high-dose MDMA sessions; the other practitioner can be unlicensed. Dryer was the licensed practitioner in the therapist dyad; Yensen was unlicensed. The implementation of a therapist dyad (one male, one female) was partially in response to historical issues of sexual abuse in psychedelic therapy settings (Passie, 2018); obviously these allegations have raised doubts as to whether current protocols are sufficient to protect participants from sexual abuse. In any case, we have well-

documented knowledge of sexual abuse (specifically with MDMA) beginning in the 1980s as well as in recent years. Moreover, in his 2000 Harvard doctoral thesis, MAPS founder Rick Doblin acknowledged: “The loving and trusting feelings that can be induced by MDMA can make patients more vulnerable to sexual pleasure” (Doblin, 2000). Given this long history, it is a wonder as to why these events did not prompt an update to psychedelic research policy before the large-scale restart of P-AT trials. Meanwhile, FDA has moved forward with approving expanded access for MDMA-assisted therapy research treating PTSD (Goldhill, 2020).

In March 2022, MAPS published an update¹³ on its website entitled *Public Announcement of Ethical Violation by Former MAPS-Sponsored Investigators* (maps.org), saying that Yensen and Dryer were barred from all MAPS-related activities as of 2018 as a result of ethical misconduct. MAPS also reported that it had notified FDA of the re-opened investigation into ethical misconduct via a compliance review initiated and conducted by the MAPS compliance team in November 2021 (maps.org). Recent reporting by *New York Magazine’s* podcast *Cover Story: Power Trip* about sexual abuse in the psychedelic above- and below-ground communities covered Buisson’s case over two episodes. *Cover Story’s* investigation into the MDMA MAPS trials uncovered several

¹³ Original public announcement by MAPS was published May 24, 2019. <https://maps.org/2019/05/24/statement-public-announcement-of-ethical-violation-by-former-maps-sponsored-investigators/>

other complaints by trial participants (Busby, 2022). A complaint was also submitted by the producers of *Cover Story* to Health Canada imploring a review into potential MAPS investigator misconduct. This complaint alleged abuses beyond sexual abuse and cited three other patients across other PA-T trials reporting worsening suicidal thoughts but whose accounts were left out of the trials' logs of adverse events (Busby, 2022). In April 2022 Health Canada announced that it would undertake a comprehensive review of all MDMA trials (Lindsay, 2022). FDA has yet to announce a similar review, although the agency has been called upon to do so by David Nickles (an affiliate of Psymposia¹⁴ and *Cover Story*). Nickles expressed concern that "regulatory agencies involved in overseeing this research are not attending to the psychotherapy aspect of MDMA clinical trials" and argued that a "full audit of all video footage and trial data is necessary with particular attention to psychotherapy" (Busby, 2022). A psychotherapist who worked on the MAPS MDMA trials echoed this concern (anonymously—out of fear of retribution), asserting that [MAPS] is "trying to be too many things" and "they need to slow down and focus on the research that's actually being done, and doing quality long-term follow-ups while listening to and providing for their trial participants when they're saying 'I need extra support'" (Busby, 2022).

¹⁴ Psymposia is a 501(c)(3) non-profit media organization that offers leftist perspectives on drugs, politics, and culture) Psymposia publishes news, essays, and investigative journalism, while challenging those in power on behalf of the public. (psymposia.com)

While slowing down the research that is currently in process would be a beneficial first step, it would not address the unique issues posed by P-AT research that the current regulatory system is inadequate to deal with, nor would it ensure the necessary level of care for participants struggling with acute PTSD symptoms. The current director of communications at MAPS (Betty Aldworth) has indirectly acknowledged this latter issue: “Any treatment that involves processing trauma might lead to worsening symptoms. Knowing all of that, we have worked to develop a treatment protocol that is supportive for most participants within the constraints of clinical trials but look forward to a day when MDMA-assisted therapy may be approved and clinicians can collaborate with patients to individualize the timing of treatments and integration approaches” (Busby, 2022). This vague statement does little more than whitewash an emergent ethical imperative and ignores the fact that adequate safety protocols should have already long since existed within the clinical research setting. In a recent interview on the *Psychedelics Today* podcast, Rick Doblin further acknowledged the limitations of P-AT research and its inability to offer continued care for participants in need as an unfortunate part of the research process. He said that one “can’t do that [offer more sessions] in the research setting” (Drapkin, 2022). Doblin further suggested that continued care will only be a possibility post-approval. A fourth MDMA session may not be an option to offer participants in need, but what of the other

kinds of resources and support that could be extended? What of the ethical codes disallowing client abandonment? How does this not apply to therapists working in P-AT trials? If I were the therapist employed in these trials, I would be in violation of my own governing body per two codes: The American Association of Marriage and Family Therapy (AAMFT) declares in section 1.11 (Non-abandonment) "Marriage and family therapists do not abandon or neglect clients in treatment without making reasonable arrangements for the continuation of treatment" and 5.2 (Protection of Research Participants) "Marriage and family therapists are responsible for making careful examinations of ethical acceptability in planning research. To the extent that services to research participants may be compromised by participation in research, marriage and family therapists seek the ethical advice of qualified professionals not directly involved in the investigation and observe safeguards to protect the rights of research participants" (AAMFT Code of Ethics, 1.11, 2015). I cannot help but wonder how therapists and organizations working in P-AT trials are can credibly claim immunity from these codes for their research trials¹⁵, especially in the presence of a trauma-related diagnosis.

¹⁵ Across disciplines (e.g. psychologist, licensed clinical social worker, licensed professional counselor, licensed marriage and family therapist) there are similar codes. For example, the American Psychological Association code 1.7 "If a therapist is unable or unwilling to continue to provide professional services, the therapist will assist the client/patient in making clinically appropriate arrangements for continuation of treatment."

MAPS has released other public statements regarding the abuse occurring in their MDMA PTSD trials prior to the Health Canada investigation, including a statement addressing the ethical violations and actions that it would take to modify its protocols. I address these modifications in the analysis section. Rick Doblin addressed other topics related to the allegations by *Cover Story* and Buisson's case directly on the *Psychedelics Today* podcast (Episode #327: *Confronting Abuse in Clinical Trials and the Future of Psychedelic Medicine*, June 2022); relevant details of this interview are covered in Appendix A.

Alongside above-ground abuse under investigation in the MAPS trials, voices of survivors who experienced underground psychedelic therapy abuse have begun to surface, often receiving a distinct lack of support from people within the psychedelic community. In another *Cover Story* report, one survivor of sexual and emotional abuse during a psychedelic experience in Ecuador said that after seeking support from members of the psychedelic underground community in the US, she was repeatedly discouraged from going public with her experience; she was told that she would "singlehandedly re-instigate the war on drugs and undo decades of research," or that she would "pretty much just kill the psychedelic renaissance or revolution and that would be on her" (Wright & Ross, 2021). I have attended several conferences and events related to psychedelics and P-AT and have overheard this narrative perpetuated

numerous times, variations of which include: concerns that overfocusing on past and current abuse may provide fuel for what has already been long road toward destigmatizing psychedelics; fears about the impact on public perception; less funding for research; and less access to potentially healing treatment for the thousands (or perhaps millions) struggling with mental health issues.

Burying past abuse to protect an agenda is, by nature, another form of abuse. We are ethically obligated to bring awareness to past abuse in order to recognize and prevent future abuse. Participants engaging in a P-AT clinical trial should be made aware of: the dubious history of psychedelic research; the investigators' credentials and their organization's policies regarding protection of participants from sexual and other abuses of power; the warning signs of abuse of power; the process for reporting; and available support resources in the event of abuse.

3. Investigating Informed Consent

Despite many differing rules governing human subjects research, it is widely agreed upon that research subjects should be fully informed about the experiments they may be participating in before entering a study (*International Ethical Guidelines for Health-Related Research Involving Humans*, 2016). Informed consent is often the first line of communication conveying the risks and benefits of experimental treatment in a clinical trial that may determine a prospective participant's choice to engage with the trial.

I chose to focus on examining MDMA-assisted therapy trials for the treatment of PTSD, as they are the closest to achieving a legalized status (pending FDA approval) and offer the greatest number of registered trials to examine. Additionally, the MDMA PTSD trials are a group of investigations regulated by FDA and FDA rules governing institutional review boards (IRBs). IRBs examining protocols and informed consent processes for clinical trials are often regulated (or mandated, depending on the funding source) by federal regulation referred to as the Common Rule (45 CFR 46), which requires informed consent from participants and appropriate documentation of the informed consent procedures (45 CFR 46, *Protection of Human Subjects*, hhs.gov, 2018). However, FDA is one of the few government agencies that oversees human subjects research but that is not a signatory to the Common Rule. Rather, FDA has its own set of regulations that I discuss in the next section.

3.1 Regulation of MDMA-assisted Therapy for PTSD

Though the MDMA PTSD trials are subject to FDA regulation rather than that of the Common Rule, a comparison document created in 2000 outlining differences between FDA and HHS Human Subject Protection regulations found that FDA regulations are largely compliant with the Common Rule in the sections related to informed consent, i.e., “50.20 and 46.116 General requirements for informed consent are virtually identical” (Lee, 2000). Of note, this comparison document was authored prior to substantial Common Rule revisions in 2018. Following those revisions, the FDA issued “Guidance for the Impact of the Revised Common Rule on FDA-Regulated Clinical Investigations” to reduce confusion about the two different sets of human subject protection regulations. Trials that: 1) involve an FDA-regulated product; and 2) are supported by HHS are subject to *both* 45 CFR part 46 (the Common Rule) and 21 CFR parts 50 and 56 (FDA regulations). Per the guidance: “...where the regulations differ, the regulations that offer the greater protection to human subjects should be followed” (*Use of Electronic Informed Consent Questions and Answers Guidance for Institutional Review Boards, Investigators, and Sponsors*, 2016). The FDA created another document as guidance for sponsors, investigators, and institutional review boards under the title *Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations*. This document acknowledges that the 2018 Common Rule revisions contained several

informed consent requirements, “including changes relating to the content, organization, and presentation of information included in the consent form and process to facilitate a prospective subject’s decision about whether to participate in research as well as changes to the basic and additional elements of consent” (*Impact*, 2018).

Though the impact document is described as non-binding “guidance for sponsors, investigators, and Institutional Review Boards,” the information communicated is stated as representative of “the current thinking of the Food and Drug Administration (FDA or Agency) on this topic” (*Impact*, 2018). Per Table 1 and Table 2, general requirements and basic and additional elements of informed consent from the 2018 *Common Rule* update communicated to FDA as relevant to their regulations are as follows:

Table 1. FDA guidance on the updated 2018 Common Rule revisions and general requirements for informed consent

Regulation	Description
46.116(a)(4)	“The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.” (<i>Impact</i> , 2018)
46.116(a)(5)(i)	Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension. (<i>Impact</i> , 2018)

46.116(a)(5)(ii)	“Informed consent as a whole must present information in sufficient detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.” (<i>Impact</i> , 2018)
46.117(b)(2)	A short form written informed consent form stating that the required elements of informed consent required by 45 CFR 46.116 have been presented orally to the subject or the subject's legally authorized representative and that the key information required by 45 CFR 46.116(a)(5)(i) was presented first to the subject, before other information, if any, was provided. (<i>Impact</i> , 2018)

Table 2. FDA guidance on the updated 2018 Common Rule revisions and basic and additional elements of informed consent.

Regulation	Description
45 CFR 46.116(b)(9) (New Basic Element)	<p>“One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:</p> <p>(i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or</p> <p>(ii) A statement that the subject’s information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.” (<i>Impact</i>, 2018)</p>
46.116(c)(7) (New Additional Element)	<p>“A statement that the subject’s biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;” (<i>Impact</i>, 2018)</p>
46.116(c)(8) (New Additional Element)	<p>A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions;” (<i>Impact</i>, 2018)</p>

Though MAPS MDMA PTSD trials span a timeline prior to and after the 2018 Common Rule revisions, clarification can be found in the same *Impact* document, which states that “...the provisions of the 2018 requirements related to the content, organization, and presentation of information included in the informed consent form and process as well as the basic and additional elements of informed consent are not inconsistent with FDA’s current policies and guidelines,” and therefore “may avoid the need for sponsors or investigators to develop, and IRBs to review, two separate informed consent forms” (*Impact*, 2018).

With the second phase of MAPS Phase III trials beginning, the “hopeful approval in 2023 [by FDA] of MDMA-assisted therapy for PTSD¹⁶, and in light of MAPS statements supporting open science, the process of gaining access to informed consent forms, in theory should have been easy and allowed me to examine how risk and accountability are communicated to P-AT trial participants. The MAPS open science principle states: “We commit to sharing what we learn and create, including our findings, protocols, and finances. Transparency creates a culture of accountability and contributes to the public domain, facilitating ethical collaboration toward a greater

¹⁶ Reported by MAPS news release May 3, 2021. “MAPS’ Phase 3 Trial of MDMA-Assisted Therapy for PTSD Achieves Successful Results for Patients with Severe, Chronic PTSD.” <https://maps.org/news/media/maps-phase-3-trial-of-mdma-assisted-therapy-for-ptsd-achieves-successful-results-for-patients-with-severe-chronic-ptsd/>

shared purpose” (*Multidisciplinary Association for Psychedelic Studies: Open Science, Open Books*, 2022).

However, the task of gathering IC documents related to MAPS and other P-AT trials proved to be difficult. Only one IC for MAPS MDMA PTSD trials surfaced publicly for review¹⁷. Following this discovery, I reached out to MAPS directly in May 2022 to request IC documents for all eligible trials¹⁸. MAPS confirmed that the IC for the MAPP1 study found on clinicaltrials.gov¹⁹ is the only IC form posted publicly. MAPS’ response to me went on to reiterate its commitment to open science and offered assurances that it was in the process of uploading more IC forms to clinicaltrials.gov under its associated trial numbers but said that the organization unfortunately did not “have a timeline for when that might take place.” In this same message MAPS offered assistance with any additional resources I might need and then followed up in June 2022, notifying me that all IC forms had been uploaded to its related trials. Unfortunately, the review period for documents uploaded to clinicaltrials.gov²⁰ did not afford access to the additional IC

¹⁷ ClinicalTrials.gov Identifier: NCT03537014 (clinicaltrials.gov)
https://clinicaltrials.gov/ProvidedDocs/14/NCT03537014/ICF_000.pdf

¹⁸ See methodology section for selection criteria.

¹⁹ [Clinicaltrials.gov](https://clinicaltrials.gov) is a database of privately and publicly funded clinical studies conducted around the world and a resource provided by the U.S. National Library of Medicine. Through the search function you can review studies status, results, descriptions, funding/sponsorship, associated investigators, and study documents.

²⁰ In a statement found on the document *ClinicalTrials.gov Results Quality Control Review Criteria: Introduction and Overview*, it states: “Note: uploaded study documents will be posted on the [ClinicalTrials.gov](https://clinicaltrials.gov) website after a quality control review.” It does not state the timelines or protocol for the review process, and no

documents for examination by the deadlines related to completion of this thesis. As of July 1, 2022, the IC forms had yet to be made available on clinicaltrials.gov. More broadly, during this process of collection, I was surprised to learn that accessing all but a small minority of IC forms related to *any* trials listed on clinicaltrials.gov would be difficult. I discuss this in the following section.

3.2 Acquiring Informed Consent Documents for Clinical Trials

Under the revised Common Rule (45 CFR 46.116(h)), it is required that for “each clinical trial conducted or supported by a federal department or agency, one IRB-approved consent form used to enroll subjects must be posted on a publicly available federal website by the awardee or the federal department or agency component conducting the trial” (Office for Human Research Protections, 2022). However, the FDA has never adopted this requirement. That said, even without FDA adoption of this provision, one might still assume that a simple search on clinicaltrials.gov would yield informed consent forms for a great number of trials given that 19 government agencies (including, most notably, NIH) are beholden to the 45 CFR 46.116(h) IC upload requirement. In reality, the number of available IC forms for not only P-AT-related trials,

other associated documents with that information were found.
<https://prsinfo.clinicaltrials.gov/ResultsDetailedReviewItems.pdf>

but *all* clinical trials listed on clinicaltrials.gov, remains extremely small (Table 3). While it's true that only three years of government-funded trials are bound by the new Common Rule posting requirement, there is no rule prohibiting sharing informed consent forms and protocols publicly.

Table 3. Number of studies overall and associated number of uploaded IC documents. (clinicaltrials.gov)

Total Studies (unfiltered) on clinicaltrials.gov	Total with Informed Consent Documents* <small>*as of June 19, 2022</small>
415,358 ²¹	4,869 (1.17%)

Alas, for this study, I was able to access few such forms via either clinicaltrials.gov or by petitioning investigators directly, despite repeated efforts to do so.

3.2.1 Methodology

Using clinicaltrials.gov, I began by using the search function to query for “post-traumatic stress disorder” in the field for “condition or disease.” Trials whose status was marked as “terminated” or “withdrawn” were filtered out along with the “no longer available” and “temporarily not available” categories under “expanded access.” Filters

²¹ Of the 415,358 studies listed, 35,675 are funded by the NIH, 7,841 funded by “Other U.S. Federal Agency,” making a total of 43,516 studies subject to Common Rule regulation. 1,485 studies filtered by “NIH,” and “Other U.S. Federal Agency” funders were found to have an IC form uploaded to the trial record.

for eligibility criteria, study type, study results, study phase, and funder type were not used. This initial search yielded 1,494 studies related to PTSD. To further filter the 1,494 studies, I sorted by the category “drug interventions, alphabetical,” and limited “psychedelic” substances to those most commonly studied in current research where participants are receiving a high dose to invoke an altered state of consciousness, which include: MDMA, psilocybin, LSD, and ketamine²². Once sorted by substance, the final filter was implemented for trials containing an uploaded IC form, yielding the following results:

Table 4. Number of studies examining PTSD treatment by psychedelic (or psychedelic-adjacent) drug intervention with uploaded informed consent forms. (clinicaltrials.gov)

PTSD Study by Drug Intervention	Number of Active or Completed Studies* <i>*as of June 19, 2022</i>	Number of Uploaded IC Forms* <i>*as of June 19, 2022</i>
<u>3,4-Methylenedioxyamphetamine (MDMA)</u>	15	1 (6.66%)
<u>Ketamine</u>	21	0
<u>Psilocybin</u>	3	0
Lysergic acid diethylamide (LSD)	0	0

²² Ketamine, though not classified as a psychedelic is classified as a hallucinogen with dissociative properties and when given at higher doses invokes an altered state of consciousness. (dea.gov)

With the search yielding only one informed consent form, I eliminated the filter limiting trial results exclusive to the examination of PTSD and expanded the search for trials examining individual psychedelic or psychedelic-adjacent (ketamine) substances for all purposes²³:

Table 5. Number of studies listed by psychedelic (or psychedelic-adjacent) drug, with an uploaded informed consent form (clinicaltrials.gov)

Drug Intervention	Number of Active or Completed Studies* <small>*as of June 19, 2022</small>	Number of Uploaded IC Forms* <small>*as of June 19, 2022</small>
3,4-Methylenedioxyamphetamine (MDMA)	84	3 (3.57%)
Psychedelic ²⁴	368	13 (3.53%)
Ketamine	1,211	16 (1.32%)
Psilocybin	97	5 (5.15%)
Lysergic acid diethylamide (LSD)	28	0

²³ Psychedelics studies include investigations into the substances impact neurologically and for other varying medical and mental health diagnoses which may or may not have included a psychotherapeutic element to the study

²⁴ Definition and substances associated with the tag "Psychedelic" on clinicaltrials.gov is unclear. If the process of tagging clinical trials is a task for the sponsor, responsible party, or principal investigator, then this tag is subjective to the person/organization associating the tag with their trial.

To gain a deeper understanding of how funding (and thus IC posting requirements) might influence access to IC forms, and how the MAPS MDMA trials compare to other organizations in this respect, I expanded the query on clinicaltrials.gov by organization and compiled the results by psychedelic research sponsors with registered clinical trials. These results also depicted a dismal picture of access to IC forms, with only three organizations having uploaded an IC: Heffter Research Institute, Usona Institute, and MAPS. Notably, these three organizations' stated commitments to open science are publicly on record on their respective websites.

Table 6. Number of documents available by organizations sponsoring psychedelic research. (clinicaltrials.gov)

Psychedelic Research Sponsor	Company Status	Number of Sponsored Studies* *as of June 19, 2022	Number of Informed Consent Uploads* *as of June 19, 2022
Beckley Psytech Limited	Private	3	0
COMPASS P-AThways NASDAQ: CMPS	Public	9	0
Eleusis Therapeutics	Private	1	0
Entheon Biomedical Corp. CSE: ENBI	Public	1	0
GH Research Ireland Limited NASDAQ: GHRS	Public	3	0
Halucenex Life Sciences Inc. (Red Light Holland Corp) CSE: TRIP FSE: 4YX	Public	1	0

OTC Pink: TRUFF			
Heffter Research Institute	Private	13	1 (7.69%)
Mind Medicine, Inc. NASDAQ: MNMD NEO: MMEDFRA: MMQ.F	Public	2	0
Multidisciplinary Association for Psychedelic Studies (MAPS) MAPS Public Benefit Corporation (PBC)	Private	37	1 (2.7%)
Optimi Health Corporation CSE: OPTI	Public	1	0
PharmaTher Inc. CSE: PHRM	Public	1	0
Revive Therapeutics, Ltd. CSE: RVV	Public	1	0
Seelos Therapeutics, Inc. NASDAQ: SEEL	Public	3	0
Small Pharma Ltd TSXV: DMT OTC: DMTTF	Public	1	0
TRYP Therapeutics CSE: TRYP	Public	2	0
Usona Institute	Private	7	1 (14.29%)
Wake Network, Inc.	Private	1	0

3.2.2 Limitations

Literature validating data related to IC forms is limited, though one study by Tse et. al. in 2021 on the “Characterization of Informed Consent Forms Posted on Clinicaltrials.gov” also addressed the revised Common Rule form-posting requirement

(45 CFR 46.116(h)) and examined if access to forms increased on clinicaltrials.gov since the revisions and through mid-2021 (Tse et al., 2021). The authors undertook a cross-sectional analysis using two data sets downloaded from clinicaltrials.gov to: 1) characterize all registered clinical trials with at least one US site and a posted form; and 2) gather the number of registered US trials with start dates on or after January 21, 2019 (the date by which new trials must have comported with revised Common Rule upload requirements) (Tse et al., 2021). Though the investigation by Tse et. al. was limited to US trials, while my query did not limit the country of origin, the results were similar. As of July 7, 2021, Tse et. al. uncovered 2100 US trials for a range of intervention types and conditions sponsored by mostly non-industry entities that had IC form available for public view (Tse et al., 2021). Notably, federally funded trials mandated to comply with the Common Rule IC posting requirement were not terribly compliant, with “fewer than 87 of 529 trials (16.5%) listing a key funder type of ‘NIH’ or ‘other US federal agency’ having posted forms” (Tse et al., 2021). Moreover, the authors reported that most forms appear to have been posted voluntarily; this was attributed to the low number of federally funded trials initiated since the Common Rule compliance date in 2019 (Tse et al., 2021). They further acknowledged that the trials they identified were “likely skewed toward those required by federal reporting requirements,” and that some trials “may have also been miscategorized because of errors or incomplete information in data self-

reported by study sponsors” (Tse et al., 2021). This latter limitation may also apply to my queries for public IC forms on clinicaltrials.gov. I agree with the authors that further research is needed, and it may be too soon to appreciate the full impact of the revised Common Rule posting requirement (Tse et al., 2021). However, given that initiating a study record on clinicaltrials.gov takes place *after* IRB approval (including the associated IC form), it shouldn’t be an onerous task to add these forms upon creating the initial record; a further look into why IC forms are held back from this initial process would be beneficial to understanding general barriers to accessing IC forms.

Another consideration specific to P-AT is that no psychedelic research trials received funding by the United States government between 1971 and 2021 (Barnett et al., 2022). This changed only recently with the first government funding award in fifty years to Johns Hopkins University in 2022 by NIH. The Hopkins study appears to be exceptional; without funding from Common Rule agencies like NIH, current P-AT trials are not subject to revised Common Rule informed consent form posting requirements for public view. Unsurprisingly, IC forms for privately funded clinical trials, including those under review by the FDA, remain largely absent from clinicaltrials.gov.

As I mentioned, results from my inquiry and the investigation by Tse et. al. illuminated that a paucity of posted informed consent documents is not unique to trials related to P-AT. This raises existential research questions about the protection of human

research subjects. For example, can safety be ensured or accountability enforced without document transparency requirements? IRBs are responsible for adherence to ethical research practice rules, but who reviews the reviewers? How are these documents shared with institutions internally beyond local IRBs? How might this lack of document sharing impact replicability? What are the benefits and risks of public document sharing with prospective and active clinical trial participants? For a researcher seeking to examine these questions, the time required to track down the information simply to inquire about receiving a copy of these documents (often to receive either no answer or be told no) proved to be substantial and limiting. Could this be a contributor to the limitation of existing literature on ethical P-AT research practices and a barrier to future research? We are left with more questions than answers.

4. Identifying Gaps

The number of available forms for examination was limited due to the reasons outlined above. Ultimately, five study forms met the following criteria: 1) involved the use of a psychedelic in tandem with psychotherapeutic intervention; and 2) had a status of “completed,” “recruiting,” or “active.” These were reviewed to determine what risks, benefits, and safety protocols were communicated to participants in their respective trials:

Table 7. Clinical Trials Used for Informed Consent Analysis

Study Title	Listed Affiliated Parties	Clinicaltrials.gov ID
A Multi-Site Phase 3 Study of MDMA-Assisted Psychotherapy for PTSD (MAPP1)	Sponsor: Multidisciplinary Association for Psychedelic Studies (MAPS)	NCT03537014
Comparing the Effects of Psilocin and Psilocybin in Healthy Adults	Sponsor: University of California San Francisco Collaborator: Filament Health	NCT05317689
Psilocybin Therapy for Depression in Bipolar II Disorder	Sponsor: University of California, San Francisco	NCT05065294

<p>Psilocybin Therapy for Depression and Anxiety in Parkinson's Disease</p>	<p>Sponsor: Joshua Woolley, MD/PhD University of California, San Francisco</p>	<p>NCT04932434</p>
<p>Psilocybin-assisted Group Therapy for Demoralization in Long-term AIDS Survivors</p>	<p>Sponsor: Joshua Woolley</p> <p>Collaborators: Heffter Research; Institute River Styx; Foundation; Usona Institute; Stupski Foundation</p>	<p>NCT02950467</p>

4.1 Existing Themes and Compliance

The five informed consent (IFC) documents from trials utilizing high-dose psychedelics alongside a psychotherapeutic intervention were analyzed and assessed under four categories: risks, benefits, safety, and accountability. They were also evaluated with respect to their perceived compliance with FDA regulations outlined in 21 CFR 50.

For studies that are subject to FDA regulation (and are not eligible for exemption), IC forms must meet requirements of 21 CFR 50.20, which states that “no investigator may involve a human being as a subject in research covered by these

regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence” (fda.gov). Given the greater-than-minimal risk associated with P-AT trials, none of the studies evaluated are eligible for exemption from this statute. The Common Rule was revised in 2017²⁵ (the first significant changes since it was first published in 1991) to enhance protections for human subjects enrolled in “greater-than-minimal-risk trials” and to reduce administrative burden for low-risk research (LeCompte & Young, 2020). Minimal risk is defined as “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological

²⁵ Its revisions were phased in in 2018 and 2019 after several delays.

examinations or tests” (CFR 21 50.3(k)). Though this broad definition of minimal risk leaves a greater-than-minimal-risk designation open to subjective and variable interpretation, it would be difficult to imagine how any P-AT trial would not be categorized as greater-than-minimal risk requiring additional support for participants.

FDA addresses research involving more than minimal risk and requires “an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained” (CFR 50.25(6)), though the definition of “injury” is not clarified as to whether this includes psychological injury or is limited to physical harm. Additionally, information required by each IC form must include eight basic elements as defined by 21 CFR 50.25(a) and elements of 21 CFR 50.25(b) that are appropriate to, in this case, any P-AT study (fda.gov). The local IRB has final authority to ensure the compliance and adequacy of information in the IC forms (fda.gov).

Overall, each IC form examined demonstrated compliance with FDA elements of informed consent regulations. Thematically, there were more commonalities than differences among forms likely due to four of the five trials available having the same institutional affiliation (University of San Francisco, [USCF]). IC documents ranged in length from 10 to 14 pages (for UCSF) and 33 pages for the MAPS trial. The MAPS IC

form obtained was the most updated version²⁶ from its Phase III study. Prior IC documents were solicited from MAPS directly, as mentioned before; however, the most recent IC form uploads (from past Phase I and Phase II trials) were unavailable at the time of this study for comparison.

4.1.1 Common Themes Related to Risk

Table 8. Common Themes Related to Risk

Theme and FDA Code of Regulation	Example
Cognitive 21CFR50.25(2) A description of any reasonably foreseeable risks or discomforts to the subject.	"Alteration of perception, mood, consciousness, cognition, or behavior."
Physical 21CFR50.25 (a)(2) A description of any reasonably foreseeable risks or discomforts to the subject.	"Nausea, "blurred vision," "elevated heart rate."
Information-based 21CFR50.25 (a)(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may	Storage of HIPAA-protected data. Sensitive genetic material stored for future research purposes. Video and/or audio footage of P-AT trial participants

²⁶ As of June 19, 2022.

inspect the records.	
<p>Statement of potential unknown risks</p> <p>21CFR50.25(b) <i>Additional elements of informed consent.</i> When appropriate, one or more of the following elements of information shall also be provided to each subject:</p> <p>21CFR50.25(b)(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.</p>	<p>“It is important to note that psilocybin may have side effects that no one knows about yet.”</p>
<p>Emotional</p> <p>21CFR50.25 (a)(2) A description of any reasonably foreseeable risks or discomforts to the subject.</p>	<p>“Questions about sensitive issues (such as alcohol use, illegal drug use, and your mood): questions could make you feel uncomfortable and lead to feelings such as anxiety, distress, sadness, or embarrassment.”</p>

While many components of the research protocols were communicated as risk to participants, other components, like the length of time involved in a high-dose session of psilocybin or MDMA, were not overtly recognized as areas of risk but could still carry potential for harm. For example, each study analyzed required two or more six-to-eight-hour visits requiring an overnight stay in a private room in the research unit and included study staff retrieving participant belongings to store in a secure location. While

this part of the protocol was intended as a safety measure, it also limited the ability of the participant to vacate the premises in the event they want to terminate their participation. All UCSF IC forms examined stated: "Study staff will put your belongings (e.g., phone, wallet, keys) in a secure location. This is to ensure your safety while you are on psilocybin. Items will be returned to you once the effects of psilocybin have worn off, after about 6 hours." If a participant decides to terminate treatment due to harm or discomfort while experiencing an altered state of consciousness, forced stay has the potential to invoke feelings of being trapped or disempowered, and may be psychologically damaging. However, UCSF consent forms indicated that each participant must identify a trusted support person (from their life outside the trial) while they are enrolled in the study, thereby creating an additional level of safety that may be called upon in the case of early termination.

The MAPS IC form did not offer the additional safety measure of a support person. In the event a participant had difficulty, for example, by being "confused or upset 8 or more hours after the start of an Overnight Test Session," it would be the therapy team that stayed with the subject until they fully recovered; there would be an attendant on staff who stays in an adjacent room for support as well. In the event the therapy team believed the participant may be at risk of harming themselves or others, the therapists would "either remain with you or admit you to a hospital until you are no

longer at risk.” Depending on the rapport built among the participant, therapist team, and staff, this protocol may or may not feel secure or comforting to the participant. While communicating this risk is compliant with what is required by the FDA, agreeing to the potential for risk and negotiating the impact of the risk itself if it actually happens are different considerations for a participant to weigh. IC forms as written were intended to allow for educated decision making in order to secure the safety of the participant during the trial. Of course, P-AT risks may also happen post-trial and without the support of trial staff; this sort of eventuality could be difficult to fully understand based on the information provided in all IC forms examined in this investigation.

Since the allegations of abuse brought forth in the MAPS Phase II trial by Yensen and Dryer, changes to the MAPS informed consent policy were published on the MAPS website under the section “What We’ve Done,” which stated that “[We have fully] informed participants in MAPS-sponsored trials through additions to the Informed Consent Form of the risks of psychedelic-assisted therapy including, but not limited to, greater participant suggestibility, the particular need for sensitivity regarding consent, and the likelihood of stronger and more complex transference and countertransference.” The MAPS MDMA trial IC form examined in this investigation was from a Phase III trial and included an enhanced section addressing “emotional openness,” which stated that

“MDMA is considered an ‘empathogenic’ drug. This means people who use it may experience increased empathy and sociability. After taking the study drug, you may feel more emotionally open, friendly, extroverted, or talkative. You may also feel closer to your therapists or more trusting of them, or you may even feel love and sexual feelings toward your therapist(s). This can happen with any psychotherapy but may be heightened by MDMA.” Without IC forms to examine from Phase I and Phase II as comparison, it was not possible to verify if this is part of the “enhanced” consent process MAPS referred to in its public statement.

4.1.2 Common Themes Related to Benefits

Table 9. Common Themes Related to Benefits

Theme and FDA Code of Regulation	Example
<p>Contribution to Society</p> <p>21CFR50.25 (a)(3) A description of any benefits to the subject or to others which may reasonably be expected from the research.</p>	<p>“You may enjoy the feeling of contribution to knowledge in the health or social sciences field.”</p> <p>“We do know that the information from this study will help doctors learn more about psilocybin therapy as a treatment for bipolar II disorder. This information could help other patients.”</p> <p>“Information obtained from this study may help doctors and researchers to improve treatment for PTSD and relationships in the future.”</p>
Financial	

<p>21CFR50.25 (a)(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.</p>	<p>Treatment at no cost with financial compensation.</p> <p>“In return for your time and effort, you will be paid up to \$500 for completing all parts of this study.” (UCSF)</p> <p>“Payment for participation: Overnight Test Session 1 Up to \$70 Overnight Test Session 2 Up to \$70 Overnight Test Session 3 Up to \$70 Visit 3 Psychological Testing Up to \$70 Visit 19 Psychological Testing Up to \$70 TOTAL Up to \$350” (MAPS)</p>
<p>Substance- or symptom-specific</p> <p>21CFR50.25 (a)(3) A description of any benefits to the subject or to others which may reasonably be expected from the research.</p>	<p>“Administration of psilocin²⁷ may lead to more consistent beneficial effects and have fewer negative effects compared to psilocybin.”</p> <p>“Recent studies have shown that psilocybin may improve depression and anxiety in people with cancer. We believe that it may also be helpful for people living with bipolar II disorder.”</p> <p>“Your symptoms of PTSD may improve while taking part in this study.”</p>

In general, IC documents examined here offered minimal discussion of benefits and focused primarily on risks and safety. As most psychedelic research remains

²⁷ Psilocin and psilocybin, which are structurally related to the neurotransmitter serotonin, are the compounds responsible for the hallucinogenic properties of “magic mushrooms” [24]. From: Bioprocessing for Value-Added Products from Renewable Resources, 2007

experimental, benefits have yet to be proven empirically. Thus far there is scant literature on the benefits perceived by participants in these trials. Benefits, not unlike risks, safety, and accountability can also be in the eye of the beholder. For example, a study examining participant response through interviews about their experience learning about neurodevelopmental/psychiatric disorders (NPD) through genomic screening found that participants considered the information to be highly valuable, despite concerns in the field that participants who received such information might experience increased anxiety, negative impact, self-image, or decreased agency over one’s mental health needs (Wain et al., 2021).

4.1.3 Common Themes Related to Safety

Table 10. Common Themes Related to Safety

Theme and FDA Code of Regulation	Example
<p>Preparation</p> <p>21CFR50.25 (a)(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.</p>	<p>“[You will have] one preparation session with your facilitator. This will be in person. We will familiarize you with what to expect during your psilocybin session including the physical space where you will take psilocybin.” (UCSF)</p> <p>“A preparatory session is where you meet with a facilitator (trained therapist) to prepare for the drug experience, by discussing expectations, practicing therapeutic touch, and listening to music. An integration session is where you meet with the same facilitator the morning after your drug experience to discuss</p>

	<p>how the session went for you and any side affects you experienced after or are currently experiencing.” (UCSF)</p>
<p>Physical Safety</p> <p>21CFR50.25 (a)(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.</p>	<p>“While you are on study drug, your facilitator will monitor your heart, blood pressure, temperature, and how you are feeling. EEG measures will also be collected during the first hour and a half of each dosing session. A study physician will be available at all times.” (UCSF)</p>
<p>Designated Outside Support</p>	<p>“You will be asked to provide the name and contact information for your designated support person who will take you home after your dosing session.</p> <p>“Your designated support person will meet you at our research unit and escort you home. This is for your safety, because you should avoid operating heavy machinery, driving home, etc.”</p>
<p>Participation Withdrawal</p> <p>21CFR50.25 (a)(8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.</p> <p>21CFR50.25 (b)(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without</p>	<p>“Your Other Options: You do not have to participate in this study. Your other choices may include:</p> <ul style="list-style-type: none"> • Getting treatment or care for your condition without being in a study. • Taking part in another study. • Getting no treatment” • Not taking part in a study.” <p>“Important Note: While you are under the effects of psilocybin (which last about 5-6 hours), you will not be able to stop being in the study. If you tell a study doctor, your facilitators, or another study staff member that</p>

<p>regard to the subject's consent.</p> <p>21CFR50.25 (b)(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.</p>	<p>you wish to stop being in the study, you will still have to stay at the research unit until the drug effects have worn off and it is safe for you to leave. This is because we must prioritize your safety while you are under the effects of psilocybin. It is important to tell a study doctor if you are thinking about stopping so any risks from the psilocybin dose can be monitored. Another reason to tell a study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you. One of the study doctors may stop you from taking part in this study at any time if they believe it is in your best interest, if you are not able to follow the study rules, or if the study is stopped."</p>
<p>Comprehension Quiz</p>	<p>"1. Participation in this study is voluntary and I may withdraw at any time."</p> <p>"3. I will complete four drug dosing sessions, each followed by an integration session."</p>
<p>Supervision</p> <p>25CFR50.25 (a)(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.</p>	<p>"You will be paired with a team of trained facilitators for the duration of the study"</p> <p>"Your facilitators will be present all day, study staff will be available overnight, and the study doctor will be available the entire time."</p>

Safety protocols related to sexual feelings and safety within the participant/therapist relationship were addressed only in the MAPS MDMA-assisted

therapy form: “You may also feel closer to your therapists or more trusting of them, or you may even feel love and sexual feelings toward your therapist(s). This can happen with any psychotherapy but may be heightened by MDMA. Your therapists are aware of the effects of the drug. They have been through training on how to appropriately care for someone who has taken MDMA and on a code of ethics that prohibits any sexual relations between therapists and participants, including after participation in the study has ended.”

4.1.4 Common Themes Related to Accountability

Table 11. Common Themes Related to Accountability

Theme and FDA Code of Regulation	Example
<p>Video Recording & Data Collection</p> <p>21CFR50.25 (a)(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.</p> <p>45 CFR 46.116(b)(9) (New Basic Element)</p> <p>“One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:</p> <p>(i) A statement that identifiers might be removed from the identifiable private</p>	<p>“Any data transferred outside of UCSF will involve a legally binding, signed agreement to make sure that collaborators use appropriate procedures to protect your privacy. We will not share your name or any additional personal information. When possible, we will only share de-identified data (i.e., data that does not contain your personal information). Any data that we share with collaborators will be destroyed when we finish the analysis. Your data, including audiovisual recordings, will never be accessible to the general public.”</p> <p>“We will be audio and video recording you during this study. We will use these recordings to understand your symptoms and also to make sure our study staff meet quality requirements”</p>

<p>information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility.</p>	<p>“We may share recordings with researchers at our university/other universities who are collaborating with us, or companies that are helping with data analysis (for example, we may have a HIPAA-compliant, secure service transcribe audio recordings to text). Any data transferred outside of UCSF will involve a legally binding, signed agreement to make sure that collaborators use appropriate procedures to protect your privacy. We will not share your name or any additional personal information. When possible, we will only share de-identified data. Any data that we share with collaborators will be destroyed when we finish the analysis. Your data, including audiovisual recordings, will never be accessible to the general public.”</p>
<p>Protocol in the event of harm or issues</p> <p>25CFR50.25 (a)(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.</p>	<p>“What happens if I am injured because I took part in this study? It is important that you tell the study leaders.”</p> <p>“If you wish to ask questions about the study or your rights as a research participant to someone other than the study leaders or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at _____”</p>
<p>Legal Rights</p> <p>25CFR50.25 (a)(8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.</p>	<p>“In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.”</p>

While the forms alluded to a process for accountability, they offered little detail about how one might go about initiating a complaint as compared to the steps for terminating participation. Participants experiencing discomfort or perceived abuse were directed to contact the principal investigator or the IRB directly, but there was no option to report to an external party unaffiliated with the trial. In the event of abuse during a trial, participants might not feel comfortable reporting to those in positions of power within the trial.

4.2 Ethical Challenges in P-AT Research and Informed Consent Gaps

Several ethical challenges related to the common themes in the examined IC forms exist within psychedelic research. It is unclear what conversations establishing consensus of informed consent protocols have taken place across P-AT trials involving various diagnoses. The literature remains limited with respect to how safety and risk have been conceptualized by the institutions enacting P-AT trials outside of the regulations they are mandated to follow. Moreover, there is no clear picture as to how IRBs evaluate informed consent and what ethical considerations unique to P-AT trials are named and communicated in informed consent forms. An IRB might review P-AT

trials for compliance with the associated regulations, but are the rules sufficient to ensure safe, ethical, and replicable research protocols? The following sections discuss ethical gaps in the P-AT research trials that should shape the informed consent process based on the (admittedly limited) number of documents I examined. I also offer recommendations for improvement.

4.2.1 Abuse of Power

There is an inherent power differential that exists between practitioner and participant; this differential is even more pronounced in P-AT trials. Many who enter a research setting have never experienced one before, let alone a research setting where they will undergo long periods of time in an altered state of consciousness. For participants without any experience with therapy, research, or psychedelics, the relevant signs of an abuse of power may be unknown or misunderstood. It is the responsibility of the clinicians and investigators to protect participants from harm by making the ethical practice and codes of conduct explicit to those whom they will be caring for. In the psychedelic-assisted therapy setting, these power differentials are heightened by the decreased capacity of participants for long periods of time and states of enhanced suggestibility and openness.

4.2.1.1 Ethical Use of Touch

Multiple ethical challenges have been identified in the literature related to psychedelic research, many of which lie in the realm of sexual misconduct. For as long as psychedelic therapy has been an underground practice, the field has contained several ingredients that have made it susceptible to sexual misconduct; aboveground practice is just as susceptible to these challenges (Goldhill, 2020). The boundaries between therapist and participant aren't always clearly defined even without the influence of a substance (MDMA) known for fostering deep connection. These blurred boundaries complicate issues of power and influence. As psychedelic therapy moves toward becoming a legal reality, there are growing demands (Kirsh, 2021) for revisions to protocols to protect against and discipline sexual misconduct (Goldhill, 2020).

Challenges related to the ethical use of touch have been at the heart of the conversation about the consent process in P-AT trials (Smith & Sisti, 2020). Touch is considered by some practitioners working with psychedelics to be integral to their work; others have stated that the omission of touch may limit the types of healing that can occur (Brennan et al., 2021). The use of touch has been controversial in traditional psychotherapy settings as well; many psychotherapists who received traditional training have not received training in the ethical use of touch or somatic practice, thereby making the use of touch potentially out of their comfort zone as practitioners and therefore

outside their scope of practice/competence. Ethical codes of conduct governing the varying types of psychotherapists (e.g., family therapists) determine that treating, diagnosing, or advising on problems outside the recognized boundaries of their competencies is an ethical violation (AAMFT Code of Ethics, 3.6s, 2015). Touch in the therapeutic relationship between participant and clinician can lead to increased relational ethical risk relative to talk therapy (Brennan et al., 2021). The current prevailing narrative in the psychedelic research community is that the consent for touch should be led by the participant; however, this does not account for what happens when touch initiated by the participant may be out of the scope of practice or comfort zone of the practitioner. This issue is compounded by the vulnerable state of the participant in an altered state of consciousness that calls their decision-making capacity into question, thereby impairing client autonomy (Brennan et al., 2021) (Smith & Sisti, 2020). It is through touch that the boundaries between therapist and participant may be blurred, and the door left open for the exploitation of the participant's vulnerability. Power differentials are particularly amplified in MDMA-assisted therapy; this approach requires extra caution on touch and boundaries and demands a clearly defined protocol to communicate to participants.

4.2.2 Training and Competency

Though MAPS has its own MDMA-assisted therapy training program, there are many P-AT trials that are unaffiliated with MAPS that may or may not be employing clinicians with specific training for P-AT practice. The risk of enhanced sexual feelings and transference are stated in the MAPS IC form, though the process of creating boundaries related to these feelings are unaddressed outside of indicating that the therapists have been trained in how to manage them. Explicitly stating what type of training the therapists have received to handle transference, countertransference, and the use of therapeutic touch should be communicated clearly in the IC form and participant-onboarding process. While a step-by-step process of what establishing boundaries related to touch need not be tediously outlined in the IC form, it should be indicated that there *is* a process and at what point in the study participation those boundaries will be discussed and agreed upon before entering the therapy room for any and all sessions, not just the ones involving high doses of psychedelics. Further, providing brief education regarding what types of touch are considered appropriate and inappropriate should be outlined for participants alongside the protocol for reporting boundary violations and resources for support. A formalized process for reporting misconduct, abuse, adverse experiences and an independent ethics council for third-party review of complaints has been requested by over 200 practitioners in the

psychedelic community (myself included) in the publication *Addressing abuse and repair: An open letter to the psychedelic community* (2022). These frameworks, once active, should be among the resources listed on IC forms.

The development of specialty skills within clinical practice requires appropriate education, training, and supervised experience. Clinicians providing care in P-AT trials should not only be required to document and submit their training experience with the use of therapeutic touch to a governing body, they should also be assessed for their competency with those skills prior to engaging with P-AT participants without supervision; a formalized process for assessing that competency should be established and adopted across all P-AT trials.

4.2.3 Long-term to Permanent Personality Shifts

Though experiences involving changes to personality are discussed in the literature on psilocybin, changes to personality have also been associated with trials involving MDMA and LSD. The phenomenon of life-altering and long-term-to-permanent changes to personality after undergoing a psychedelic-assisted therapy trial remains under investigation (Smith & Sisti, 2020). Several studies related to P-AT trials have had participants rank the level of meaning of the experience; many ranked psychedelic treatment as “one of the most meaningful events of their lives” (Smith & Sisti, 2020). That said, the risk of changes in values and personality, and the possibility of

associated “mystical experiences” that might have created this enhanced meaning, may cause unintended or unwelcome existential turmoil to participants. A change in beliefs precipitated by a high-dose psychedelic experience may be in direct conflict with the prior beliefs of the participant and belief systems they share in their intimate and familial relationships (Smith & Sisti, 2020). The “ineffable” qualities of a high-dose psychedelic experience poses challenges to the consent process. How can one be “informed” if the experience cannot be adequately described?

Changes to personality are not only life-altering to an individual’s internal experience, but they can also be disruptive relationally. Many aspects of psychedelic experience, like nuances of risk related to personal and relational shifts, can be difficult for participants without prior experience to understand and should involve more than signing a document with a brief synopsis. Reviewing the content of IC forms alongside participants in the onboarding process offers an opportunity for the participant to ask additional questions and for the clinicians/investigators to begin developing rapport in a supportive role. As with other IC processes for research, the P-AT consent process should provide participants with a better understanding of risk and a chance to gauge their comfort level with every aspect of the intervention.

4.2.4 Culturally Responsive Informed Consent

Calls for greater inclusion of more diverse ethnoracial groups in empirically supported posttraumatic stress disorder treatment research have brought forward how little diversity exists among participants in past and current P-AT trials (Grau et al., 2022). Increasing these numbers will not only require more effective recruitment strategies (Smith et al., 2022), but will also require systemic changes to prevent participants of color and other marginalized identities from being further harmed (Strauss et al., 2021).

The ramifications of ethnoculturally insensitive care in psychedelic-assisted therapy research are too great to dismiss, especially in consideration of the presence of trauma. Psychedelic research has almost exclusively been conducted on White populations in North America and Western Europe (Fogg et al., 2021) (Smith et al., 2022). Further, the IC process in P-AT forms examined in this study does not address unconscious bias, microaggressions, or other forms of discrimination as risk or offer explicit reporting protocols and supportive structures for participants in the event of racial harm. For example, for Black people in the U.S. and Canada racial mistreatment is frequently experienced via a variety of macro and micro insults, with such experiences triggering physiological responses of anxiety and fear, which are associated with the

chronically elevated stress hormone levels²⁸ similar to levels experienced among populations with an anxiety disorder (Smith et al., 2022). Statements from the research study on the IC form acknowledging the risk of discrimination and asserting a no tolerance policy and protocol for reporting discrimination would be simple place to start. Further, the literature suggests that disregarding these contextual factors leads to negative outcomes, including higher risks for BIPOC to have challenging drug experiences, poorer long-term outcomes, and less trust for future participants and stakeholders in P-AT due to the influence of negative public perceptions reinforcing stigma within the broader sociopolitical and legal landscape (Fogg et al., 2021). Missteps and abuse reported within an historically stigmatized field like psychedelic research threatens support for and access to this type of care. Proactive accounting for ethnoracial factors ensures better outcomes for the future of P-AT research and the individuals participating in it (Fogg et al., 2021).

While the informed consent documents I examined covered several important areas related to risk, benefits, safety, and accountability, the framework of the informed consent process is worth further critique and investigation not only to increase safety in the face of continued abuse, but to take steps to reform outdated practices inhibiting equity, justice, inclusion, and safety for participants of all cultural backgrounds who

²⁸ For example cortisol and epinephrine (Smith et al., 2022)

have already endured a level of trauma, mistreatment, and impairment to flourishing for far too long. We need further examination of how IC forms—and the IC process as a whole—can address the risks related to cultural and racial discrimination.

4.2.5 Ethical challenges addressed by examined IC Forms

Table 12. Ethical Challenges addressed by examined IC forms.²⁹

Ethical Challenge	Addressed by Forms Examined
Abuse of Power	Trial #NCT03537014 (MAPS): Partial Trial #NCT05317689 (UCSF): No Trial #NCT05065294 (UCSF): No Trial #NCT04932434 (UCSF): No Trial #NCT02950467 (UCSF): No
Use of Touch	Trial #NCT03537014 (MAPS): Partial Trial #NCT05317689 (UCSF): No Trial #NCT05065294 (UCSF): No Trial #NCT04932434 (UCSF): No Trial #NCT02950467 (UCSF): No
Training and Competency	Trial #NCT03537014 (MAPS): Partial Trial #NCT05317689 (UCSF): Partial Trial #NCT05065294 (UCSF): Partial Trial #NCT04932434 (UCSF): Partial Trial #NCT02950467 (UCSF): Partial
Longterm to Permanent Personality Shift	Trial #NCT03537014 (MAPS): No Trial #NCT05317689 (UCSF): No Trial #NCT05065294 (UCSF): No Trial #NCT04932434 (UCSF): No Trial #NCT02950467 (UCSF): No

²⁹ Yes: IC Form directly addresses ethical challenge.

No: IC form does not mention or have indirect mention of ethical challenge.

Partial: IC form made an acknowledgment of importance, or an indirect, or brief mention of ethical challenge.

Culturally Responsive Care or Consent

Trial #NCT03537014 (MAPS): **No**

Trial #NCT05317689 (UCSF): **No**

Trial #NCT05065294 (UCSF): **No**

Trial #NCT04932434 (UCSF): **No**

Trial #NCT02950467 (UCSF): **No**

5. Challenging Informed Consent Per Se

Risk of harm is inherent to many clinical research trials. Informed consent requirements were created to ensure that participants have the ability to choose to participate with full understanding of what they may or may not be subjecting themselves to. Unfortunately, the history of research involving human subjects has been dominated by scandals (Fost & Levine, 2007) and so-called informed consent has not always guaranteed safety or participant understanding.

Many believe that mandating informed consent fails because too much is asked of it (Schneider, 2015). When consent is fully realized, it is a “communicative act that alters moral relations, authorizing activities that would otherwise be forbidden” (Koenig, 2014). Yet mounting evidence suggests that there are large disparities between the ideal of consent and its actual practice (Koenig, 2014). For example, in a cancer trial reviewed by Carl Schneider in *The Censor’s Hand: The Misregulation of Human-Subject Research*, major deficiencies in participants’ knowledge were detected even after they were given what was considered to be optimal informed consent resources (Schneider, 2015). The trial investigators conceded that important misunderstandings occurred as a result (Schneider, 2015). The major deficiencies included “not being aware of non-standard treatment, the potential for incremental risk or discomfort, the unproven nature of treatment and the uncertainty of the benefits to self” (Schneider, 2015). Many

“did not realize that the treatment being researched was not proven to be the best for their cancer, that the study used non-standard treatments or procedures, that participation may carry incremental risk or that they might not receive direct medical benefit from participation” (Schneider, 2015). Over half of participants in another study reported that they believed that consent was used to protect the institution or investigator from liability (Schneider, 2015). Some IRB professionals have agreed that consent is more concerned with protecting institutions than subjects (Fost & Levine, 2007) and many critics have asserted that research participants are inadequately protected (Fost & Levine, 2007). Participants may also be inadequately protected by virtue of the language used in the informed consent process. Prospective participants should be receiving information at a level understandable to average person. In the U.S. the average American reads at the seventh to eighth grade level; it has been suggested by the 2015 Institute of Medicine report “Informed Consent and Health Literacy,” to reflect this standard (Grant, 2021). It is worth considering placing greater emphasis on the whole of the consent process while deemphasizing the role of the consent form itself (Grant, 2021).

In the cases of historical and current P-AT trials, it is clear that protecting participants must move beyond them reading and agreeing to risks outlined in an IC form. Though the P-AT IC forms examined in this thesis were shown to play by the

letter of the rules for governance of human subjects, it is worth asking whether the rules (as constructed) are really up to the task of protecting participants from harm driven by the ethical complexities involved in P-AT research.

6. Conclusions: Future Research

The inability to obtain informed consent documents for study created limitations for a more robust analysis across trials examining psychedelic-assisted therapy interventions. Further good-faith efforts to collaborate and collect documents from willing investigators and organizations would provide more insight into the common themes being addressed by the field at large, and where the holes remain. Investigation into IRB processes of approval and the makeup of IRB committees approving forms and methodology may offer valuable insight. Performing interviews with all stakeholders involved, including IRB members, funding organizations, sponsors, and principal investigators, could help us glean where consensus (if any) is occurring, and what issues stakeholders are confronting in improving the informed consent process and research protocols at large. Lastly, seeking feedback from participants themselves should be prioritized. There is (as of yet) no research into participant understanding of risks and benefits going into a P-AT trial and the feelings of security they may (or may not) have experienced prior to, during, and after trial participation. It is through the eyes of those who have firsthand experience navigating P-AT trial protocols that we may learn and be most effectively guided towards how to create safe environments and better informed consent processes for future participants.

Appendix A

The *Psychedelics Today* podcast episode 327: *Confronting Abuse in Clinical Trials and the Future of Psychedelic Medicine* featured an interview with Rick Doblin (founder of MAPS) that focused on confronting the allegations and ethical issues revealed by the Buisson case. While Doblin acknowledged that one case of abuse is “one too many,” and that enhanced safety and changes to policy are necessary, he seemed strongly focused on ensuring that the audience knew that a transparent response to Buisson’s allegations was initiated by MAPS as soon as its leadership was made aware of the complaint. Doblin felt that *Cover Story* unfairly characterized MAPS as having malicious intent by withholding or hiding information (Drapkin, 2022).

Doblin went on to discuss MAPS’ process of quality control, explaining that reviews are administered by “adherence raters” who are trained to watch the videos and rate therapists’ adherence to the treatment manual. Doblin reported that during the study under legal scrutiny in which Buisson participated, Yensen and Dryer’s initial videos were reviewed, no concerns related to abuse were reported, and thus there was no further review of subsequent videos. It was not until Buisson (who was given her session videos by request) went forward publicly with complaints of ethical violations that the remaining sessions were reviewed. Doblin said that he believes it was a mistake to not have reviewed the videos related to the Buisson case sooner, but also argued that

it likely would not have prevented what happened since the original allegations were not related to the therapy itself but to the sexual misconduct that was initiated “after the fact” (Drapkin, 2022). After complaints of Yensen’s therapeutic misconduct in Buisson’s sessions surfaced, the associated videos were reviewed. Doblin stated: “What was going on in the video tapes [released by the media] is disturbing, however it was selectively edited,” and “what I would just say is that you get the impression from looking at the videos that these therapists are actively abusing this patient, they’re restraining her,” but it was “more of this technique related to Salvador Roquet (a Mexican psychiatrist) who developed a very ‘provocative’ approach, his idea being that when people are in non-ordinary states of consciousness, you can provoke people to bring buried emotions up to the surface.” Doblin did not condone the use of this technique, agreeing that there were certain elements of touch in Buisson’s sessions that were over a certain line. Doblin also noted that there was “a lack of double-checking consent,” and said he believes that Yensen’s behavior in the videos deviated from the treatment approaches outlined by the MAPS therapist manual (Drapkin, 2022). While this information about Yensen and his lack of adherence to the MAPS treatment protocols is relevant to this thesis, what felt most salient to me was Buisson’s experience of the therapy rather than MAPS’ evaluation of Yensen’s adherence to the manual. Regardless of the content of the therapy in question, Buisson felt harmed and she was sexually assaulted. Even if adherence

raters found no issue with Yensen's treatment of Buisson, Buisson's experience of harm should automatically trigger an evaluation of existing protocols to ensure they were and are sufficiently protecting participants.

Actions that have been taken by MAPS in response to Yensen's misconduct in Buisson's case that Doblin reported included: immediately cutting ties with both Yensen and Dryer; communicating what happened to all other therapists; issuing a public statement; and, based on feedback from Buisson, adding "a sentence or two" to the informed consent form warning about sexual or inappropriate feelings that may develop in the therapeutic relationship (Drapkin, 2022). Doblin disclosed that he was aware that after the filing of the lawsuit against Yensen and Dryer, Buisson asked for support for therapy while waiting for the trial to resolve and accepted \$15,000 CAD from MAPS to cover additional therapy until her trial reached a resolution. Doblin went on to state that MAPS lawyers originally had a non-disclosure agreement for Buisson to sign but did not feel Buisson should be constrained by an NDA, and removed this provision; Buisson was, however, asked to sign a document stating she would not sue MAPS further.

Doblin discussed changes in policies to review all videos related to any case that has reported misconduct of any kind but indicated that no other cases related to MAPS trials have received complaints of ethical misconduct at this time (as of June, 2022). A commentary will be published publicly regarding the content of the videos in the

Buisson case, though no timeline of its release was indicated. Enhanced training on the foundations of consent for MAPS therapists will also be initiated.

The FDA and Health Canada were notified at the time of complaint received by MAPS about Buisson's case and have not shut down any part of the MAPS trials as of June 2022, despite additional complaints filed by the *Cover Story* staff. Health Canada will be reviewing all trial records in the U.S. in June 2022, along with the regularly scheduled audits related to approval by the FDA, Health Canada, and the Israeli Ministry of Health³⁰. Though audits are happening prior to approval by the associated governing bodies, it would be useful to understand what elements the audit evaluates and the criteria with which they use to evaluate the trials, and what (if any) recommendations can be made for future treatment and research protocols in the event of the audit identifying ethical problems in one or more trials.

³⁰ MAPS MDMA-assisted therapy trials are comprised of 11 sites in the U.S., 2 sites in Canada, and 2 in Israel.

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