

## PREFACE

This dissertation has three parts, each of which focuses on a different aspect of the regulation of the medical uses of psychedelic drugs and marijuana in the United States. Part 1 examines the history and current status of the regulation of medical research using psychedelic drugs and marijuana. Part 2 analyzes various ethical, regulatory and methodological issues addressed in designing and evaluating the research studies that FDA will require to investigate the safety and efficacy of psychedelics and marijuana. Part 3 proposes a hypothetical regulatory regime governing the potential prescription use of psychedelic drugs for a variety of clinical indications.

The primary emphasis of this dissertation will be on regulatory issues of consequence for psychedelic psychotherapy research and potential prescription use of psychedelic drugs. Regulation of the medical uses of marijuana will also be examined, though to a lesser extent, due to the close interplay between the political pressures, laws, and regulatory dynamics that govern the medical uses of marijuana and the psychedelics.

### What is a Psychedelic Drug?

The word “psychedelic” was coined in 1956 by psychiatric researcher Dr. Humphry Osmond, who combined the Greek word *psyche* (mind) with *delein* (to make manifest) to create a new word meaning “mind manifesting.”<sup>1</sup> Dr. Osmond created the word “psychedelic” to describe a class of substances that catalyze the emergence into conscious awareness of previously unconscious, subconscious, repressed or filtered cognitions, perceptions and emotions, in a manner somewhat similar to dream states. Dr. Stanislav Grof, the world’s foremost psychedelic researcher, described LSD as a non-specific amplifier of the unconscious.<sup>2</sup> The effects of psychedelic drugs are distinct pharmacologically and psychologically from stimulants, sedatives, analgesics, inebriants (alcohol), anti-depressants and anti-anxiety drugs. Other terms that have been used to describe this class of drugs include hallucinogens, delirients, fantasticants, psychotomimetics, and entheogens.

Psychedelic drugs include LSD (d-lysergic acid diethylamide), a synthetic drug modified from compounds present in ergot, psilocybin (extracted from certain mushrooms), mescaline (extracted from the peyote cactus), ibogaine (extracted from the

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<sup>1</sup>Osmond H. A Review of the Clinical Effects of Psychotomimetic Agents. *Annals New York Academy of Science*. 66 (1957):418. Dr. Osmond first proposed the term psychedelic in 1956 within a poem he sent to Aldous Huxley, “To fathom hell or soar angelic, just take a pinch of psychedelic.” For more background on the development of the word, “psychedelic,” see: Osmond H. *Predicting the Past: Memos on the Enticing Universe of Possibility*. New York: Macmillan Publishing Co., 1981: 81-82.

<sup>2</sup>Grof S. *LSD Psychotherapy*. New York: Hunter House, 1980: 32.

iboga root), MDMA (methylenedioxyamphetamine, a synthetic drug modified from compounds present in nutmeg and saffron), ketamine (a synthetic drug), DMT (dimethyltryptamine, extracted from plants, present in certain toad excretions and the only psychedelic substance that is endogenous to the human brain), and other related substances. Extended back into pre-history, psychedelics have been used by humankind primarily as part of religious/healing rituals in which the participants sought and frequently reported obtaining a direct experience of a mystical/spiritual nature, with associated healing benefits both physical and psychological. Modern scientific research has primarily focused on the use of psychedelics within either a psychotherapeutic context or as tools better to understand the contents and processes of the mind.

While marijuana can be considered to have some psychedelic effects, the term “psychedelic” as used within this dissertation will not include marijuana. Marijuana’s impact on mental processes has not been the focus of most modern medical marijuana research, and almost all proposed medical applications of marijuana are based on its direct physiological effects.

### Part 1– Historical Review

Chapters 1 (pp.5-70) and 2 (pp. 71-129) of this dissertation focus on the history of the regulation of psychedelic drug and medical marijuana research on human subjects in the United States. Emphasis is placed on the gradual accretion of state, federal and international regulations governing the conduct of scientific research with psychedelics and marijuana, and on the ebb and flow of internal bureaucratic and external political forces that have worked to facilitate or limit such research. Chapter 1 covers the period 1874-1988, concluding at a time when psychedelic and medical marijuana research had been completely halted. Chapter 2 covers the period 1989 to the summer of 2000, beginning with the establishment of the Food and Drug Administration’s (FDA) Pilot Drug Evaluation Staff (PDES), the organizational unit within FDA that approved the renewal of psychedelic and medical marijuana research.

Chapter 3 (pp. 130-190) investigates the Pilot Drug Evaluation Staff itself, herein after referred to as Pilot Drug. Chapter 3 is based on a series of interviews conducted in 1999 and 2000 with key FDA personnel involved in Pilot Drug’s establishment, operation and elimination, on published trade press literature, media, and peer-reviewed journals, on publicly available as well as unpublished governmental investigations of Pilot Drug (General Accounting Office (GAO) and Office of Inspector General (OIG) reports), and on an “Internal Assessment” of Pilot Drug not available in the public record or obtainable through FOIA request.

The historical analysis seeks to demonstrate that government policy toward human clinical research into the potential medical applications of psychedelics has varied over the decades from open acceptance (1874-1962), growing concern (1963-1964), near total prohibition (1965-1989), cautious acceptance (1989-1996), reevaluation and retreat (1997-mid-1999) and, beginning in mid-1999 and for the foreseeable future, a return to a policy

of cautious acceptance.

From 1906-1989, FDA's changing policies of psychedelic research acceptance and growing disapproval closely track the social and political concerns about the non-medical use of psychedelics. From 1990 to the present, FDA's fluctuating policies of renewed openness, retreat and reevaluation, and return to cautious acceptance have been primarily determined not by external political pressures but by the choices and legacy of the small number of FDA personnel who authorized, created and worked within Pilot Drug.

Medical marijuana research followed a somewhat different pattern. The period of open acceptance of research into marijuana's medical uses began when research started around 1850 and ended in 1941, when marijuana was removed from the United States Pharmacopeia and National Formulary. Since that time, five research studies conducted from 1979-1983 examined smoked marijuana's medical use in controlling nausea in cancer chemotherapy patients. In the 1990s, Pilot Drug permitted the renewal of medical marijuana research, but only one study has so far been initiated, in HIV+ patients. The regulatory environment for medical marijuana research has been more restrictive than for psychedelic research due to the monopoly by the National Institute on Drug Abuse (NIDA) of the supply of marijuana (but not psychedelics) that can be used in FDA-approved research.<sup>3</sup>

## Part 2– Regulatory, Ethical and Methodological Issues in Psychedelic Research

As medical marijuana and psychedelic psychotherapy research is gradually conducted, both in the United States and abroad, the task of evaluating the data generated will be complicated by challenging methodological issues and passionately divisive political controversy. In order to protect and promote the health and safety of research subjects, patients, and the general public, a variety of difficult regulatory, ethical and methodological issues need to be examined carefully. Part 2 is a contribution toward that effort.

Chapter 4 (pp.191-254) begins by reviewing different standards of proof that FDA could use to evaluate whether data about the medical use of marijuana or a psychedelic drug are sufficient to justify approval for prescription use. The analysis addresses regulatory, ethical and methodological considerations. Chapter 4 focuses in large part on problems with and alternatives to the use of randomized placebo-controlled double-blind studies with substances whose powerful subjective effects usually enable patients and experimenters to pierce the blind. Chapter 4 concludes that there are no compelling justifications for using any different standard of proof than the one FDA uses with most other drugs it reviews, that

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<sup>3</sup>There will be occasional references throughout this dissertation to a non-profit organization called the Multidisciplinary Association for Psychedelic Studies (MAPS). MAPS was founded in 1986 and is currently directed by this author. MAPS raises funds from its over 1700 members and supports government-approved clinical research into the risks and benefits of psychedelic drugs and marijuana. MAPS supports projects in a variety of countries, primarily the United States, Switzerland, and Russia, and is seeking to support studies in Spain and Israel. For more information, see [www.maps.org](http://www.maps.org).

being the comparison of the medical use of the test drug, in this case psychedelic psychotherapy or marijuana, with placebo.

Chapter 5 (pp. 255-298) recognizes that the controversial nature of claims about beneficial uses of psychedelics and marijuana will necessitate a higher standard of proof and more complex protocol designs. Chapter 5 includes a critical evaluation of all currently-approved psychedelic psychotherapy protocols around the world and proposes an enhanced design for any large-scale Phase III trials on the safety and efficacy of psychedelic psychotherapy. The economic implications of this enhanced design are evaluated and determined not to impose an unreasonable burden on sponsors of research into potential medical uses of psychedelics or marijuana.

### Part 3– A Proposal for the Regulation of Psychedelic Psychotherapy

Chapter 6 (pp.299-368) is an exercise in regulatory policy design. This chapter begins with the assumption that FDA has been presented with sufficient data proving the safety and efficacy of psychedelic psychotherapy for at least one clinical indication. The chapter then reviews the range and limits of FDA power to control the medical use of prescription medicines. The authority of the Drug Enforcement Administration (DEA) to control the prescription use of controlled substances is also evaluated. In an attempt to learn by analogy, the regulatory systems for the control of the medical use of methadone, thalidomide and electroconvulsive therapy are analyzed.

Chapter 6 proposes a rigorous regulatory regime for the control of psychedelic psychotherapy. The primary features of this proposal are the limitation of prescribing power to board-certified psychiatrists, the requirement that all prescribers participate in a specialized training and educational program, the licensing of facilities within which psychedelic psychotherapy can take place, mail-order distribution from a single source, and a national patient registry to record all treatment sessions. Within such a regulatory system, psychedelic psychotherapy could possibly make a positive contribution to the health and welfare of the American public.