No. 21-70544

In the United States Court of Appeals for the Ninth Circuit

ADVANCED INTEGRATIVE MEDICAL SCIENCE INSTITUTE, PLLC, DR. SUNIL AGGARWAL, MD, PHD, MICHAL BLOOM, AND ERINN BALDESCHWILER,

Petitioners,

v.

U.S. DRUG ENFORCEMENT ADMINISTRATION; MERRICK GARLAND, IN HIS OFFICIAL CAPACITY AS ATTORNEY GENERAL; AND D. CHRISTOPHER EVANS, IN HIS OFFICIAL CAPACITY AS ACTING ADMINISTRATOR OF THE U.S. DRUG ENFORCEMENT ADMINISTRATION,

Respondents.

PETITIONERS' OPENING BRIEF

Kathryn L. Tucker
Emerge Law Group
621 SW Morrison Street
Suite 900
Portland, OR 97205
Phone: 206.595.0097
kathryn@emergelawgroup.com

Matthew C. Zorn
Yetter Coleman LLP
811 Main Street, Suite 4100
Houston, Texas 77002
Phone: 713.632.8000
Fax: 713.632.8002
mzorn@yettercoleman.com

James F. Williams
Andrew J. Kline
Thomas J. Tobin
Holly Martinez
Perkins Coie LLP
1201 Third Avenue, Suite 4900
Seattle, WA 98101-3099
Phone: 206.359.8000
Fax: 206.359.9000
jwilliams@perkinscoie.com
akline@perkinscoie.com
ttobin@perkinscoie.com
hmartinez@perkinscoie.com

Shane Pennington
Vicente Sederberg LLP
1115 Broadway, 12th Floor
New York, NY 10010
Phone: 917.338.5455
Fax: 303.860.4504
s.pennington@vicentesederberg.com

Attorneys for Petitioners

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INTRODUCTION

This case, like *Gonzales v. Oregon*, 546 U.S. 243 (2006), before it, arises from a federal law-enforcement agency's attempt to use the Controlled Substances Act ("CSA") to thwart state medical practice to the detriment of dying patients.

In *Oregon*, the Court held that the CSA did not permit the Attorney General—the nation's chief law-enforcement officer—to "bar dispensing controlled substances for assisted suicide in the face of a state medical regime permitting such conduct." 546 U.S. at 275. Here, dying patients seek access to promising new treatments still in the investigative process—access expressly permitted under both state and federal law—to help them live in peace. Once again, the CSA blocks the way. Framing its effort to undermine democratic processes at the state and federal levels as an act of administrative *restraint*, DEA claims it lacks authority to waive the CSA's requirements to permit therapeutic use for these patients.

DEA's refusal comes in the wake of a significant paradigm shift in federal and state law. In less than a decade, a democratic movement swept the nation, with a supermajority of states voting to empower terminally ill patients with a "Right to Try" ("RTT") certain unapproved, investigational drugs for therapeutic use. Forty-one states have passed these laws since

2014. And in 2018, the federal government followed the states' lead. To "expand[ ] the scope of individual liberty and agency among patients, in limited circumstances," Congress added § 561B to the Federal Food Drug and Cosmetic Act ("FDCA"), "establish[ing] national standards and rules by which investigational drugs may be provided to terminally ill patients" and providing an exemption to permit therapeutic use of unapproved drugs by terminally ill patients under specified conditions.

In early 2021, Petitioner Dr. Sunil Aggarwal sought to vindicate these changes in the law to provide psilocybin, an investigational drug, to his terminally ill patients for therapeutic use under Washington's RTT. In recent years, psilocybin has shown enormous promise in early clinical trials in relieving debilitating anxiety and depression suffered by terminally ill patients. But because FDA has not approved psilocybin for interstate marketing, it remains a schedule I controlled substance. No supplier would provide psilocybin to Dr. Aggarwal without DEA's blessing.

Dr. Aggarwal sought DEA's guidance regarding how to proceed. DEA responded with a perfunctory letter ("the final decision") categorically refusing to accommodate medical practice under RTT laws. "Absent an explicit statutory exemption to the Controlled Substances Act (CSA)," it

explained, "DEA has no authority to waive any of the CSA's requirements pursuant to the RTT."

This Court should set aside DEA's determination, which rests on unsound interpretations of the FDCA and the CSA. In substance, DEA's final decision marks yet another impermissible intrusion by federal law-enforcement into the states' sovereign authority to regulate the practice of medicine—the very sort of intrusion rebuked by this Court and the Supreme Court in *Oregon*.

First, the CSA's text and federal drug law more generally compel DEA to accommodate federal and state RTT laws. DEA says "[a]bsent an explicit statutory exemption" to the CSA it cannot accommodate these laws. But the CSA itself forbids DEA from construing CSA provisions "in any way" that would "affect[ ], modify[ ], repeal[ ], or supersed[e]" FDCA provisions. 21 U.S.C. § 902. By construing the CSA to supersede the FDCA's RTT provisions, however, DEA's final decision does just that. DEA's faulty interpretation also threatens core federalism values and poses constitutional questions demanding avoidance.

Second, the CSA's text, DEA's regulations and past practice administering that text, and controlling judicial precedent all refute DEA's denial of authority to waive the CSA's requirements absent "explicit statutory

exemption." DEA's unexplained conclusion to the contrary is arbitrary, capricious, and contrary to law.

Third, DEA can make exceptions and has done so in the past. As a result, its failure to accommodate RTT marks an unexplained departure from past practice. And while DEA has for decades invoked FDCA standards when administering the CSA, here, in the final decision, it does an abrupt about face—abandoning those standards in the RTT context without explanation. Reasoned decision-making under the Administrative Procedure Act requires more of an agency seeking to change a long-settled policy—especially one that has engendered serious reliance interests like those of patient Petitioners here.

For these and other reasons discussed further below, Petitioners urge this Court to grant the petition for review.

JURISDICTIONAL STATEMENT

"[A]ny person aggrieved" by a final DEA determination may seek review of the decision in the United States Court of Appeals in the circuit in which his principal place of business is located within thirty days after notice of the decision. 21 U.S.C. § 877. On March 8, 2021, Petitioners timely petitioned for review of DEA's final decision concluding that it had "no authority to waive" the CSA's requirements to accommodate state or federal

RTT laws. *See* 21 U.S.C. § 360bbb, *et seq.*; RCW 69.77, *et seq* ; Petition for Review, ECF No. 1.

Each Petitioner suffers an injury from the final decision and seeks to vindicate interests within the CSA's zone-of-interests. *See PDK Labs. Inc. v. DEA*, 362 F.3d 786, 793 (D.C. Cir. 2004). Petitioners the Advanced Integrative Medical Science ("AIMS") Institute and its Co-Director, Dr. Sunil Aggarwal, seek to access psilocybin therapy with patients under RTT laws. Petitioners Erinn Baldeschwiler and Michal Bloom are patients with advanced cancer under Dr. Aggarwal's care.

PERTINENT STATUTES AND CONSTITUTIONAL PROVISIONS

Pertinent statutes and constitutional provisions appear in the addendum.

STATEMENT OF THE ISSUES

1. Can DEA refuse to accommodate RTT based on a construction of the CSA that supersedes the FDCA's RTT provisions? *No*.

2. The CSA empowers DEA to waive its requirements, and DEA has exercised that exception-making power repeatedly in the past. Is DEA's conclusion to the contrary in the final decision contrary to law? *Yes*.

3. Given DEA's (A) past practice of waiving CSA requirements in various circumstances and (B) steadfast reliance on FDCA standards when

administering the CSA, does the agency's failure to explain its refusal to accommodate the FDCA's RTT provisions render the final decision arbitrary and capricious? *Yes*.

STATEMENT OF THE CASE

I. Statutory and Regulatory Background

"[O]ur Nation has long expressed interest in drug regulation, calibrating its response in terms of the capabilities to determine the risks associated with both drug safety and efficacy." *Abigail All. for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695, 703 (D.C. Cir. 2007) (en banc), *cert. denied*, 128 S. Ct. 1069 (2008). This case involves four such calibrations:

A. **1938**. The FDCA, which first empowered FDA to prohibit interstate marketing of unsafe drugs.

B. **1962**. The 1962 FDCA Amendments, which required FDA to evaluate both the safety and efficacy of new drugs before approving them for interstate marketing.

C. **1970**. The CSA, which Congress enacted to curb drug abuse and diversion by, among other things, prohibiting unauthorized distribution of controlled substances.

D. **2018**. Federal RTT law, which amended the FDCA to dial back the 1962 efficacy requirement to permit terminally ill patients to access drugs that, while safe, have not yet been proven efficacious.

A. The FDCA

Enacted in 1938 as a consumer-protection measure, the FDCA established the modern premarket-approval system for drug distribution. *Abigail All.*, 495 F.3d at 705. Under this system, no new drug can enter interstate commerce without FDA approval.

Before premarket approval, the federal government regulated drug distribution under the Pure Federal Food and Drugs Act of 1906, 34 Stat. 768 ("FFDA").[1] The FFDA prohibited the manufacture or interstate shipment of "adulterated" or "misbranded" drugs, "supplement[ing] the protection for consumers already provided by state regulation and common-law liability." *Wyeth v. Levine*, 555 U.S. 555, 566 (2009). Under the FFDA, however, FDA was limited to after-the-fact enforcement. David F. Cavers, *The Food, Drug, and Cosmetic Act of 1938: Its Legislative History and Its Substantive Provisions,* Law & Contemp. Probs. 2, 6 (1938) (under the FFDA, FDA effectively served as "a policing organization, acting after the event to detect violations of the law").

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[1] Before that, few federal laws regulated the domestic manufacture and distribution of drugs. P.B. Hutt, 42 Food Drug & Cosmetic L.J. 1, 1 (1987). That changed in the early 1900s after reports of the adulteration of the food and drug supply proliferated. *See generally* Hutt at 2-3 (citing legislative history). Since then, "Congress has enacted a series of comprehensive laws to regulate every aspect of commerce in food, drugs, and cosmetics." *Id.*

This reactive paradigm changed with the introduction of premarket approval in the 1938 Act, Pub. L. 75-717, 52 Stat. 1040. The innovation followed the 1937 "Elixir Sulfanilamide" tragedy, where at least 100 people died as a direct result of taking a drug that had been tested for flavor but not for its effect on human life. *See Abigail All.*, 495 F.3d at 725 (Rogers, J., dissenting) (citing legislative history); Cavers, Law & Contemp. Probs. 2, 20 (calling tragedy "directly responsible" for premarket approval). To prevent another similar tragedy, Congress added § 505 to the 1938 Act, which stated that "[n]o person shall introduce or deliver for introduction into interstate commerce any new drug" unless a new drug application ("NDA") for the drug was approved. 52 Stat. 1052–53. The statute charged FDA with reviewing applications to determine if drugs were "safe for use." *Id.*

Although these provisions required FDA to control drugs available for prescribing, "Congress did not intend the [FDA] to interfere with medical practice and references to the understanding that the bill did not purport to regulate the practice of medicine as between the physician and the patient." *See* 35 Fed. Reg. 16,503 (Aug. 15, 1972) (discussing legislative history).

B. The 1962 FDCA Amendments

Since the 1938 Act, Congress has recalibrated the FDCA to reflect changes in medicine, emerging technologies, and new societal norms. *See,*

e.g., Food Additives Amendment of 1958, Pub. L. 85-929, 72 Stat. 1784; Radiation Control for Safety and Health Act, Pub. L. 90-602, 82 Stat. 1173 (1968); Dietary Supplement Health and Education Act, P.L. 103-417, 108 Stat. 4332 (1994). The most consequential change was the Drug Act Amendments of 1962, 76 Stat. 780, which revolutionized drug development nationwide by requiring manufacturers to demonstrate a drug's safety *and* efficacy before marketing it interstate.

This recalibration came on the heels of another national tragedy. In the late 1950s, Thalidomide was hailed as a wonder drug for morning sickness and a panoply of other conditions. *See* Sue McGrath, *Only A Matter of Time: Lessons Unlearned at the Food and Drug Administration Keep Americans at Risk*, 60 Food & Drug L.J. 603, 607 (2005) (Thalidomide touted "not only as a sedative, but also as a treatment for anxiety, asthma, cancer, alcoholism, marital discord, poor school work, and premature ejaculation"). By 1961, the drug was connected to birth defects, prompting Congress to "greatly widen the powers of the Secretary to adopt regulations pertaining to interstate distribution and sale of new drugs." *Turkel v. FDA*, 334 F.2d 844, 845 (6th Cir. 1964).

Congress's key change was requiring FDA "to scrutinize and evaluate drugs for effectiveness as well as safety." *Weinberger v. Hynson, Westcott &*

Dunning, Inc., 412 U.S. 609, 630 (1973). Through "adequate and well-controlled clinical studies conducted by qualified experts," manufacturers must show both a drug's safety and efficacy—i.e., "substantial evidence" that a drug would "have the effect it purports or is represented to have"—before introducing it into interstate commerce. 21 U.S.C. § 355(d).

Current FDA regulations expand on these requirements. After preliminary studies identify a promising drug, the sponsor of a clinical trial may submit an investigational new drug ("IND") application to FDA to begin human testing. *Id.* § 355(i). INDs must include a proposed study design and detailed information about the drug. 21 C.F.R. § 312.23. An Institutional Review Board must approve and supervise each clinical trial to ensure participants are aware of the drug's investigative status and associated risks. *Id.* § 312.23(a)(1)(iv).

Once FDA approves an IND, the drug's sponsor may begin clinical trials. IND investigations typically proceed in three phases. *Id.* § 312.21. Phase 1 trials typically include twenty to eighty subjects and focus on safety and early evidence of efficacy. *Abigail All.*, 495 F.3d at 698 (citing 21 C.F.R. § 312.21(a)(1)). If a drug successfully completes Phase 1 trials, its sponsor may proceed with Phase 2 and Phase 3 trials, which include more subjects and focus more heavily on efficacy. *See* 21 C.F.R.§§ 312.21(b)–(c).

On average, this process takes nearly seven years, start to finish. *Abigail All.*, 495 F.3d at 697.

C. The CSA

Congress enacted the CSA in 1970 "to conquer drug abuse and to control the legitimate and illegitimate traffic in controlled substances." *Gonzales v. Raich*, 545 U.S. 1, 12 (2005). According to William Vodra, DEA's former chief counsel and principal author of the CSA's initial implementing regulations, the law's "raison d'etre is to enable the U.S. Government to minimize the quantity of drugs of abuse which are available to persons who are prone to abuse drugs." ER-71 (William Vodra, *The Controlled Substances Act*, 2 Drug Enforcement 2 (1975)).

1. Limitations on Regulating Medical Practice

Congress "clearly" intended to limit the CSA to problems associated with drug abuse, addiction, and diversion. *Oregon v. Ashcroft*, 368 F.3d 1118, 1128 (9th Cir. 2004). "In concept, in spirit, and in detail," it is a "law-enforcement measure," *see* 116 Cong. Rec. 973 (1970), and "manifests no intent to regulate the practice of medicine generally," *Oregon*, 546 U.S. at 270. Indeed, Congress legislated against the backdrop of federalism and presumed competent regulation of the medical profession under the states' police powers. *Id.*

Congress was especially uncomfortable with entrusting law-enforcement with determining the appropriateness of medical practice. *See Ashcroft*, 368 F.3d at 1128 (quoting legislative history); *Oregon*, 546 U.S. at 266 (explaining that the CSA "conveys unwillingness to cede medical judgments to an executive official who lacks medical expertise"). Although the Attorney General retained final authority on drug scheduling, legislators found compromise by carefully allocating authority to administer the CSA among HHS, the Attorney General (or his delegee, DEA), and the states. "To the limited extent that the CSA does authorize federal regulation of medical practice," it "carefully circumscribe[s]" DEA's role. *Ashcroft*, 368 F.3d at 1126. In administering the schedules, for example, DEA is bound by HHS determinations on medical and scientific matters. *See* 21 U.S.C. § 811(b). In addition, with two limited exceptions, nothing in the CSA may be "construed as in any way affecting, modifying, repealing, or superseding the provisions of the [FDCA]." And finally, the CSA's preemption provision expressly preserves traditional state authority over the practice of medicine. *Id.* § 903. *See also Oregon*, 546 U.S. at 270; *Ashcroft*, 368 F.3d at 1116.

These provisions and others prohibit DEA from making "anterior judgment[s]" about what constitutes accepted medicine or medical treatment. *Oregon*, 546 U.S. at 272. While DEA can establish controls

"against diversion," it cannot "define diversion based on [its] view of legitimate medical practice." *Id.* at 260. Nor does the CSA "set general, uniform standards of medical practice." *Id.* at 271.

2. The Closed System and Schedules

To aid law-enforcement, the CSA "consolidate[d] various drug laws on the books into a comprehensive statute." *Raich*, 545 U.S. at 10. To this end, the statute establishes a "closed system" of drug distribution and a uniform drug-classification framework.

First, under the "closed system," it is unlawful to manufacture, distribute, dispense, or possess any controlled substance except as authorized by the CSA. *Id.* at 12–13 (citing 21 U.S.C. §§ 841(a)(1), 844(a)); *see also United States v. Moore*, 423 U.S. 122, 141 (1975) (quoting H.R. Rep. No. 91–1444 (1970)). Every handler of a controlled substance must register with DEA and is subject to a set of administrative controls. *See* 21 C.F.R. § 1301.11; *see also Wedgewood Vill. Pharm. v. DEA*, 509 F.3d 541, 543 (D.C. Cir. 2007). Registrants must keep complete records of all manufacturing, purchases, sales, and inventories of the substance. *See* 21 C.F.R. § 1304.04.

Second, the CSA introduced drug schedules to replace the patchwork of drug laws that preceded it. This uniform drug-classification framework is

the CSA's "cardinal feature." *Nat'l Org. for Reform of Marijuana Laws ("NORML") v. Ingersoll*, 497 F.2d 654, 656 (D.C. Cir. 1974).

Restrictions on the manufacture, distribution, and possession of a controlled substance depend on the where it appears in the schedules. *See* 21 U.S.C. §§ 821–29. Controls and penalties track the schedules—the lower the number the more restrictive the controls and the more severe the penalties. *See* ER-75-76. Placements of drugs on the five schedules are based on factual findings related to accepted medical uses, potential for abuse, and effects on the body. 21 U.S.C. § 812(b). Congress made these findings initially and tasked DEA with updating the schedules going forward. *Raich*, 545 U.S. at 13.

Schedule I drugs are deemed to have (1) "a high potential for abuse," (2) "no currently accepted medical use in treatment in the United States," and (3) "a lack of accepted safety for use … under medical supervision." 21 U.S.C. § 812(b)(1). Schedule II drugs differ in only one meaningful respect: While schedule I and II drugs are subject to nearly identical, severe restrictions, because schedule I drugs are deemed to have "no currently accepted medical use in treatment in the United States," doctors may not prescribe them. *Id.* § 812(b)(1)(B). Schedule II drugs, by contrast, are available for prescription. 21 U.S.C. § 829(a). As the table from Vodra on the

next page illustrates, registration, control, and penalty provisions for schedules I and II drugs are otherwise *identical*:

Schedule	Registration	Recordkeeping	Manufacturing Quotas	Restrictions	Dispensing Limits	Import-Export	Security	Manufacturer/ Distributor Reports to DEA	Criminal Penalties
I	Required	Separate	Yes	Order forms	Research use only	Permit	Vault	Yes	15 years/ $25,000 (narcotic) 5 years / $15,000 (non-narcotic)
II	Required	Separate	Yes	Order forms	Rx: no written refills	Permit	Vault	Yes	15 years/ $25,000 (narcotic) 5 years / $15,000 (non-narcotic)
III	Required	Readily retrievable	No but some drugs limited by schedule I quotas	DEA registration number	Rx: written or oral; with medical authorization, refills up to 5 times in 6 months	Permit (narcotic) Notice (non-narcotic)	Surveillance	Yes (narcotic) No (non-narcotic)	5 years / $15,000
IV	Required	Readily retrievable	No but some drugs limited by schedule I quotas	DEA registration number	Rx: written or oral; with medical authorization, refills up to 5 times in 6 months	Permit (narcotic) Notice (non-narcotic)	Surveillance	Yes (narcotic) No (non-narcotic)	3 years / $10,000
V	Required	Readily retrievable	No but some drugs limited by schedule I quotas	DEA registration number	OTC (Rx drugs limited to MD's order)	Permit (import, narcotic) Notice (export, narcotic) Notice (non-narcotic)	Surveillance	Manufacture only (narcotic) No (non-narcotic)	1 year / $5,000

ER-75–76.

In practice, whether a drug belongs in schedule I or II hinges entirely on whether clinical trials have shown it to be safe and effective. According to DEA, a drug has a "currently accepted medical use in treatment in the United States" for purposes of 21 U.S.C. § 812(b)(1)(B) if it has FDA approval or satisfies a five-part test drawn from FDA standards:

(1) the drug's chemistry must be known and reproducible;

(2) there are adequate safety studies;

(3) there are adequate and well-controlled studies proving efficacy;

(4) the drug is accepted by qualified experts; and

(5) the scientific evidence must be widely available.

See All. for Cannabis Therapeutics v. DEA, 15 F.3d 1131, 1135 (D.C. Cir. 1994). As DEA has explained, this test reflects the core safety and efficacy standards "developed under the FDCA" for approving drugs for interstate marketing. 57 Fed. Reg. 10,499–04 (Mar. 26, 1992).

3. Exceptions

Despite the CSA's "closed" and "comprehensive" nature, DEA has wide discretion to make exceptions and issue exemptions, for example, under 21 C.F.R. § 1307.03:

> **§ 1307.03 Exceptions to regulations.** Any person may apply for an exception to the application of any provision of this chapter by filing a written request with the Office of Diversion Control, Drug Enforcement Administration, stating the reasons

> for such exception. See the Table of DEA Mailing Addresses in Sec. 1321.01 of this chapter for the current mailing address. The Administrator may grant an exception in his discretion, but in no case shall he/she be required to grant an exception to any person which is otherwise required by law or the regulations cited in this section.

See also 21 U.S.C. § 822(d) (authorizing waiver of registration requirements if consistent with public health and safety).

As the following examples show, DEA has often exercised these powers (as well as the agency's broad rulemaking authority under the Act, *see, e.g.*, 21 U.S.C. §§ 821, 871(b)), to grant partial or full exceptions to CSA requirements. Indeed, these exceptions have proven instrumental in maintaining the flexibility and integrity necessary to achieve the CSA's goals in light of Congress's key findings that while many controlled drugs "have a useful and legitimate medical purpose and are necessary to maintain the health and general welfare of the American people[,]...improper use of controlled substances have a substantial and detrimental effect on the health and general welfare of the American people." *Id.* § 801(1), (2).

a. Peyote and Religious Use

DEA has long permitted use of peyote—a schedule I substance—for religious use. *See Gonzales v. O Centro Espirita Beneficente Uniao do Vegetal*, 546 U.S. 418, 433 (2006) ("*UDV*") (citing 21 CFR § 1307.31). A 1981 memo from the Department of Justice's ("DOJ") Office of Legal Counsel

explains that DEA regulations exempting peyote use accurately reflect Congress' intent to exempt bona fide religious use of peyote. Memo Op. for the Chief Counsel, DEA, Peyote Exemption for Native American Church, 5 Op. O.L.C. 403, 404 (Dec. 22, 1981) ("DOJ Memo"). Not surprisingly, DEA once noted the exemption "has nothing to do with the vast and violent traffic in illegal narcotics that plagues this country" and that "it is unaware of the diversion of peyote to any illicit market." H.R. Rep. 103—675, at 4 (1994) (summarizing DEA testimony).

Likewise, following *UDV*, DEA issued guidance to parties wishing to petition for a religious exemption to DEA's regulations implementing the CSA. *See Arizona Yage Assembly v. Barr*, 2020 WL 5629833, at *2 (N.D. Cal. Sept. 21, 2020). [2] This guidance provides that those who seek religious exemptions must agree to comply with all applicable laws and CSA regulations governing registration, labeling and packaging, quotas, recordkeeping and reporting, security and storage, and periodic inspections.

[2] *See* Guidance Regarding Petitions for Religious Exemption from the Controlled Substances Act Pursuant to the Religious Freedom Restoration Act, at https://www.deadiversion.usdoj.gov/GDP/(DEA-DC-5)%20Guidance%20Regarding%20Petitions%20for%20Religious%20Exemptions.pdf.

b. Partial Control

The CSA permits DEA to exempt controlled substances from certain control mechanisms. ER-78. One longstanding DEA exemption, for example, relates to chemical preparations and mixtures containing controlled substances not intended for human consumption. *See id.* (citing 21 C.F.R. §§ 1308.23-.24). As Vodra explains, this "exemption authority does not specifically appear in the statute but derives from inherent powers of DEA to provide for the efficient execution of the statute pursuant to 21 U.S.C. § 871(b)." ER-80.

c. Public Health Waivers

Over the years, DEA has invoked its waiver power under 21 U.S.C. § 822(d) to make discrete exceptions to the CSA's otherwise-closed distribution scheme.

Start with the very first regulations promulgated to implement the CSA. In 1971, DEA's predecessor, the Bureau of Narcotic and Dangerous Drugs ("BNDD") invoked § 822(d) to permit "limited, irregular distribution of controlled substances by a practitioner for the purpose of accommodating and servicing another practitioner, without the supplying practitioner's being registered as a distributor" to the extent "consistent with public health and safety." 36 Fed. Reg. 18,727 at 18,727–28 (Sept. 21, 1971). Permitting

practitioners to distribute less than five percent of a practitioner's total volume of controlled drugs without having to register as a distributor, BNDD explained, was "not encouraging pharmacies and other practitioners to expand their distribution activities." *Id.* Already-registered practitioners were providing a service—not "engaging in a commercial activity." *Id.*

More recently, DEA proposed waiving the requirement that narcotic treatment programs carry separate registrations at each principal place of business or professional practice where controlled substances are dispensed. *See* 85 Fed. Reg. 11,008 (Feb. 26, 2020). Under the proposed rule, registrants would not need a separate registration for mobile components registrants use to transport controlled substances. *Id.* This would "make maintenance or detoxification treatments more widely available, while ensuring that safeguards are in place to reduce the likelihood of diversion." *Id.*

Similarly, DEA waived the CSA's registration requirements to permit use of a radiopharmaceutical schedule II drug. 79 Fed. Reg. 70,085 (Nov. 25, 2014). Because of its radioactive nature, the drug was already strictly controlled under other federal and state laws, thus limiting distribution to certain licensed medical facilities. *Id.* at 70,087. DEA thus concluded that a

waiver for persons administering the drug directly to patients was consistent with the public health and safety under § 822(d). *Id.* at 70,086.

d. The Federal Medical Marijuana Program

For nearly fifty years, DEA has provided marijuana for therapeutic use, despite its schedule I classification. *See* Erwin Chemerinsky et al., *Cooperative Federalism and Marijuana Regulation*, 62 UCLA L. Rev. 74, 110, n. 114 (2015) (discussing the history of the federal medical marijuana program); *Kuromiya v. United States*, 78 F. Supp. 2d 367, 368–70 (E.D. Pa. 1999).

In 1972, twenty-four-year-old Robert Randall was diagnosed with a severe form of glaucoma and told he would be blind within five years. Lewis A. Grossman, *Life, Liberty, (and the Pursuit of Happiness): Medical Marijuana Regulation in Historical Context*, 74 Food & Drug L.J. 280, 292 (2019). One year later, Randall smoked marijuana cigarettes he received from a friend and noticed that the halos that normally impaired his vision disappeared. *See id.* Randall then began cultivating his own marijuana to treat his glaucoma. *See id.* In 1975, he was arrested and tried. *See id.* Randall's doctor and the researcher who had first linked marijuana use with reducing eye pressure testified on his behalf, and the court dismissed the charges after concluding that Randall had established a case of medical

necessity. *Id. See also United States v. Randall*, 104 Wash. L. Rep. 2249 (D.C. Sup. Ct. 1976).

In parallel, Randall's attorneys also successfully petitioned FDA to have him included in a research program that would afford him ten marijuana cigarettes per day. Patient's History of Medical Cannabis, Americans for Safe Access, *available at* https://www.safeaccessnow.org/patients_history_of_medical_cannabis (describing Randall case). Under this nominal research program, Randall received a monthly supply of medical marijuana cigarettes from the federal government's cultivation site at the University of Mississippi. D. Oberhaus, The US Government Has Sent This Guy 300 Joints Each Month for 34 Years, Vice (Sept. 8, 2016) *available at* https://www.vice.com/en/article/dp3e4y/the-us-government-has-sent-this-guy-300-joints-each-month-for-34-years (stating that the University of Mississippi is the sole grower for all federal marijuana). When Randall's doctor moved in 1978, the federal government tried to cut off Randall's supply. Randall sued, and the government settled, resulting in FDA creating the Compassionate IND Program to allow Randall sustained access to this unapproved schedule I drug. *See Kuromiya*, 37 F. Supp. 2d at 720. Known

as a "Single-Patient IND," the program was a kludge to provide single patients access to unapproved drugs—even schedule I controlled substances:

> Single patient INDs cannot establish the scientific efficacy of new drugs; nor are they intended to permit the widespread distribution of unapproved drugs. The INDs are not conducted in controlled clinical settings, nor are they blinded or closely monitored by FDA or the clinical investigators. Thus, reports resulting from single patient INDs are merely anecdotal, and are not designed in a manner to provide the type of scientific data necessary to establish the safety and efficacy of a new drug.

Id. at 369 (quoting government witness affidavit).

To apply, an applicant had to find a physician sponsor, submit paperwork to FDA, and provide a letter from the supplier confirming the drug's availability. *See* ER-57–67 (Ltr. from Dr. James Mason, Asst. Sec'y for Health, HHS to Dr. Louis Sullivan, HHS Sec'y re: Therapeutic Use of Marijuana—Decision (Jan. 31, 1992; approved Mar. 4, 1992) (cited as Ex. 3 at *Kuromiya*, 78 F. Supp. at 369–70)). In the case of marijuana, because the federal government monopolizes cultivation, the National Institute of Drug Abuse ("NIDA") had to supply. *See* Oberhaus, *supra* (describing Rosenfeld case and IND program). In addition, DEA was required to conduct a site investigation for security, a criminal background check, and "register all physicians who *prescribe Schedule I drugs*." ER-59 (emphasis added). Approved applicants had to file annual reports documenting the effects of the drug and a statement from a physician regarding whether the patient

should continue with the experimental therapy. *Id.* *See also* Alex Kreit, *The Future of Medical Marijuana: Should the States Grow Their Own?*, 151 U. Pa. L. Rev. 1787, 1795 (2003) (describing paperwork).

Only about a dozen people were ever admitted to the "anomalous" program before DEA and FDA jointly terminated it. *Kuromiya*, 78 F. Supp. 2d at 369. In a letter to HHS, DEA contended that marijuana smokers were "using the suffering of people with serious medical problems as a means of making marijuana more readily available for their own use" and that having to respond to applications for single-patient INDs placed "an undue burden of work on the DEA." ER-66–67 (Ltr. from Stephen Greene, Acting Dep'y Admin., DEA, to Dr. James Mason, Asst. Sec'y Health, HHS (Mar. 4, 1992)). DEA further claimed that "the use of marijuana in the single patient studies being pushed will not demonstrate the medical utility of the substance." *Id.* DEA proposed working with HHS to "formulate policies on regulatory issues related to the use of marijuana in the treatment of disease." *Id.*

A month later, FDA declared that marijuana would no longer be available through single-patient IND. ER-68–70 (Memo Re: Letters to IND Investigators Receiving Marijuana Out from D. Spyker to F. Cook (Apr. 23, 1992)). FDA terminated the program to "find a balance between providing

everything possible to ease the suffering of chronically ill patients while at the same time adhering to best medical practice." ER-70.

D. Right to Try Laws

In 2018, following a wave of state RTT enactments, Congress enacted a federal RTT law "[t]o authorize the use of unapproved medical products by patients diagnosed with a terminal illness in accordance with State law." Pub. L. 115-176. The Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 added § 360bbb-0a to the FDCA, establishing an exception to the statute's safety/efficacy requirements for premarket approval for unapproved investigational drugs that have successfully completed Phase 1 trials. Where it applies, the law permits distribution of unapproved drugs for therapeutic use by patients with life-threatening illness who have exhausted available treatment options.

Federal RTT effects a paradigm shift in the availability of investigational drugs for patients with life threatening illness, effectively reverting to the 1938 Act's safety-only paradigm for these individuals. Rather than impose the general safety/efficacy norm, federal RTT allows states to choose whether and to what extent this patient population should have the right to try EIDs.

1. *Abigail Alliance*

Like many recalibrations of federal drug control law, the RTT movement began with tragedy. One year into treatment, teenager Abigail Burroughs had exhausted all conventional treatment options for her cancer. Her oncologist urged FDA to allow her to try an unapproved investigational treatment. *See* Valarie Blake, *The Terminally Ill, Access to Investigational Drugs, and FDA Rules*, 15 AMA J. of Ethics 687, 687 (2013). FDA denied the request, and in 2001, Abigail died of cancer at age 21. Years later, FDA approved the drug to treat her type of cancer. *See FDA Approval for Cetuximab for Late-Stage Head & Neck Cancer*, 33 Oncology Times 24 (2011).

After Abigail's death, her father formed the Abigail Alliance for Better Access to Developmental Drugs and sued FDA to enjoin enforcement of its policy barring the sale of new drugs that have completed Phase 1 trials and received FDA clearance for later-stage trials. The plaintiffs argued that terminally ill patients lacking alternative treatment options have a fundamental constitutional right to access post-Phase 1 (safe) investigational new drugs. A panel of the D.C. Circuit initially agreed, but the en banc court reversed, holding that our nation's history, tradition, and practices do not support a fundamental due process right for the terminally ill to access

unapproved treatments. *Abigail All.*, 495 F.3d at 702-13. Nonetheless, it emphasized that federal law could be subject to democratic recalibration:

> [T]his is not to say that the FDA's balance can never be changed. The Alliance's arguments about morality, quality of life, and acceptable levels of medical risk are certainly ones that can be aired in the democratic branches, without injecting the courts into unknown questions of science and medicine.

Id. at 714.

The court emphasized that it sought to "ensure that this debate among the Alliance, the FDA, the scientific and medical communities, and the public may continue through the democratic process"—a point we take up next. *Id.* (citing *Washington v. Glucksberg*, 521 U.S. 702, 735 (1997) ("Our holding permits this debate to continue, as it should in a democratic society.")).

2. The Democratic Right to Try Movement

The *Abigail Alliance* decision catalyzed a nationwide democratic movement rooted in the understanding that FDA's program for access to investigational drugs was insufficient to safeguard the rights of the terminally ill to access promising investigational drugs. Forty-one states enacted RTT laws in six years. *See generally* Goldwater Institute, Right To Try In Your State, https://righttotry.org/in-your-state/ (last accessed May 2021). These laws provide exactly what *Abigail Alliance* denied: access to

safe but federally unapproved investigational drugs for therapeutic use with terminally ill patients.

Washington's RTT law, which is at issue in this case, provides that "the process for approval of investigational drugs … often takes many years" and that patients with terminal illnesses do not have the luxury of waiting until an investigational drug obtains final approval the FDA. RCW 69.77.010. Washington legislators voted unanimously to approve access to investigational drugs for "patient[s] with a terminal illness in consultation with the patient's health care provider." *Id.*

After a supermajority of states passed RTT legislation, Congress embraced the "will of the American people." 164 Cong. Rec. H4355, H4356 (2018). "To open the door to innovative, experimental drugs for terminally ill patients without necessarily compromising the vital work and mission of [FDA]," *id.*, federal RTT exempts investigational drugs from FDCA premarketing approval requirements, permitting state law to govern. Federal RTT thus "empower[s] terminally ill patients and their doctors who, together with the cooperation of the developers of potentially life-saving therapies, should be in charge of making a determination about their own course of treatment." *Id.* at H4360 (quoting federal RTT's primary drafter).

To accomplish these goals, federal RTT adds § 561B to the FDCA, creating an "alternative pathway" for terminally ill patients to access investigational drugs. *Id.* at H4356. According to FDA, § 561B "amends the [FDCA] to establish an option for patients who meet certain criteria to request access to certain unapproved medical products, and for sponsors and manufacturers who agree to provide certain unapproved medical products other than through FDA's expanded access program." 85 Fed. Reg. 44,804 at 44,805 (July 24, 2020).

Under § 561B, an "eligible patient" may use an "eligible investigational drug" ("EID") exempt from certain parts of the FDCA and FDA regulations, 21 U.S.C. § 360bbb-0a(b), and "no liability in a cause of action shall lie" against a manufacturer, sponsor, prescriber, or dispenser providing EIDs to an eligible patient in compliance with § 561B, 21 U.S.C. § 360bbb-0a(b) note, 132 Stat. 1374. To qualify as an "eligible patient," a person must have (1) been diagnosed with a life-threatening disease or condition, (2) exhausted approved treatment options and is unable to participate in a clinical trial involving the EID and (3) given informed consent regarding the drug. 21 U.S.C. § 360bbb-0a(a)(1). To qualify as an EID, a drug must (1) have completed an FDA-approved Phase 1 clinical trial; (2) not be approved or licensed for any use through the FDCA or the Public Health Service Act

("PHSA"), 42 U.S.C. § 201 *et seq.*; (3) either have an application filed under the FDCA or PHSA, or be under investigation in a clinical trial that is "intended to form the primary basis of a claim of effectiveness in support of approval" and be the subject of an active IND application; and (4) have ongoing active development and production. *Id.* § 360bbb-0a(a)(2).

A Sense of the Senate provision, 21 U.S.C. §360bbb-0a(b) note, 132 Stat. 1374–75, explains that federal RTT:

> (1) does not establish a new entitlement or modify an existing entitlement, or otherwise establish a positive right to any party or individual;
>
> (2) does not establish any new mandates, directives, or additional regulations;
>
> (3) only expands the scope of individual liberty and agency among patients, in limited circumstances;
>
> (4) is consistent with, and will act as an alternative pathway alongside, existing expanded access policies of the [FDA];
>
> (5) will not, and cannot, create a cure or effective therapy where none exists;
>
> (6) recognizes that the eligible terminally ill patient population often consists of those patients with the highest risk of mortality, and use of experimental treatments under the criteria and procedure described in such section 561A involves an informed assumption of risk; and
>
> (7) establishes national standards and rules by which investigational drugs may be provided to terminally ill patients.

II. Factual Background

A. Psilocybin

Psilocybin is a naturally occurring compound found in more than 200 fungus species. Congress placed psilocybin in schedule I when first enacting the CSA, 84 Stat. 1249 (1970), and it remains there today. Effects of ingested psilocybin can include euphoria, changes in perception, and profound spiritual experiences. *See generally* Charles S. Grob, Alicia L. Danforth, & Gurpreet S. Chopra, *Pilot Study of Psilocybin Treatment for Anxiety in Patients with Advanced-Stage Cancer*, 68 Arch Gen. Psych. 71, 71 (2011).

Recent research has rekindled interest in psilocybin as medicine. Studies have consistently found that psilocybin treatment can significantly and rapidly reduce symptoms of mental and emotional distress in patients with life-threatening cancer with no clinically significant adverse effects.[3] A 2020 randomized clinical trial found that psilocybin-assisted therapy produced "large, rapid, and sustained antidepressant effects in patients with major depressive disorder." *See* Alan K. Davis, *et al.*, *Effects of Psilocybin-*

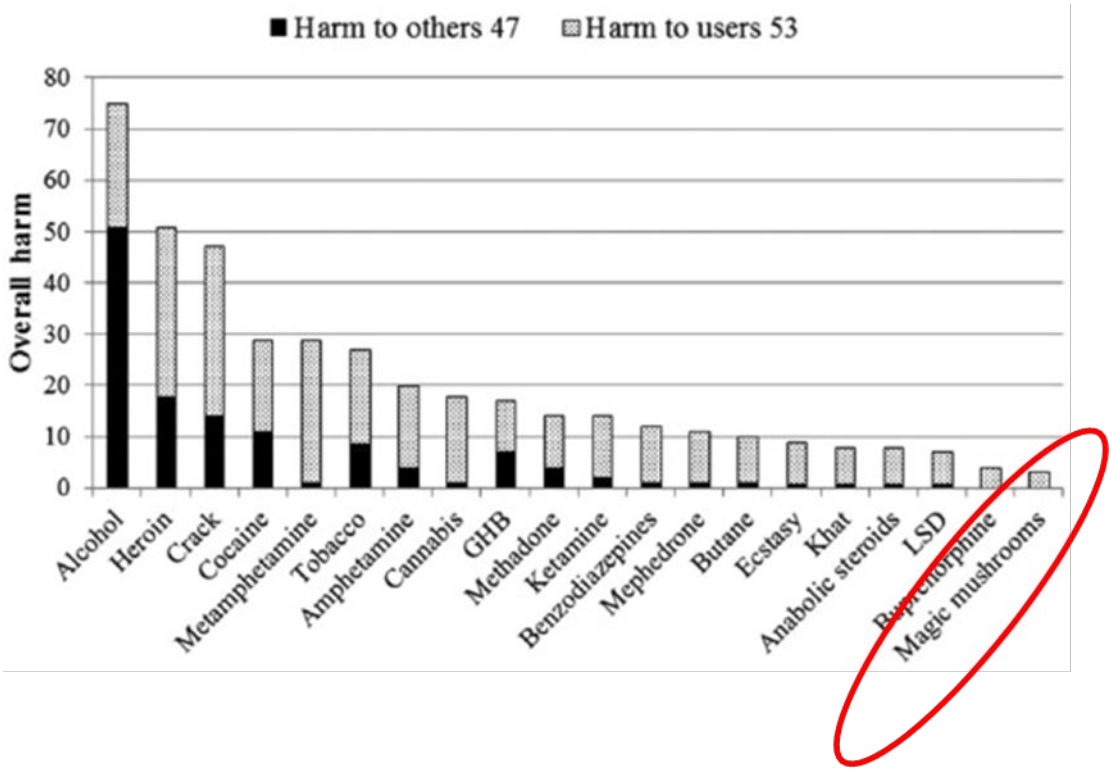
[3] *See* Grob, 68 Arch Gen. Psych. at 71; Roland R. Griffiths et al., Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial, 30 J. of Psychopharm. 1181, 1195 (2016). *See* Stephen Ross S, *et al.*, *Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial.* 30 J Psychopharmacol. 1165 (2016).

Assisted Therapy on Major Depressive Disorder: A Randomized Clinical Trial, JAMA Psych. (2020). "[C]ompelling evidence" of psilocybin's safety and efficacy continues to mount, especially for addressing end-of-life psychiatric distress secondary to cancer. Matthew W. Johnson & Roland R. Griffiths, *Potential Therapeutic Effects of Psilocybin*, 14 Neurotherapeutics 734, 734 & 739 (2017) (collecting studies).

Psilocybin also showed potential to help such patients find meaning. Researchers found that "the psilocybin-induced mystical experience mediated the therapeutic effect of psilocybin on anxiety and depression" among cancer patients, suggestive of a causal effect. Ross, 30 J. Psychopharmacol. at 1177. Months after treatment, these patients reported decreased cancer-related existential distress and increased spiritual wellbeing. *Id.* at 1175.

Phase 1 clinical trials have shown that psilocybin was "well tolerated." *See* Michael W. Jann, *Psilocybin Revisited: The Science Behind the Drug and Its Surprising Therapeutic Potential*, 38 Psychiatric Times (Mar. 9, 2021). Phase 2 trials are underway, and plans for Phase 3 trials are already in place. *Id.* Psilocybin has thus been shown to be safe per FDA standards, and it has also shown significant indications of effectiveness.

Indeed, although a schedule I drug,[4] psilocybin is remarkably safe compared to many other drugs:



B. Dr. Aggarwal's Seattle Practice and His Patients

Petitioner Dr. Sunil Aggarwal is the Co-Founder and Co-Director of the Advanced Integrative Medical Science ("AIMS") Institute, an integrative oncology clinic based in Seattle, Washington. A well-credentialed palliative care specialist, Dr. Aggarwal holds a DEA license to prescribe schedule II-V drugs. ER-27 (Aggarwal Declaration).

[4] Some state RTT laws exclude schedule I substances from their ambit. *See* RSMo 191.480(2). Washington's RTT and federal RTT do not. RCW 69.77, *et seq*; 21 U.S.C.A. § 360bbb-0a.

In his professional practice, Dr. Aggarwal treats many patients with advanced-stage cancer, including some who suffer from severe anxiety and depression that does not respond to therapy with approved medicines. ER-28.

Petitioners Michal Bloom and Erinn Baldeschwiler are two such patients. Bloom, a DOJ attorney who retired due to her illness, has been undergoing extensive treatment for advanced ovarian cancer since 2017 with a multitude of burdensome complications. She experiences severe anxiety and depression, which approved FDA therapies have not abated. ER-12 (Bloom Declaration). Baldeschwiler has Stage IV metastatic breast cancer with tumors all over her body. ER-11. A mother of two, the prospect of an imminent death preventing her from raising her children to adulthood causes her severe mental and emotional pain. ER-12. She suffers from anxiety and depression which has not been addressed by currently approved treatments. *Id.*

Based on his professional experience and assessment of (1) Bloom and Baldeschwiler's condition and symptoms and (2) recent research on psilocybin therapy, including successful clinical trials, Dr. Aggarwal discussed the possibility of psilocybin therapy, including the risks and rewards, with Bloom and Baldeschwiler, including the risks and rewards.

ER-26. Both patients indicated a desire to try the treatment and gave informed consent. ER-26; ER-19-20 (Baldeschwiler Declaration).

III. DEA's Final Decision

In January 2021, Dr. Aggarwal requested DEA provide instructions and guidance on how he could obtain permission to order psilocybin for therapeutic use with his suffering terminally ill patients under Washington and federal RTT. ER-4–7. He advised that a DEA-registered manufacturer and distributor of psilocybin had agreed to provide the investigational drug on receipt of evidence of DEA's approval. ER-6.

DEA responded on February 12, 2021, declaring that it could not accommodate Dr. Aggarwal's RTT request. ER-8–9. According to DEA, it has "no authority to waive" any of the CSA's requirements to accommodate RTT. ER-8. DEA provided no avenue to obtain an exception, exemption, or waiver. Instead, it suggested Dr. Aggarwal consider registering as a schedule I researcher under the CSA. ER-9. In response to this proceeding, DEA confirmed it would accommodate RTT only "[w]hen research demonstrates that a drug is both safe and effective, and the FDA recognizes it as a legitimate treatment." ER-55.

DEA's final decision gives rise to this action.

STANDARD OF REVIEW

Under the Administrative Procedure Act ("APA"), "a reviewing court shall … hold unlawful and set aside agency action, findings, and conclusions" found to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A).

Courts generally review agency interpretations of statutes they administer under *Chevron U.S.A., Inc. v. Nat. Res. Def. Council, Inc.*, 467 U.S. 837 (1984). "Even under *Chevron*," however, courts "owe an agency's interpretation of the law no deference unless, after 'employing traditional tools of statutory construction,' [they] find [them]selves unable to discern Congress's meaning." *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1358 (2018) (cites omitted).

Nor does *Chevron* deference apply when an agency interprets a statute it does not administer. *See Epic Sys. Corp. v. Lewis*, 138 S. Ct. 1612, 1629 (2018). "[R]econciliation of distinct statutory regimes is a matter for the courts, not agencies." *Id.* (quot. omitted).

> An agency eager to advance its statutory mission, but without any particular interest in or expertise with a second statute, might (as here) seek to diminish the second statute's scope in favor of a more expansive interpretation of its own—effectively bootstrap[ping] itself into an area in which it has no jurisdiction.
>
> *Id.* (quot. omitted).

SUMMARY OF THE ARGUMENT

I. DEA's claimed lack of "authority to waive" CSA requirements to accommodate RTT laws ignores the plain language of the FDCA and CSA, defies longstanding federalism norms, and poses constitutional concerns.

Congress considered the interaction between the FDCA and CSA and made the statutory determination that "[n]othing in [the CSA] … shall be construed as in any way affecting, modifying, repealing, or superseding the provisions of the [FDCA]." 21 U.S.C. § 902. The meaning of this statute is straightforward. The FDCA governs, and any construction of the CSA that would "in any way … affect[], modify[], repeal[], or supersed[e]" its provisions is prohibited. Now that Congress has amended the FDCA to include RTT, DEA's claim that anything in the CSA prevents it from accommodating RTT turns § 902's order of operations on its head: Not only does the CSA not prevent DEA from accommodating RTT, its plain language *compels* DEA to yield to Congress's mandate in the FDCA's RTT provisions.

In addition, basic principles of federalism counsel that the legitimate practice of medicine is left to the states' police powers. Forty-one states, including Washington, have adopted RTT laws that empower qualifying patients to try investigational drugs that may be beneficial for their terminal condition and quality of life. DEA is a law-enforcement agency with no

authority to police or regulate the practice of medicine. Its final decision impedes access to RTT, vitiates democratic efforts at the state and federal levels, and offends core federalism principles. It must be corrected immediately.

II. DEA's final decision is at odds with the CSA itself, which expressly empowers DEA to waive the statute's requirements. *See* 21 U.S.C. §§ 822(d), 871(b). Moreover, the agency's determination runs counter to recent Supreme Court precedent. Case law and agency practice counsel that DEA can—indeed must—accommodate use of schedule I EIDs in compliance with RTT laws. DEA's refusal to do so is contrary to law.

III. Finally, DEA's claimed lack of authority to waive the CSA's requirements marks an abrupt departure from the agency's consistent historical practice under the Act. Yet DEA did not acknowledge its change in policy, much less attempt to provide a reasoned explanation for it. Nor did DEA distinguish Petitioners' request for accommodation from numerous similar requests the agency has granted in the past. Reasoned decision-making under the APA requires more.

Petitioners therefore urge the Court to grant the petition for review, hold DEA's final decision unlawful, and remand to DEA with instructions to promptly accommodate RTT.

ARGUMENT

I. DEA Must Accommodate RTT.

A. The CSA's Plain Language Compels Accommodation.

Addressing the interplay between the CSA and the FDCA, Congress declared that "[n]othing in [the CSA] … shall be construed as in any way affecting, modifying, repealing, or superseding the provisions of the [FDCA]." 21 U.S.C. § 902. Section 902's unambiguous aim is to prohibit any construction of the CSA that would interfere with the FDCA. Yet DEA's final decision does just that.

The FDCA greenlights EID use "by patients diagnosed with a terminal illness in accordance with State law." *Id.* § 360bbb-0a. It then exempts (with limited exceptions not relevant here) anyone acting "pursuant to … and in compliance with [§ 360bbb-0a]" from liability. Pub. L. 115-176, § 2(b), May 30, 2018, 132 Stat. 1374. By insisting that those very acts remain categorically prohibited under the CSA, DEA's final decision construes the CSA as "superseding the provisions of the [FDCA]"—precisely what § 902 forbids.

Nor can there be any doubt that Congress intended the protection from liability in the FDCA's RTT provisions to include liability under the CSA. Congress expressly identified certain forms of liability that survived the no-

liability provision, but liability under the CSA isn't among them. Pub. L. 115-176, § 2(b), May 30, 2018, 132 Stat. 1374.

DEA's own regulations reflect this order of operations between the FDCA and the CSA. Take 21 C.F.R. § 1316.24. It provides that DEA may exempt registered researchers "from prosecution under Federal, State, or local laws for offenses relating to possession, distribution or dispensing of those controlled substances within the scope of this exemption" but immediately adds that "this exemption does not diminish any requirement of compliance with the [FDCA]." This discretionary exemption makes sense in light of 21 U.S.C. § 872(e), which permits DEA to "authorize the possession, distribution, and dispensing of controlled substances by persons engaged in research" and to exempt "[p]ersons who obtain this authorization … from State or Federal prosecution …." Notably missing from § 872(e), however, is any clarification that the exemption from liability does "not diminish any requirement of compliance with the [FDCA]." 21 C.F.R. § 1316.24. That DEA went out of its way to avoid construing § 872(e) to "supersede the [FDCA]" is a testament to the agency's awareness of § 902's background rule prohibiting constructions of the CSA's provisions that would interfere with the FDCA.

FDA's public statements regarding federal RTT confirm that it displaces otherwise-applicable CSA requirements. In response to the "frequently asked question," "Can patients gain access to cannabis"—another schedule I substance—"for medical use through Right to Try?," FDA encourages the inquiring public to consult their "licensed physician," emphasizing that the agency "is not involved in these decisions":

> **19. Can patients gain access to cannabis or cannabis-derived products for medical use through Right to Try?**
>
> A. Information for patients on Right to Try (RTT) is available on our website. RTT is designed to facilitate access to certain investigational drugs through direct interactions between patients, their physicians and drug sponsors – FDA is not involved in these decisions. Sponsors developing drugs for life-threatening conditions are responsible for determining whether to make their products available to patients who qualify for access under RTT. If you are interested in RTT, you should discuss this pathway with your licensed physician. Companies who develop drugs and biologics, also known as sponsors, can provide information about whether their drug/biologic is considered an eligible investigational drug under RTT and if they are able to provide the drug/biologic under the RTT Act.

https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd#righttotry. If FDA had any doubt that the CSA's requirements yield to the FDCA's RTT provision, this response would make little sense. FDA would not advise the public to leave a decision of whether to commit a federal crime up to their physician.

Other statutory clues reinforce this interpretation. Section 902 is one of four "General Provisions" in Part F of the CSA. *See* 21 U.S.C. §§ 901–904. Together, these General Provisions establish background principles to govern the interplay between the CSA and other sources of law. *See id.* § 901 (interplay between the CSA and judicial precedent construing its terms); *id.* § 902 (interplay between CSA and FDCA); *id.* § 903 (interplay between provisions of subchapter I of the CSA and state law); *id.* § 904 (interplay between provisions of subchapter I of CSA and certain tort issues arising abroad).

Comparing § 902 to the CSA's other General Provisions underscores § 902's remarkable breadth. Section 902 is, for example, one of just two "General Provisions" in the CSA that applies to the *entire* Act—both the "Drug and Abuse and Control" provisions of subchapter I *and* the "Import and Export" provisions of subchapter II.[5] Even more remarkable, § 902 is

[5] The first two "general provisions"—§§ 901 and 902—address themselves to "this chapter." 21 U.S.C. §§ 901, 902 (beginning "[i]f a provision of *this chapter*" and "[n]othing in *this chapter*," respectively) (emphases added). The second two "general provisions"—§§ 903 and 904—refer instead to "this subchapter." *Id.* §§ 903, 904 (referencing "[n]o provision of *this subchapter*" and "the functions of the Department of Justice under *this subchapter*, respectively) (emphases added). The "chapter" referenced in §§ 901 and 902 is chapter 13 of Title 21, entitled "Drug Abuse Prevention and Control." And the "subchapter" referenced in §§ 903 and 904 is subchapter I, entitled "Control and Enforcement (§§ 801-904)."

the *only* "General Provision" applicable to nearly *everything* in the Act. Unlike § 901, which applies only if "a provision of [chapter 13] is held invalid" or "if a provision of [chapter 13] is held invalid in one or more of its applications," § 902 contains no similar limitation. *Compare id.* § 901 ("If *a provision of this chapter* is held invalid, all valid provisions that are severable shall remain in effect…") *and id.* § 902 ("*Nothing in this chapter* … shall be construed as in any way affecting …") (emphases added).

When enacting the CSA, Congress knew that conflicts between the CSA and other sources of law within the broader tapestry of our nation's drug laws would inevitably arise. That each of the four "General Provisions" in Part F of the CSA, *see* 21 U.S.C. § 901-904, addresses the interplay between the CSA and a different one of those related bodies of law is proof enough. It is therefore no accident that Congress reserved its most sweeping and categorical language for § 902—the General Provision specifically addressing the interplay between the CSA and the FDCA.

Although no court has previously addressed § 902's applicability to a conflict between the CSA and FDCA, cases addressing similar statutes reinforce this interpretation. Consider, for example, *McIntyre v. United States*, 222 F.3d 655, 660 (9th Cir. 2000). That case involved the savings provision from the Employees Retirement Income Security Act (ERISA),

which is nearly identical in relevant part to § 902 of the CSA. *See* 29 U.S.C. § 1144(d) ("Nothing in this subchapter shall be construed to alter, amend, modify, invalidate, impair, or supersede any law of the United States."). The Court held that prohibiting the garnishment of ERISA plan benefits would "modify" the government's authority under another federal statute to enforce tax liens. More recently, the en banc Court reaffirmed *McIntyre's* interpretation of § 1144(d) when it held that "prohibiting the garnishment of retirement plan benefits would just as clearly 'modify' the government's authority under [under yet another federal statute] to enforce criminal restitution orders … as would such a prohibition 'modify' the government's authority [at issue in *McIntyre*] to enforce tax liens." *United States v. Novak*, 412 F.3d 1141, 1150–51 (9th Cir. 2007) (en banc).

The same reasoning applies with full force here. Just as prohibiting the garnishment of ERISA plan benefits at issue in *McIntyre* and *Novak* would "modify" the government's authority to enforce tax liens and criminal restitution orders, treating actions taken "pursuant to and in compliance with" the FDCA's RTT provisions as categorically prohibited under the CSA would "modify" or "supersede" the FDCA's mandate that those same actions be exempt from premarket approval requirements and may not serve as a basis for liability. Indeed, DEA's construction frustrates the entire purpose

of the FDCA's RTT provisions. Because DEA's final decision rests on such a construction of the CSA, it plainly violates § 902.

B. DEA's Categorical Refusal to Accommodate RTT Violates Federalism Principles.

The tapestry of drug laws within which Congress wove both the CSA and RTT reflects Hart and Wechsler's iconic encapsulation of federalism:

> Federal law is generally interstitial in its nature. It rarely occupies a legal field completely, totally excluding all participation by the legal systems of the states. Federal legislation on the whole, has been conceived and drafted on an *ad hoc* basis to accomplish limited objectives. It builds upon legal relationships established by the states, altering or supplanting them only so far as necessary for the special purpose. … Congress acts, in short, against the background of the total corpus juris of the states in much the way that a state legislature acts against the background of the common law, assumed to govern unless changed by legislation.

Hart & Wechsler, *The Federal Courts and the Federal System*, 435 (1st ed. 1953).

Congress enacted the CSA against a backdrop of long-extant drug-control laws at both the state and federal level that included a settled division of authority between the state and federal governments with respect to drug regulation. The Act "presume[s] and relies upon a functioning medical profession regulated under the States' police powers," *Oregon* 546 U.S. at 270, prohibits the federal government from making "anterior judgment[s]" about what constitutes accepted medicine or medical treatment, *id.* at 272,

and "manifests no intent to regulate the practice of medicine generally," *id.* at 270.

As the Court held in *Oregon*, proper interpretation of the CSA requires keeping federalism principles and the states' traditional authority to regulate the medical profession squarely in view. There, the Attorney General issued a directive stating that prescribing controlled substances consistent with Oregon's Death with Dignity Act was grounds for suspending or revoking a doctor's CSA registration because 'assisting suicide' was not a "legitimate medical purpose" for purposes of the Act's prescription and registration provisions. *See id.* at 253–54. *See also* 21 U.S.C. § 829(c) (defining valid prescription as one issued for a legitimate medical purpose); *id.* § 824(a) (authority to deregister). Affirming the decisions below, the Court rejected that interpretation and explained that the CSA does not provide "a single executive officer [would have] the power to effect a radical shift of authority from the States to the Federal Government to define general standards of medical practice in every locality." *Oregon*, 546 U.S. at 275.

Such a result, the Court reasoned, would ignore federalism principles: the "regulation of health and safety is 'primarily, and historically, a matter of local concern.'" *Id.* at 271 (citation omitted). The Court was not persuaded that Congress had intended the CSA to assert "expansive federal authority to

regulate medicine." *Id.* Instead, it explained, the Act had a far more limited aim: preventing drug abuse and drug trafficking while relying on State regulation of medical practice. *Id.* at 273. After *Oregon*, DEA itself acknowledged that it "does not act as the Federal equivalent of a State medical board overseeing the general practice of medicine" and that the "scope of the CSA (and therefore role of DEA) is much narrower." 71 Fed. Reg. 52,716, 52,717 (2006)

DEA's refusal to accommodate RTT laws usurps the same traditional state authority over the practice of medicine that the Court held was impermissible in *Oregon*. Exercising their traditional authority over matters of local health and the medical practice, the states have adopted different approaches to RTT. Some, like Washington, have adopted RTT laws that allows use of schedule I substances as a legitimate medical practice when RTT's criteria are met. RCW 69.77.020(4). Others, like Missouri, do not. *See* RSMo 191.480(2).

This diversity of approaches to RTT is a classic example of the laboratories of democracy in action and has implications for DEA's obligations under the CSA. Because the states—and not DEA—decide what qualifies as legitimate medical practice in the United States, DEA must respect the varying lines states have drawn regarding access to schedule I

substances under RTT laws. *Oregon*, 546 U.S. at 270 (CSA does not "does not authorize the Attorney General to bar dispensing controlled substances for assisted suicide in the face of a state medical regime permitting such conduct"). By failing to do so, the final decision has an impermissible leveling effect, reducing diverse state-law approaches to the most restrictive common denominator. *See Nat'l Fed'n of Indep. Bus. v. Sebelius*, 567 U.S. 519, 536 (2012).

Even more, DEA's refusal to accommodate RTT effectively nullifies choices made by states like Washington to permit access to schedule I substances under RTT as legitimate medical practice, leaving other RTT laws like Missouri's intact. DEA, a federal law-enforcement agency, has no authority to pick and choose which state medical practices are legitimate. Since the early days of our republic, such choices have been reserved for local sovereigns "closer to the governed." *NFIB*, 567 U.S. at 546.

Finally, DEA's attempt to override legislative enactments at both the state and federal levels demeans the democratic process. As *Abigail Alliance* explained, a crucial and intended aspect of our federal system is that citizens should vigorously debate matters like these. 495 F.3d at 702. This Court should not countenance DEA's attempt to end an ongoing public conversation of such profound complexity by administrative fiat.

C. DEA's Failure to Accommodate RTT Raises Constitutional Concerns.

Permitting DEA to interpret the CSA in a manner that stifles these substantive state rights in an area traditionally regulated by states would raise serious constitutional questions, thus implicating avoidance.

It is a "cardinal principle" that courts must ascertain whether "a construction of the statute is fairly possible" by which a constitutional question may be avoided. *Ashwander v. Tennessee Valley Auth.*, 297 U.S. 288, 348 (1936) (quot. omitted). Thus, in "choosing between competing plausible interpretations of a statutory text," courts must favor interpretations that avoid constitutional issues. *Clark v. Martinez*, 543 U.S. 371, 381 (2005). This rule is rooted in the sensible presumption that "Congress does not casually authorize administrative agencies to interpret a statute to push the limit of congressional authority." *Solid Waste Agency of N. Cook Cty. v. U.S. Army Corps of Eng'rs*, 531 U.S. 159, 172–73 (2001).

For example, in *Flores-Chavez v. Ashcroft*, 362 F.3d 1150, 1153 (9th Cir. 2004), this Court applied avoidance to reject a construction of the INS regulatory scheme for juvenile notice and release because that raised due process concerns. The government argued that INS was not required to notice the responsible adult required to appear at the hearing, but this Court

rejected that interpretation to avoid the "due process concerns [that] would [otherwise] arise":

> Were we to uphold the INS's position that notice pursuant to § 103.5a was sufficient, due process concerns would arise. Because the private liberty interests involved in deportation proceedings are indisputably substantial, we have previously held that alien minors in deportation proceedings are entitled to the fifth amendment guaranty of due process. Additionally, parental notification requirements, such as those established in 8 C.F.R. § 103.5a, further implicate the due process rights of juveniles, as minors generally cannot appreciate or navigate the rules of or rights surrounding final proceedings that significantly impact their liberty interests.

Id. at 1160 (cit./quot. omitted). The only reasonable interpretation of the regulations that comported with due process required the agency to serve notice both on juvenile and to the responsible adult.

Here, construing the CSA to admit of no exceptions for therapeutic use of schedule I substances in compliance with RTT laws raises two serious constitutional questions.

First, as explained above, an interpretation that rests on a conclusion that schedule I drugs can never be used medically would mark a significant intrusion into state authority, "alter[ing] the usual constitutional balance between the States and the Federal Government." *Gregory v. Ashcroft*, 501 U.S. 452, 460 (1991) (internal quot. omitted). Because Congress did not clearly state that a drug's schedule I classification overrides a state

determination that in particular circumstances (like those contemplated by RTT laws) use of schedule I drugs qualifies as a legitimate medical practice, the Act should not be construed to permit such a disruption to the state-federal balance. *Id. See also Bond v. United States*, 572 U.S. 844, 858, 134 S. Ct. 2077, 2089 (2014) (listing cases involving construction of federal statutes "that touched on several areas of traditional state responsibility.").

In *Gregory*, for example, the federal Age Discrimination in Employment Act ("ADEA") imposed liability on any employer, including a State or political subdivision of a State, who discharged an employee over the age of forty because of that employee's age. *Id.* at 456–57. While the ADEA provides an exemption for government officials, that exemption did not unambiguously apply to state judges. *Id.* at 466–67. Nonetheless, the Court concluded that ambiguous was enough to apply the clear statement rule: absent a clear statement, the Court would "not attribute to Congress an intent to intrude on state governmental functions." *Id.* at 470.

As explained earlier, *see* Part I *supra*, from quotas to penalties, the CSA provides nearly identical abuse and diversion controls for schedule I and schedule II drugs. The primary difference "is that the former may be used for research only, whereas the latter may be prescribed by licensed physicians." *NORML v. DEA*, 559 F.2d 735, 751 (D.C. Cir. 1977). In light of this similarity,

it cannot seriously be argued that accommodating discrete therapeutic uses of a schedule I drug that qualifies as an EID will prevent DEA from effectively preventing diversion and abuse. Permitting use of a schedule I drug under RTT amounts to treating it as a schedule II substance for that discrete purpose. DEA's contention that the CSA does not permit such an accommodation necessarily assumes that a drug's schedule I classification means it has "no medical benefits worthy of an exception," *United States v. Oakland Cannabis Buyers' Co-op.*, 532 U.S. 483, 491 (2001) ("*OCBC*"), and that strictly controlled use of an EID under RTT laws constitutes drug abuse.

This contention raises serious constitutional questions. How substances are used in medicine has traditionally been a matter for state—not federal—regulation. And at the end-of-life stage, such state regulation is "of the most fundamental sort." *Gregory*. *See also Glucksberg*, 521 U.S. at 737 (O'Connor, J., concurring); *Cruzan* v. *Missouri Dep't of Health*, 497 U.S. 261, 293 (1990) (Scalia, J., concurring). Any determination that use of schedule I drugs in compliance with state RTT laws cannot be legitimate medical practice and constitutes drug abuse would mark a significant federal intrusion into the states' traditional police powers and regulate local activity. *See Bond*, 572 U.S. at 860 (absent clear statement, declining to interpret

federal statute expansively "in a way that intrudes on the police power of the States.").

Nor did Congress expressly forbid discrete therapeutic uses of schedule I drugs, let alone forbid states from filling that gap. The CSA does, of course, forbid dispensing schedule I drugs through a *prescription*, but RTT is not prescription-based. That is precisely its point. If Congress intended to categorically foreclose all therapeutic uses of schedule I drugs, one would have expected a clear statement to that effect. But there is none. *Cf. UDV*, 546 U.S. 418 at 432–38 ("The fact that the [CSA] itself contemplates that exempting certain people from its requirements would be 'consistent with the public health and safety' indicates that congressional findings with respect to Schedule I substances should not carry the determinative weight, for RFRA purposes, that the Government would ascribe to them."). *OCBC*, 532 U.S. at 493, is not to the contrary. The Court there acknowledged that Congress's initial placement of marijuana in schedule I in 1970 reflected a legislative determination that it had "no medical benefits worthy of an exception," *Id.* at 491, but did not address whether and how DEA must act to permit use of schedule I drugs to accommodate laws like the federal and state RTT statutes at issue here. Moreover, the Court in *OCBC* acknowledged that a later legislative determination—like federal RTT—could demonstrate that

drugs without currently accepted medical uses in treatment "may nonetheless have medical benefits to a particular patient or class of patients" in a specific setting. *Id.* at 493. Because nothing in the CSA should be construed as trumping the provisions or standards of the FDCA, 21 U.S.C. § 902, this recognition operates with similar force with respect to CSA. At minimum, federal RTT creates a statutory ambiguity that puts constitutional avoidance back in play. *See Id. at* 494.

Second, while terminally ill patients may not have a fundamental federal constitutional right to non-FDA-approved drugs "deeply rooted in our Nation's history and traditions," *Abigail All.*, 495 F.3d at 711, widespread enactment of state RTT laws establishes liberty rights rooted in principles of federalism and state law. For example, in *United States v. Windsor*, 570 U.S. 744 (2013), the Court adopted a federalism approach to identifying a Fifth Amendment liberty right. In its holding, the Court relied on the core notion that state legislatures determine the boundaries of domestic-relations law, and that state law enhanced the recognition and protection of same-sex marriages in their own community, which federal law impermissibly undermined. *Id.* at 769–70. This right of recognition "was not some untethered judicial creation, but rather an entitlement to federal recognition of state law rights created in the democratic exercise of the states' reserved

powers." Ernest Young, *United States v. Windsor and the Role of State Law in Defining Rights Claims*, 99 Va. L. Rev. 39, 47 (2013).

Here, after *Abigail Alliance*, the states exercised a similar prerogative to protect liberty in an area that has traditionally been within the "exclusive province of the States.'" *See Oregon*, 546 U.S. at 270 (states enjoy "great latitude under their police powers to legislate as to the protection of the lives, limbs, health, comfort, and quiet of all persons") (citations omitted). State legislatures enacted law approving athe use of investigational drugs by the terminally ill. Because no federal law clearly states otherwise, the CSA should not be construed to undermine this protected liberty.

* * *

DEA may not refuse to accommodate RTT because it views use of schedule I drugs in compliance with state and federal RTT laws as illegitimate medical practice or "drug abuse." Rather, the scope of DEA's inquiry must be consonant with its mission: to protect "the health of the citizens by controlling the manufacture, sale, and use of dangerous or potentially dangerous drugs." *Kennedy v. Bureau of Narcotics & Dangerous Drugs*, 459 F.2d 415, 416 (9th Cir. 1972); *see also Ashcroft*, 368 F.3d at 1125 (DEA's authority under CSA limited to the "field of drug abuse"). In other words, it is limited to determining whether, how, and under what conditions

granting an exception or exemption for a valid RTT request would increase or promote drug abuse or drug diversion.

The FDCA, CSA, and DEA's history demonstrate beyond cavil that DEA can, and indeed must, accommodate use of schedule I drugs in compliance with RTT. DEA may, of course, subject such accommodation to controls that the agency, in its discretion, deems necessary to prevent unlawful abuse and diversion. It may not, however, categorically refuse to grant requests to use schedule I drugs in compliance with RTT because it has "no authority" to grant exceptions, as it did in the final decision.

II. DEA's Claimed Lack of Authority to Accommodate RTT Rests on an Impermissible Interpretation of the CSA.

DEA concluded it lacks "authority to waive any of the CSA's requirements pursuant to the RTT" because 21 U.S.C.§ 360bbb-0a(b) contains no "explicit statutory exemption to the CSA." ER-8. That determination defies the CSA's plain language as well as DEA's own regulations and past practice.

The CSA permits the Attorney General—and thus DEA—to "waive the requirement for registration of certain manufacturers, distributors, or dispensers if he finds it consistent with the public health and safety." 21 U.S.C. § 822(d). And under 21 U.S.C. § 871(b), it "may promulgate and enforce any rules, regulations, and procedures" that it deems necessary and

appropriate for the efficient execution of the CSA. *See also id.* § 821 (DEA may "promulgate rules and regulations … relating to the registration and control of the manufacture, distribution, and dispensing of controlled substances and to listed chemicals"). DEA may also waive the requirements of its own regulations. *See* 21 U.S.C. § 1307.03. DEA has invoked these authorities throughout the CSA's history to create exceptions to the statute's requirements. *See supra* Part I.B.3 (discussing some—not all—of exceptions to CSA's requirements DEA has permitted over the years).

This is not the first time DEA has ignored these authorities in the face of a request for accommodation. In *UDV*, 546 U.S. 418, the Supreme Court rebuked a near-identical DEA argument that the CSA admits of no exceptions for use of schedule I drugs. The UDV church sought individualized exceptions to use ayahuasca, a mixture containing the schedule I drug dimethyltryptamine ("DMT"), for religious purposes. DEA contended the CSA was a "closed" system that prohibits all use of controlled substances except as authorized by the Act itself. The Court rejected that argument as contrary to the plain language of § 822(d). *Id.* at 420.

Similarly, no "explicit statutory exemption" greenlighted DEA's exercise of exception-making authority at the time DEA promulgated 21 C.F.R. § 1307.31 or any of the other waivers DEA has recognized in the past.

Yet DEA did not hesitate to waive the CSA's requirements anyway. *See generally* Part I.B.3 *supra* (discussing history of exception-making); *Native American Church v. United States*, 468 F. Supp. 1247, 1249–51 (S.D.N.Y.1979) (recounting history of regulatory exception for peyote).

In the final decision, DEA notes that the federal RTT law expressly exempts sections of the FDCA but makes no mention of the CSA. ER-8–9. According to DEA, this leaves it without authority to waive the CSA's requirements to accommodate RTT. That argument fails for at least three reasons.

First, it ignores 21 U.S.C. § 902, which makes clear that CSA provisions must yield to those of the FDCA. *See* Part I.A. *supra* (discussing § 902). Second, the CSA expressly permits DEA to waive the Act's requirements even without an explicit statutory exemption. *See, e.g.*, 21 U.S.C. § 822(d). And third, religious exemptions and past practice undermine DEA's interpretation. RFRA does not expressly exempt the CSA, but DEA must accommodate bona fide religious use of schedule I substances through exemptions. Even before RFRA, there was no statutory text anywhere sanctioning the religious use of peyote or permitting DEA to accommodate such use through 21 C.F.R. § 1307.31, but DEA did so anyway. *See* DOJ Memo. The absence of an express statutory exemption has never prevented

DEA from creating exceptions to the CSA's requirements in the past. As a result, DEA cannot rely on the absence of one here to justify its refusal to accommodate state and federal RTT laws.

III. DEA's Final Decision Is Arbitrary and Capricious.

A. DEA's Final Decision Marks an Abrupt and Unexplained Departure from the Agency's Consistent Past Practice.

The APA directs courts to "hold unlawful and set aside" agency actions that are "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2). To that end, agencies must "examine the relevant data and articulate a satisfactory explanation for its action." *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 513 (2009) (quotation omitted). While "searching and careful," *Marsh v. Or. Nat. Res. Council*, 490 U.S. 360, 378 (1989) (quotation omitted), judicial review under this standard is also limited to the reasoning "articulated by the agency itself," *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 50 (1983). *Post hoc* rationalizations of the Government's counsel are irrelevant. *See id.*

These principles require that DEA's final decision be set aside for two reasons. First, it marks an unexplained departure from consistent past practice. Second, DEA failed to distinguish Petitioners' request for accommodation from similar requests it has granted in the past.

1. DEA's failure to acknowledge its change of position and supply good reasons for the change renders the final decision arbitrary and capricious.

When an agency changes its policy or practices, it must "provide a reasoned explanation for the change." *Alaska Oil & Gas Ass'n v. Pritzker*, 840 F.3d 671, 682 (9th Cir. 2016). Failure to do so renders agency action arbitrary and capricious. *Humane Soc'y of U.S. v. Locke*, 626 F.3d 1040, 1053 (9th Cir. 2010).

DEA's claimed lack of authority to accommodate state and federal RTT laws absent an "explicit statutory exemption" defies the agency's consistent past practice under the Act, including:

- permitting Robert Randall (and others) to receive and use marijuana for years;
- exempting various chemical preparations containing controlled substances from the various CSA requirements even before Congress enacted 21 U.S.C. § 811(g)(3)(B); and
- recognizing "an exemption from the Controlled Substances Act" for certain "religious organizations which use controlled substances within the free exercise of their religion."[6]

This record of exception-making reaches back to the agency's very first decisions under the CSA, and has continued uninterrupted ever since.

[6] https://www.deadiversion.usdoj.gov/GDP/(DEA-DC-5)(EO-DEA-007)(Version2)RFRA_Guidance_(Final)_11-20-2020.pdf#search=RFRAfo

DEA's "power to adjust its policies and rulings in light of experience and to announce new principles in an adjudicatory proceeding," does not permit it "to depart, sub silentio, from its usual rules of decision to reach a different, unexplained result in a single case." *W. States Petroleum Ass'n v. EPA*, 87 F.3d 280, 284 (9th Cir. 1996) (quotations omitted). "To the contrary," DEA "must clearly set forth the ground for its departure from prior norms so that [courts] may understand the basis of the [its] action and judge the consistency of that action with the [agency]'s mandate." *Id.* In the final decision, however, DEA did not even acknowledge its decades-long adherence to a dramatically different interpretation, much less attempt to explain its reasons—assuming it has any—for abruptly shifting ground. Instead, it simply declared its new view that in the absence of "an explicit statutory exemption," exceptions to the CSA's requirements are out of the question. Reasoned decision-making under the APA demands more than an agency's bare ipse dixit.

2. DEA's failure to treat like cases alike renders the final decision unlawful.

It is a bedrock principle of administrative law that an agency must "treat like cases alike." 32 Charles Alan Wright & Charles H. Koch, Federal Practice and Procedure § 8248, at 431 (2006). Thus, "[i]f the agency makes an exception in one case, then it must either make an exception in a similar

case or point to a relevant distinction between the two cases." *Agua Caliente Tribe of Cupeno Indians of Pala Rsrv. v. Sweeney*, 932 F.3d 1207, 1220 (9th Cir. 2019) (internal quotation marks omitted).

As already discussed, *see supra* Part II, DEA has consistently made exceptions to the Act's requirements in various circumstances. It was therefore duty bound either to make an exception to accommodate RTT or "point to a relevant distinction between the two cases." *Id.* Instead, it simply claimed a lack of authority to accommodate RTT without an explicit statutory exemption without even attempting to reconcile that reason with exceptions the agency has routinely made for decades. Once again, however, the APA demands more. *See Cappadora v. Celebrezze*, 356 F.2d 1, 6 (2d Cir. 1966) (Friendly, J.) ("[O]nce appropriate rules have been established, … unreasonable deviation from such rules on an *ad hoc* basis at the whim of the Administration" is arbitrary and capricious).

B. DEA Cannot Adopt the FDCA's Policies and Goals for Decades Only to Disregard Subsequent Amendments to the FDCA's Scheme.

Agencies must consider all relevant factors, *see Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 416 (1971), and may not "entirely fail[ ] to consider an important aspect of the problem," that they seek to address. *State Farm* 463 U.S. at 43. Likewise, when an agency decision fails

to account for "relevant factors" or evinces "a clear error of judgment," the APA requires courts to hold it unlawful and set it aside. *Marsh*, 490 U.S. at 378 (quotation omitted).

DEA's final decision falls short of these standards. DEA cannot adopt FDCA standards for determining "accepted medical use" under the CSA but ignore subsequent amendments to those same standards.

Of course, agencies aren't generally obligated to weigh the "policies and goals" of statutory schemes they don't administer. *See Pension Ben. Guar. Corp. v. LTV Corp.*, 496 U.S. 633, 646 (1990). So, for example, DEA need not consider the policies and goals of the Fair Housing Act when administering the CSA. But this general principle does not apply here for two reasons.

First, as explained throughout, the FDCA plainly is not a statute *unrelated* to the CSA. *See supra* Part I. On the contrary, Congress expressly addressed the *interplay* between the two statutory schemes by require the CSA's provision to yield to those of the FDCA. *See* 21 U.S.C. § 902.

Second, DEA's cherry-picking of the FDCA must be rejected. For decades, DEA has cloaked some of its most controversial policies in the mantle of the FDCA. *See, e.g.*, 81 Fed. Reg. 53,688 at 700-01 (denying petition to reschedule marijuana filed by two State governors because of the absence of adequate and well-controlled studies for safety and efficacy of a

human drug as defined under FDA regulations and based on FDA-derived test). Indeed, in response to comments on the petition for review at issue here, DEA stated that "[it] relies on and continues to support legitimate scientific research for medical treatments," and "[w]hen research demonstrates that a drug is both safe and effective, and the FDA recognizes it as a legitimate treatment, DEA will take the appropriate actions." ER-55f.

The most notorious example of DEA grafting FDCA standards onto the CSA is probably the agency's 1992 Order interpreting the statutory term "currently accepted medical use in treatment." 57 Fed. Reg. 10,499 (Mar. 26, 1992). There, DEA explained that when Congress enacted the CSA, it relied on the fact that it had previously "developed detailed Federal statutory criteria under the FDCA to determine whether drugs are acceptable for medical use." *Id.* at 10,503. DEA further explained that while "[t]he FDCA is a very complex regulatory scheme not easily summarized," drugs that fell "into one of four FDCA categories were accepted by Congress for medical use." *Id.*

Decades later, changing societal and scientific norms led Congress to create another category through the FDCA's RTT provisions. Federal RTT establishes different "national standards and rules by which investigational drugs may be provided to terminally ill patients." 21 U.S.C. § 360bbb–0a

note, 132 Stat. 1375. Congress was fully aware of DEA's longstanding adherence to FDCA standards when administering the CSA. *See, e.g.*, *Mississippi ex rel. Hood v. AU Optronics Corp.*, 571 U.S. 161, 169 (2014) ("[W]e presume that 'Congress is aware of existing law when it passes legislation'" (quoting *Hall v. United States*, 566 U.S. 506, 515 (2012)).

Having insisted for decades that FDCA standards determine what drugs are acceptable for medical use, DEA may not ignore those same standards now that they recognize the use of schedule I EIDs by terminally ill patients qualifies as legitimate medical practice in certain limited circumstances. If DEA wants to change its settled policy with respect to FDCA standards, it must at least acknowledge its change of position and provide Petitioners and the public some reasoned explanation why, in the case of dying patients seeking the benefits of the FDCA's RTT provisions, it has had an anomalous change of heart.

CONCLUSION

Petitioners request that the Court grant the Petition for Review, vacate the Final Determination, and instruct DEA to promptly accommodate RTT and provide directions to licensed practitioners on how to obtain approval from DEA necessary to obtain schedule I drugs for therapeutic use consistent with RTT laws.

Date: May 14, 2021

/s/ James F. Williams

Kathryn L. Tucker
EMERGE LAW GROUP
621 SW Morrison Street
Suite 900
Portland, OR 97205
Phone: 206.595.0097
kathryn@emergelawgroup.com

Matthew C. Zorn
YETTER COLEMAN LLP
811 Main Street, Suite 4100
Houston, Texas 77002
Phone: 713.632.8000
Fax: 713.632.8002
mzorn@yettercoleman.com

James F. Williams
Andrew J. Kline
Thomas J. Tobin
Holly Martinez
PERKINS COIE LLP
1201 Third Avenue, Suite 4900
Seattle, WA 98101-3099
Phone: 206.359.8000
Fax: 206.359.9000
jwilliams@perkinscoie.com
akline@perkinscoie.com
ttobin@perkinscoie.com
hmartinez@perkinscoie.com

Shane Pennington
Vicente Sederberg LLP
1115 Broadway, 12th Floor
New York, NY 10010
Phone: 917.338.5455
Fax: 303.860.4504
s.pennington@vicentesederberg.com

Attorneys for Petitioners

CERTIFICATE OF COMPLIANCE

Pursuant to Fed. R. App. P. 32(a)(7)(C), I certify that:

This brief complies with the type-volume limitation of Fed. R. App. P. 32(a)(7)(B) because this brief contains 13,609 words, excluding the parts of the brief exempted by Fed. R. App. P. 32(a)(7)(B)(iii). This brief com-plies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6) because this brief has been prepared in a proportionately spaced typeface using Microsoft Word Georgia 14-point font.

Perkins Coie LLP

/s/James F. Williams
James F. Williams
1201 Third Avenue, Suite 4900
Seattle, WA 98101-3099
Phone: 206.359.8000
Fax: 206.359.9000
jwilliams@perkinscoie.com

Attorney for Petitioners

CERTIFICATE OF SERVICE

I hereby certify that on May 14, 2021, I electronically filed the foregoing with the Clerk of the Court for the United States Court of Appeals for the Ninth Circuit by using the appellate CM/ECF system.

Perkins Coie LLP

/s/James F. Williams
James F. Williams
1201 Third Avenue, Suite 4900
Seattle, WA 98101-3099
Phone: 206.359.8000
Fax: 206.359.9000
jwilliams@perkinscoie.com

Attorney for Petitioners

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TRICKETT WENDLER, FRANK MONGIELLO, JORDAN MCLINN, AND MATTHEW BELLINA RIGHT TO TRY ACT OF 2017

Public Law 115–176
115th Congress

An Act

May 30, 2018
[S. 204]

To authorize the use of unapproved medical products by patients diagnosed with a terminal illness in accordance with State law, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017.
21 USC 301 note.

SECTION 1. SHORT TITLE.

This Act may be cited as the "Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017".

SEC. 2. USE OF UNAPPROVED INVESTIGATIONAL DRUGS BY PATIENTS DIAGNOSED WITH A TERMINAL ILLNESS.

(a) IN GENERAL.—Chapter V of the Federal Food, Drug, and Cosmetic Act is amended by inserting after section 561A (21 U.S.C. 360bbb–0) the following:

21 USC 360bbb–0a.

"SEC. 561B. INVESTIGATIONAL DRUGS FOR USE BY ELIGIBLE PATIENTS.

"(a) DEFINITIONS.—For purposes of this section—

"(1) the term 'eligible patient' means a patient—

"(A) who has been diagnosed with a life-threatening disease or condition (as defined in section 312.81 of title 21, Code of Federal Regulations (or any successor regulations));

"(B) who has exhausted approved treatment options and is unable to participate in a clinical trial involving the eligible investigational drug, as certified by a physician, who—

"(i) is in good standing with the physician's licensing organization or board; and

"(ii) will not be compensated directly by the manufacturer for so certifying; and

"(C) who has provided to the treating physician written informed consent regarding the eligible investigational drug, or, as applicable, on whose behalf a legally authorized representative of the patient has provided such consent;

"(2) the term 'eligible investigational drug' means an investigational drug (as such term is used in section 561)—

"(A) for which a Phase 1 clinical trial has been completed;

"(B) that has not been approved or licensed for any use under section 505 of this Act or section 351 of the Public Health Service Act;

"(C)(i) for which an application has been filed under section 505(b) of this Act or section 351(a) of the Public Health Service Act; or

"(ii) that is under investigation in a clinical trial that—

"(I) is intended to form the primary basis of a claim of effectiveness in support of approval or licensure under section 505 of this Act or section 351 of the Public Health Service Act; and

"(II) is the subject of an active investigational new drug application under section 505(i) of this Act or section 351(a)(3) of the Public Health Service Act, as applicable; and

"(D) the active development or production of which is ongoing and has not been discontinued by the manufacturer or placed on clinical hold under section 505(i); and

"(3) the term 'phase 1 trial' means a phase 1 clinical investigation of a drug as described in section 312.21 of title 21, Code of Federal Regulations (or any successor regulations).

"(b) EXEMPTIONS.—Eligible investigational drugs provided to eligible patients in compliance with this section are exempt from sections 502(f), 503(b)(4), 505(a), and 505(i) of this Act, section 351(a) of the Public Health Service Act, and parts 50, 56, and 312 of title 21, Code of Federal Regulations (or any successor regulations), provided that the sponsor of such eligible investigational drug or any person who manufactures, distributes, prescribes, dispenses, introduces or delivers for introduction into interstate commerce, or provides to an eligible patient an eligible investigational drug pursuant to this section is in compliance with the applicable requirements set forth in sections 312.6, 312.7, and 312.8(d)(1) of title 21, Code of Federal Regulations (or any successor regulations) that apply to investigational drugs.

"(c) USE OF CLINICAL OUTCOMES.—

"(1) IN GENERAL.—Notwithstanding any other provision of this Act, the Public Health Service Act, or any other provision of Federal law, the Secretary may not use a clinical outcome associated with the use of an eligible investigational drug pursuant to this section to delay or adversely affect the review or approval of such drug under section 505 of this Act or section 351 of the Public Health Service Act unless—

"(A) the Secretary makes a determination, in accordance with paragraph (2), that use of such clinical outcome is critical to determining the safety of the eligible investigational drug; or

Determination.

"(B) the sponsor requests use of such outcomes.

"(2) LIMITATION.—If the Secretary makes a determination under paragraph (1)(A), the Secretary shall provide written notice of such determination to the sponsor, including a public health justification for such determination, and such notice shall be made part of the administrative record. Such determination shall not be delegated below the director of the agency center that is charged with the premarket review of the eligible investigational drug.

Notice.
Records.

"(d) REPORTING.—

"(1) IN GENERAL.—The manufacturer or sponsor of an eligible investigational drug shall submit to the Secretary an annual summary of any use of such drug under this section. The summary shall include the number of doses supplied, the

Regulations.

number of patients treated, the uses for which the drug was made available, and any known serious adverse events. The Secretary shall specify by regulation the deadline of submission of such annual summary and may amend section 312.33 of title 21, Code of Federal Regulations (or any successor regulations) to require the submission of such annual summary in conjunction with the annual report for an applicable investigational new drug application for such drug.

"(2) POSTING OF INFORMATION.—The Secretary shall post an annual summary report of the use of this section on the internet website of the Food and Drug Administration, including the number of drugs for which clinical outcomes associated with the use of an eligible investigational drug pursuant to this section was—

"(A) used in accordance with subsection (c)(1)(A);

"(B) used in accordance with subsection (c)(1)(B); and

"(C) not used in the review of an application under section 505 of this Act or section 351 of the Public Health Service Act.".

21 USC 360bbb–0a note.

(b) NO LIABILITY.—

(1) ALLEGED ACTS OR OMISSIONS.—With respect to any alleged act or omission with respect to an eligible investigational drug provided to an eligible patient pursuant to section 561B of the Federal Food, Drug, and Cosmetic Act and in compliance with such section, no liability in a cause of action shall lie against—

(A) a sponsor or manufacturer; or

(B) a prescriber, dispenser, or other individual entity (other than a sponsor or manufacturer), unless the relevant conduct constitutes reckless or willful misconduct, gross negligence, or an intentional tort under any applicable State law.

(2) DETERMINATION NOT TO PROVIDE DRUG.—No liability shall lie against a sponsor manufacturer, prescriber, dispenser or other individual entity for its determination not to provide access to an eligible investigational drug under section 561B of the Federal Food, Drug, and Cosmetic Act.

(3) LIMITATION.—Except as set forth in paragraphs (1) and (2), nothing in this section shall be construed to modify or otherwise affect the right of any person to bring a private action under any State or Federal product liability, tort, consumer protection, or warranty law.

21 USC 360bbb–0a note.

SEC. 3. SENSE OF THE SENATE.

It is the sense of the Senate that section 561B of the Federal Food, Drug, and Cosmetic Act, as added by section 2—

(1) does not establish a new entitlement or modify an existing entitlement, or otherwise establish a positive right to any party or individual;

(2) does not establish any new mandates, directives, or additional regulations;

(3) only expands the scope of individual liberty and agency among patients, in limited circumstances;

(4) is consistent with, and will act as an alternative pathway alongside, existing expanded access policies of the Food and Drug Administration;

(5) will not, and cannot, create a cure or effective therapy where none exists;

(6) recognizes that the eligible terminally ill patient population often consists of those patients with the highest risk of mortality, and use of experimental treatments under the criteria and procedure described in such section 561A involves an informed assumption of risk; and

(7) establishes national standards and rules by which investigational drugs may be provided to terminally ill patients.

Approved May 30, 2018.

LEGISLATIVE HISTORY—S. 204:

CONGRESSIONAL RECORD:
Vol. 163 (2017): Aug. 3, considered and passed Senate.
Vol. 164 (2018): May 22, considered and passed House.
DAILY COMPILATION OF PRESIDENTIAL DOCUMENTS (2018):
May 30, Presidential remarks.

○

Chapter Listing

Chapter 69.77 RCW

INVESTIGATIONAL DRUGS, BIOLOGICAL PRODUCTS, AND DEVICES

Sections

69.77.010 Findings—Intent.

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69.77.090 Pharmacy quality assurance commission may adopt rules.

RCW 69.77.010

Findings—Intent.

The legislature finds that the process for approval of investigational drugs, biological products, and devices in the United States protects future patients from premature, ineffective, and unsafe medications and treatments over time, but the process often takes many years. Patients who have a terminal illness do not have the luxury of waiting until an investigational drug, biological product, or device receives final approval from the United States food and drug administration. The legislature further finds that patients who have a terminal illness should be permitted to pursue the preservation of their own lives by accessing available investigational drugs, biological products, and devices. The use of available investigational drugs, biological products, and devices is a decision that should be made by the patient with a terminal illness in consultation with the patient's health care provider so that the decision to use an investigational drug, biological product, or device is made with full awareness of the potential risks, benefits, and consequences to the patient and the patient's family.

The legislature, therefore, intends to allow terminally ill patients to use potentially lifesaving investigational drugs, biological products, and devices.

[2017 c 212 § 1.]

RCW 69.77.020

Definitions.

The definitions in this section apply throughout this chapter unless the context clearly requires otherwise.

(1) "Eligible patient" means an individual who meets the requirements of RCW 69.77.040.

(2) "Health care facility" means a clinic, nursing home, laboratory, office, or similar place where a health care provider provides health care to patients.

(3) "Hospital" means a health care institution licensed under chapter **70.41**, 71.12, or **72.23** RCW.

(4) "Investigational product" means a drug, biological product, or device that has successfully completed phase one and is currently in a subsequent phase of a clinical trial approved by the United States food and drug administration assessing the safety of the drug, biological product, or device under section 505 of the federal food, drug, and cosmetic act, 21 U.S.C. Sec. 355.

(5) "Issuer" means any state purchased health care programs under chapter **41.05** or **74.09** RCW, a disability insurer regulated under chapter **48.20** or **48.21** RCW, a health care service contractor as defined in RCW **48.44.010**, or a health maintenance organization as defined in RCW **48.46.020**.

(6) "Manufacturer" means a person or other entity engaged in the manufacture or distribution of drugs, biological products, or devices.

(7) "Physician" means a physician licensed under chapter **18.71** RCW or an osteopathic physician and surgeon licensed under chapter **18.57** RCW.

(8) "Serious or immediately life-threatening disease or condition" means a stage of disease in which there is reasonable likelihood that death will occur within six months or in which premature death is likely without early treatment.

[**2017 c 212 § 2**.]

RCW 69.77.030

Eligible patient and treating physician may request investigational product—Manufacturer may make for treatment—Agreement.

(1) An eligible patient and his or her treating physician may request that a manufacturer make an investigational product available for treatment of the patient. The request must include a copy of the written informed consent form described in RCW **69.77.050** and an explanation of why the treating physician believes the investigational product may help the patient.

(2) Upon receipt of the request and the written informed consent form, the manufacturer may, but is not required to, make the investigational product available for treatment of the eligible patient. Prior to making the investigational product available, the manufacturer shall enter into an agreement with the treating physician and the eligible patient providing that the manufacturer will transfer the investigational product to the physician and the physician will use the investigational product to treat the eligible patient.

[**2017 c 212 § 3**.]

RCW 69.77.040

Patient eligibility for access and treatment with investigational product.

A patient is eligible to request access to and be treated with an investigational product if:

(1) The patient is eighteen years of age or older;

(2) The patient is a resident of this state;

(3) The patient's treating physician attests to the fact that the patient has a serious or immediately life-threatening disease or condition;

(4) The patient acknowledges having been informed by the treating physician of all other treatment options currently approved by the United States food and drug administration;

(5) The patient's treating physician recommends that the patient be treated with an investigational product;

(6) The patient is unable to participate in a clinical trial for the investigational product because the patient's physician has contacted one or more clinical trials or researchers in the physician's practice area and has determined, using the physician's professional judgment, that there are no clinical trials reasonably available for the patient to participate in, that the patient would not qualify for a clinical trial, or that delay in waiting to join a clinical trial would risk further harm to the patient; and

(7) In accordance with RCW **69.77.050**, the patient has provided written informed consent for the use of the investigational product, or, if the patient lacks the capacity to consent, the patient's legally authorized representative has provided written informed consent on behalf of the patient.

[**2017 c 212 § 4**.]

RCW 69.77.050

Informed consent.

(1) Prior to treatment of the eligible patient with an investigational product, the treating physician shall obtain written informed consent, consistent with the requirements of RCW **7.70.060**(1), and signed by the eligible patient or, if the patient lacks the capacity to consent, his or her legally authorized representative.

(2) Information provided in order to obtain the informed consent must, to the extent possible, include the following:

(a) That the patient has been diagnosed with a serious or immediately life-threatening disease or condition and explains the currently approved products and treatments for the disease or condition from which the eligible patient suffers;

(b) That all currently approved and conventionally recognized treatments are unlikely to prolong the eligible patient's life;

(c) Clear identification of the investigational product that the eligible patient seeks to use;

(d) The potentially best and worst outcomes of using the investigational product and a realistic description of the most likely outcome. This description must include the possibility that new, unanticipated, different, or worse symptoms may result and that death could be hastened by the proposed treatment. The description must be based on the physician's knowledge of the proposed treatment in conjunction with an awareness of the eligible patient's condition;

(e) That the eligible patient's health benefit plan is not obligated to pay for the investigational product or any harm caused to the eligible patient by the investigational product, unless otherwise specifically required to do so by law or contract, and that in order to receive the investigational product the patient may be required to pay the costs of administering the investigational product; and

(f) That the eligible patient is liable for all expenses consequent to the use of the investigational product, except as otherwise provided in the eligible patient's health benefit plan or a contract between the eligible patient and the manufacturer of the investigational product.

(3) The document must be signed and dated by the eligible patient's treating physician and witnessed in writing by at least one adult.

[**2017 c 212 § 5**.]

RCW 69.77.060

Issuer may provide coverage for cost or administration of investigational product—Denial of coverage.

(1) An issuer may, but is not required to, provide coverage for the cost or the administration of an investigational product provided to an eligible patient pursuant to this chapter.

(2)(a) An issuer may deny coverage to an eligible patient who is treated with an investigational product for harm to the eligible patient caused by the investigational product and is not required to cover the costs associated with receiving the investigational product or the costs demonstrated to be associated with an adverse effect that is a result of receiving the investigational product.

(b) Except as stated in (a) of this subsection, an issuer may not deny coverage to an eligible patient for: (i) The eligible patient's serious or immediately life-threatening disease or condition; (ii) benefits that accrued before the day on which the eligible patient was treated with an investigational product; or (iii) palliative or hospice care for an eligible patient who was previously treated with an investigational product but who is no longer being treated with an investigational product.

[**2017 c 212 § 6**.]

RCW 69.77.070

Hospitals and health care facilities.

A hospital or health care facility:

(1) May, but is not required to, allow a health care practitioner who is privileged to practice or who is employed at the hospital or health care facility to treat, administer, or provide an investigational product to an eligible patient under this chapter;

(2) May establish a policy regarding treating, administering, or providing investigational products under this chapter; and

(3) Is not obligated to pay for the investigational product or any harm caused to the eligible patient by the product, or any care that is necessary as a result of the use of the investigational product, including under chapter **70.170** RCW.

[**2017 c 212 § 7**.]

RCW 69.77.080

Private right of action—Unprofessional conduct—Immunity from civil or criminal liability.

(1) Chapter 212, Laws of 2017 does not create a private right of action.

(2) A health care practitioner does not commit unprofessional conduct under RCW **18.130.180** and does not violate the applicable standard of care by:

(a) Obtaining an investigational product pursuant to this chapter;

(b) Refusing to recommend, request, prescribe, or otherwise provide an investigational product pursuant to this chapter;

(c) Administering an investigational product to an eligible patient pursuant to this chapter; or

(d) Treating an eligible patient with an investigational product pursuant to this chapter.

(3) The following persons and entities are immune from civil or criminal liability and administrative actions arising out of treatment of an eligible patient with an investigational product, other than acts or

omissions constituting gross negligence or willful or wanton misconduct:

(a) A health care practitioner who recommends or requests an investigational product for an eligible patient in compliance with this chapter;

(b) A health care practitioner who refuses to recommend or request an investigational product for a patient seeking access to an investigational product;

(c) A manufacturer that provides an investigational product to a health care practitioner in compliance with this chapter;

(d) A hospital or health care facility where an investigational product is either administered or provided to an eligible patient in compliance with this chapter; and

(e) A hospital or health care facility that does not allow a health care practitioner to provide treatment with an investigational product or enforces a policy it has adopted regarding treating, administering, or providing care with an investigational product.

[**2017 c 212 § 8**.]

RCW 69.77.090

Pharmacy quality assurance commission may adopt rules.

The pharmacy quality assurance commission may adopt rules necessary to implement this chapter.

[**2017 c 212 § 9**.]

21 U.S.C.A. § 355

§ 355. New drugs

Effective: April 23, 2021
Currentness

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug.

(b) Filing application; contents

(1)(A) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as part of the application--

(i) full reports of investigations which have been made to show whether such drug is safe for use and whether such drug is effective in use;

(ii) a full list of the articles used as components of such drug;

(iii) a full statement of the composition of such drug;

(iv) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug;

(v) such samples of such drug and of the articles used as components thereof as the Secretary may require;

(vi) specimens of the labeling proposed to be used for such drug;

(vii) any assessments required under section 355c of this title; and

(viii) the patent number and expiration date of each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that--

(I) claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or

(II) claims a method of using such drug for which approval is sought or has been granted in the application.

(B) If an application is filed under this subsection for a drug, and a patent of the type described in subparagraph (A)(viii) is issued after the filing date but before approval of the application, the applicant shall amend the application to include the patent number and expiration date.

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include--

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c)--

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

(3) Notice of opinion that patent is invalid or will not be infringed

(A) Agreement to give notice

An applicant that makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give notice as required by this paragraph.

(B) Timing of notice

An applicant that makes a certification described in paragraph (2)(A)(iv) shall give notice as required under this paragraph--

(i) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(ii) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(C) Recipients of notice

An applicant required under this paragraph to give notice shall give notice to--

(i) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(ii) the holder of the approved application under this subsection for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(D) Contents of notice

A notice required under this paragraph shall--

(i) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(ii) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(4)(A) An applicant may not amend or supplement an application referred to in paragraph (2) to seek approval of a drug that is a different drug than the drug identified in the application as submitted to the Secretary.

(B) With respect to the drug for which such an application is submitted, nothing in this subsection or subsection (c)(3) prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(5)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1) or under section 262 of Title 42, which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict

of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection or section 262 of Title 42 if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size--

(i)(I) of clinical trials intended to form the primary basis of an effectiveness claim; or

(II) in the case where human efficacy studies are not ethical or feasible, of animal and any associated clinical trials which, in combination, are intended to form the primary basis of an effectiveness claim; or

(ii) with respect to an application for approval of a biological product under section 262(k) of Title 42, of any necessary clinical study or studies.

The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of the clinical trials. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request.

(C) Any agreement regarding the parameters of the design and size of clinical trials of a new drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except--

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance division personnel unless such field or compliance division personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection or section 262 of Title 42 (including all scientific and medical matters, chemistry, manufacturing, and controls).

(6) An application submitted under this subsection shall be accompanied by the certification required under section 282(j)(5)(B) of Title 42. Such certification shall not be considered an element of such application.

(c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(1) Within one hundred and eighty days after the filing of an application under subsection (b), or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either--

(A) approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) applies, or

(B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) Not later than 30 days after the date of approval of an application submitted under subsection (b), the holder of the approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii), except that a patent that is identified as claiming a method of using such drug shall be filed only if the patent claims a method of use approved in the application. If a patent described in subsection (b)(1)(A)(viii) is issued after the date of approval of an application submitted under subsection (b), the holder of the approved application shall, not later than 30 days after the date of issuance of the patent, file the patent number and the expiration date of the patent, except that a patent that claims a method of using such drug shall be filed only if approval for such use has been granted in the application. If the patent information described in subsection (b) could not be filed with the submission of an application under subsection (b) because the application was filed before the patent information was required under subsection (b) or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii). If the holder of an approved application could not file patent information under subsection (b) because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) because no patent of the type for which information is required to be submitted in subsection (b)(1)(A)(viii) had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it. Patent information that is not the type of patent information required by subsection (b)(1)(A)(viii) shall not be submitted under this paragraph.

(3) The approval of an application filed under subsection (b) which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined by applying the following to each certification made under subsection (b)(2)(A):

(A) If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) or in both such clauses, the approval may be made effective immediately.

(B) If the applicant made a certification described in clause (iii) of subsection (b)(2)(A), the approval may be made effective on the date certified under clause (iii).

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) before the date on which the application (excluding an amendment or supplement to the application) was submitted. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under subsection (b)(3) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that--

(i) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on--

(I) the date on which the court enters judgment reflecting the decision; or

(II) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(ii) if before the expiration of such period the district court decides that the patent has been infringed--

(I) if the judgment of the district court is appealed, the approval shall be made effective on--

(aa) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(bb) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(II) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of Title 35;

(iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in clause (i); or

(iv) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in clause (ii).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(D) Civil action to obtain patent certainty

(i) Declaratory judgment absent infringement action

(I) In general

No action may be brought under section 2201 of Title 28 by an applicant referred to in subsection (b)(2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (C) unless--

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) Filing of civil action

If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of Title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) Offer of confidential access to application

For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant referred to in subsection (b)(2) for the purpose of determining whether an action referred to in subparagraph (C) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and

disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under subsection (b)(2)(A)(iv) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) Counterclaim to infringement action

(I) In general

If an owner of the patent or the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or this subsection on the ground that the patent does not claim either--

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) No independent cause of action

Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) No damages

An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(E)(i) Repealed. Pub.L. 117-9, § 1(b)(1)(A), Apr. 23, 2019, 135 Stat. 258

(ii) If an application submitted under subsection (b) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under subsection (b), is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under subsection (b) after the expiration of four years from the date of

the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A). The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application approved under subsection (b), is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) if the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailabilty [1] studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) if the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval for the drug prior to manufacture of the drug in a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.

(5)(A) The Secretary may rely upon qualified data summaries to support the approval of a supplemental application, with respect to a qualified indication for a drug, submitted under subsection (b), if such supplemental application complies with subparagraph (B).

(B) A supplemental application is eligible for review as described in subparagraph (A) only if--

(i) there is existing data available and acceptable to the Secretary demonstrating the safety of the drug; and

(ii) all data used to develop the qualified data summaries are submitted to the Secretary as part of the supplemental application.

(C) The Secretary shall post on the Internet website of the Food and Drug Administration and update annually--

(i) the number of applications reviewed solely under subparagraph (A) or section 262(a)(2)(E) of Title 42;

(ii) the average time for completion of review under subparagraph (A) or section 262(a)(2)(E) of Title 42;

(iii) the average time for review of supplemental applications where the Secretary did not use review flexibility under subparagraph (A) or section 262(a)(2)(E) of Title 42; and

(iv) the number of applications reviewed under subparagraph (A) or section 262(a)(2)(E) of Title 42 for which the Secretary made use of full data sets in addition to the qualified data summary.

(D) In this paragraph--

(i) the term "qualified indication" means an indication for a drug that the Secretary determines to be appropriate for summary level review under this paragraph; and

(ii) the term "qualified data summary" means a summary of clinical data that demonstrates the safety and effectiveness of a drug with respect to a qualified indication.

(d) Grounds for refusing application; approval of application; "substantial evidence" defined

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b), do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b); or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As

used in this subsection and subsection (e), the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence. The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decisionmaking, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for marketing approval of a drug.

(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the application contains any untrue statement of a material fact: *Provided*, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based. The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk evaluation and mitigation strategy for the drug under section 355-1(g)(2)(D) of this title.

(f) Revocation of order refusing, withdrawing or suspending approval of application

Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

(g) Service of orders

Orders of the Secretary issued under this section shall be served (1) in person by any officer or employee of the department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last-known address in the records of the Secretary.

(h) Appeal from order

An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals for the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and file in the court the record upon which the order complained of was entered, as provided in section 2112 of Title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of Title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

(i) Exemptions of drugs for research; discretionary and mandatory conditions; direct reports to Secretary

(1) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon--

(A) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

(B) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings;

(C) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b); and

(D) the submission to the Secretary by the manufacturer or the sponsor of the investigation of a new drug of a statement of intent regarding whether the manufacturer or sponsor has plans for assessing pediatric safety and efficacy.

(2) Subject to paragraph (3), a clinical investigation of a new drug may begin 30 days after the Secretary has received from the manufacturer or sponsor of the investigation a submission containing such information about the drug and the clinical investigation, including--

(A) information on design of the investigation and adequate reports of basic information, certified by the applicant to be accurate reports, necessary to assess the safety of the drug for use in clinical investigation; and

(B) adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from animal or human studies.

(3)(A) At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a "clinical hold") if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is that--

(i) the drug involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation, the condition for which the drug is to be investigated, and the health status of the subjects involved; or

(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish (including reasons established by regulation before November 21, 1997).

(C) Any written request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

(4) Regulations under paragraph (1) shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where it is not feasible, it is contrary to the best interests of such human beings, or the proposed clinical testing poses no more than minimal risk to such human beings and includes appropriate safeguards as prescribed to protect the rights, safety, and welfare of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs. The Secretary shall update such regulations to require inclusion in the informed consent documents and process a statement that clinical trial information for such clinical investigation has been or will be submitted for inclusion in the registry data bank pursuant to subsection (j) of section 282 of Title 42.

(j) Abbreviated new drug applications

(1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.

(2)(A) An abbreviated application for a new drug shall contain--

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (7) (hereinafter in this subsection referred to as a "listed drug");

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (ii) through (vi) of subsection (b)(1)(A);

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c)--

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B) Notice of opinion that patent is invalid or will not be infringed

(i) Agreement to give notice

An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give notice as required by this subparagraph.

(ii) Timing of notice

An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall give notice as required under this subparagraph--

(I) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(II) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(iii) Recipients of notice

An applicant required under this subparagraph to give notice shall give notice to--

(I) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(II) the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(iv) Contents of notice

A notice required under this subparagraph shall--

(I) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(II) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds--

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

(D)(i) An applicant may not amend or supplement an application to seek approval of a drug referring to a different listed drug from the listed drug identified in the application as submitted to the Secretary.

(ii) With respect to the drug for which an application is submitted, nothing in this subsection prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(iii) Within 60 days after December 8, 2003, the Secretary shall issue guidance defining the term "listed drug" for purposes of this subparagraph.

(3)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1), which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size of bioavailability and bioequivalence studies needed for approval of such application. The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of such studies. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant.

(C) Any agreement regarding the parameters of design and size of bioavailability and bioequivalence studies of a drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except--

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance office personnel unless such field or compliance office personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection (including scientific matters, chemistry, manufacturing, and controls).

(4) Subject to paragraph (5), the Secretary shall approve an application for a drug unless the Secretary finds--

(A) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(B) information submitted with the application is insufficient to show that each of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

(C)(i) if the listed drug has only one active ingredient, information submitted with the application is insufficient to show that the active ingredient is the same as that of the listed drug;

(ii) if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or

(iii) if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show--

(I) that the other active ingredients are the same as the active ingredients of the listed drug, or

(II) that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 321(p) of this title,

or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

(D)(i) if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or

(ii) if the application is for a drug whose route of administration, dosage form, or strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);

(E) if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;

(F) information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

(G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

(H) information submitted in the application or any other information available to the Secretary shows that (i) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or (ii) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

(I) the approval under subsection (c) of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e), the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) for grounds described in the first sentence of subsection (e), the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph (6), or the Secretary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

(J) the application does not meet any other requirement of paragraph (2)(A); or

(K) the application contains an untrue statement of material fact.

(5)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii):

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that--

(I) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on--

(aa) the date on which the court enters judgment reflecting the decision; or

(bb) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(II) if before the expiration of such period the district court decides that the patent has been infringed--

(aa) if the judgment of the district court is appealed, the approval shall be made effective on--

(AA) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(BB) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(bb) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of Title 35;

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in subclause (I); or

(IV) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in subclause (II).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(iv) 180-day exclusivity period

(I) Effectiveness of application

Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

(II) Definitions

In this paragraph:

(aa) 180-day exclusivity period

The term "180-day exclusivity period" means the 180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.

(bb) First applicant

As used in this subsection, the term "first applicant" means an applicant that, on the first day on which a substantially complete application containing a certification described in paragraph (2)(A)(vii)(IV) is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a certification described in paragraph (2)(A)(vii)(IV) for the drug.

(cc) Substantially complete application

As used in this subsection, the term "substantially complete application" means an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required by paragraph (2)(A).

(dd) Tentative approval

(AA) In general

The term "tentative approval" means notification to an applicant by the Secretary that an application under this subsection meets the requirements of paragraph (2)(A), but cannot receive effective approval because the

application does not meet the requirements of this subparagraph, there is a period of exclusivity for the listed drug under subparagraph (F) or section 355a of this title, or there is a 7-year period of exclusivity for the listed drug under section 360cc of this title.

(BB) Limitation

A drug that is granted tentative approval by the Secretary is not an approved drug and shall not have an effective approval until the Secretary issues an approval after any necessary additional review of the application.

(v) 180-day exclusivity period for competitive generic therapies

(I) Effectiveness of application

Subject to subparagraph (D)(iv), if the application is for a drug that is the same as a competitive generic therapy for which any first approved applicant has commenced commercial marketing, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the competitive generic therapy (including the commercial marketing of the listed drug) by any first approved applicant.

(II) Limitation

The exclusivity period under subclause (I) shall not apply with respect to a competitive generic therapy that has previously received an exclusivity period under subclause (I).

(III) Definitions

In this clause and subparagraph (D)(iv):

(aa) The term "competitive generic therapy" means a drug--

(AA) that is designated as a competitive generic therapy under section 356h of this title; and

(BB) for which there are no unexpired patents or exclusivities on the list of products described in section 355(j)(7)(A) of this title at the time of submission.

(bb) The term "first approved applicant" means any applicant that has submitted an application that--

(AA) is for a competitive generic therapy that is approved on the first day on which any application for such competitive generic therapy is approved;

(BB) is not eligible for a 180-day exclusivity period under clause (iv) for the drug that is the subject of the application for the competitive generic therapy; and

(CC) is not for a drug for which all drug versions have forfeited eligibility for a 180-day exclusivity period under clause (iv) pursuant to subparagraph (D).

(C) Civil action to obtain patent certainty

(i) Declaratory judgment absent infringement action

(I) In general

No action may be brought under section 2201 of Title 28, by an applicant under paragraph (2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (B)(iii) unless--

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) Filing of civil action

If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of Title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) Offer of confidential access to application

For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant under paragraph (2) for the purpose of determining whether an action referred to in subparagraph (B)(iii) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access,

and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) Counterclaim to infringement action

(I) In general

If an owner of the patent or the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) on the ground that the patent does not claim either--

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) No independent cause of action

Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) No damages

An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(D) Forfeiture of 180-day exclusivity period

(i) Definition of forfeiture event

In this subparagraph, the term “forfeiture event”, with respect to an application under this subsection, means the occurrence of any of the following:

(I) Failure to market

The first applicant fails to market the drug by the later of--

(aa) the earlier of the date that is--

(AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) is withdrawn by the holder of the application approved under subsection (b).

(II) Withdrawal of application

The first applicant withdraws the application or the Secretary considers the application to have been withdrawn as a result of a determination by the Secretary that the application does not meet the requirements for approval under paragraph (4).

(III) Amendment of certification

The first applicant amends or withdraws the certification for all of the patents with respect to which that applicant submitted a certification qualifying the applicant for the 180-day exclusivity period.

(IV) Failure to obtain tentative approval

The first applicant fails to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

(V) Agreement with another applicant, the listed drug application holder, or a patent owner

The first applicant enters into an agreement with another applicant under this subsection for the drug, the holder of the application for the listed drug, or an owner of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV), the Federal Trade Commission or the Attorney General files a complaint, and there is a final decision of the Federal Trade Commission or the court with regard to the complaint from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the agreement has violated the antitrust laws (as defined in section 12 of Title 15, except that the term includes section 45 of Title 15 to the extent that that section applies to unfair methods of competition).

(VI) Expiration of all patents

All of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.

(ii) Forfeiture

The 180-day exclusivity period described in subparagraph (B)(iv) shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.

(iii) Subsequent applicant

If all first applicants forfeit the 180-day exclusivity period under clause (ii)--

(I) approval of any application containing a certification described in paragraph (2)(A)(vii)(IV) shall be made effective in accordance with subparagraph (B)(iii); and

(II) no applicant shall be eligible for a 180-day exclusivity period.

(iv) Special forfeiture rule for competitive generic therapy

The 180-day exclusivity period described in subparagraph (B)(v) shall be forfeited by a first approved applicant if the applicant fails to market the competitive generic therapy within 75 days after the date on which the approval of the first approved applicant's application for the competitive generic therapy is made effective.

(E) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(F)(i) Repealed. Pub.L. 117-9, § 1(b)(1)(B), Apr. 23, 2021, 135 Stat. 258

(ii) If an application submitted under subsection (b) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under subsection (b), is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application approved under subsection (b), is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) for such drug.

(iv) If a supplement to an application approved under subsection (b) is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b).

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from September 24, 1984.

(6) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended--

(A) for the same period as the withdrawal or suspension under subsection (e) or this paragraph, or

(B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(7)(A)(i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public--

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) before September 24, 1984;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(ii) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (c) respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(iv) For each drug included on the list, the Secretary shall specify any exclusivity period that is applicable, for which the Secretary has determined the expiration date, and for which such period has not yet expired, under--

(I) clause (ii), (iii), or (iv) of subsection (c)(3)(E);

(II) clause (iv) or (v) of paragraph (5)(B);

(III) clause (ii), (iii), or (iv) of paragraph (5)(F);

(IV) section 355a of this title;

(V) section 355f of this title;

(VI) section 360cc(a) of this title; or

(VII) subsection (u).

(B) A drug approved for safety and effectiveness under subsection (c) or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under paragraph (6) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list--

(i) for the same period as the withdrawal or suspension under subsection (e) or paragraph (6), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(D) In the case of a listed drug for which the list under subparagraph (A)(i) includes a patent for such drug, and any claim of the patent has been cancelled or invalidated pursuant to a final decision issued by the Patent Trial and Appeal Board of the United States Patent and Trademark Office or by a court, from which no appeal has been, or can be, taken, if the holder of the applicable application approved under subsection (c) determines that a patent for such drug, or any patent information for such drug, no longer meets the listing requirements under this section--

(i) the holder of such approved application shall notify the Secretary, in writing, within 14 days of such decision of such cancellation or invalidation and request that such patent or patent information, as applicable, be amended or withdrawn in accordance with the decision issued by the Patent Trial and Appeal Board or a court;

(ii) the holder of such approved application shall include in any notification under clause (i) information related to such patent cancellation or invalidation decision and submit such information, including a copy of such decision, to the Secretary; and

(iii) the Secretary shall, in response to a notification under clause (i), amend or remove patent or patent information in accordance with the relevant decision from the Patent Trial and Appeals Board or court, as applicable, except that the Secretary shall not remove from the list any patent or patent information before the expiration of any 180-day exclusivity period under paragraph (5)(B)(iv) that relies on a certification described in paragraph (2)(A)(vii)(IV).

(8) For purposes of this subsection:

(A)(i) The term "bioavailability" means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(ii) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may assess bioavailability by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or therapeutic ingredient becomes available at the site of drug action.

(B) A drug shall be considered to be bioequivalent to a listed drug if--

(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

(C) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may establish alternative, scientifically valid methods to show bioequivalence if the alternative methods are expected to detect a significant difference between the drug and the listed drug in safety and therapeutic effect.

(9) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of--

(A) the name of the applicant,

(B) the name of the drug covered by the application,

(C) the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

(D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

(10)(A) If the proposed labeling of a drug that is the subject of an application under this subsection differs from the listed drug due to a labeling revision described under clause (i), the drug that is the subject of such application shall, notwithstanding any other provision of this chapter, be eligible for approval and shall not be considered misbranded under section 352 of this title if--

(i) the application is otherwise eligible for approval under this subsection but for expiration of patent, an exclusivity period, or of a delay in approval described in paragraph (5)(B)(iii), and a revision to the labeling of the listed drug has been approved by the Secretary within 60 days of such expiration;

(ii) the labeling revision described under clause (i) does not include a change to the "Warnings" section of the labeling;

(iii) the sponsor of the application under this subsection agrees to submit revised labeling of the drug that is the subject of such application not later than 60 days after the notification of any changes to such labeling required by the Secretary; and

(iv) such application otherwise meets the applicable requirements for approval under this subsection.

(B) If, after a labeling revision described in subparagraph (A)(i), the Secretary determines that the continued presence in interstate commerce of the labeling of the listed drug (as in effect before the revision described in subparagraph (A)(i)) adversely impacts the safe use of the drug, no application under this subsection shall be eligible for approval with such labeling.

(11)(A) Subject to subparagraph (B), the Secretary shall prioritize the review of, and act within 8 months of the date of the submission of, an original abbreviated new drug application submitted for review under this subsection that is for a drug--

(i) for which there are not more than 3 approved drug products listed under paragraph (7) and for which there are no blocking patents and exclusivities; or

(ii) that has been included on the list under section 356e of this title.

(B) To qualify for priority review under this paragraph, not later than 60 days prior to the submission of an application described in subparagraph (A) or that the Secretary may prioritize pursuant to subparagraph (D), the applicant shall provide complete, accurate information regarding facilities involved in manufacturing processes and testing of the drug that is the subject of the application, including facilities in corresponding Type II active pharmaceutical ingredients drug master files referenced in an application and sites or organizations involved in bioequivalence and clinical studies used to support the application, to enable the Secretary to make a determination regarding whether an inspection of a facility is necessary. Such information shall include the relevant (as determined by the Secretary) sections of such application, which shall be unchanged relative to the date of the submission of such application, except to the extent that a change is made to such information to exclude a facility that was not used to generate data to meet any application requirements for such submission and that is not the only facility intended to conduct one or more unit operations in commercial production. Information provided by an applicant under this subparagraph shall not be considered the submission of an application under this subsection.

(C) The Secretary may expedite an inspection or reinspection under section 374 of this title of an establishment that proposes to manufacture a drug described in subparagraph (A).

(D) Nothing in this paragraph shall prevent the Secretary from prioritizing the review of other applications as the Secretary determines appropriate.

(12) The Secretary shall publish on the internet website of the Food and Drug Administration, and update at least once every 6 months, a list of all drugs approved under subsection (c) for which all patents and periods of exclusivity under this chapter have expired and for which no application has been approved under this subsection.

(13) Upon the request of an applicant regarding one or more specified pending applications under this subsection, the Secretary shall, as appropriate, provide review status updates indicating the categorical status of the applications by each relevant review discipline.

(k) Records and reports; required information; regulations and orders; access to records

(1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e). Regulations and orders issued under this subsection and under subsection (i) shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(3) Active postmarket risk identification

(A) Definition

In this paragraph, the term "data" refers to information with respect to a drug approved under this section or under section 262 of Title 42, including claims data, patient survey data, standardized analytic files that allow for the pooling and analysis of data from disparate data environments, and any other data deemed appropriate by the Secretary.

(B) Development of postmarket risk identification and analysis methods

The Secretary shall, not later than 2 years after September 27, 2007, in collaboration with public, academic, and private entities--

(i) develop methods to obtain access to disparate data sources including the data sources specified in subparagraph (C);

(ii) develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including, in aggregate--

(I) at least 25,000,000 patients by July 1, 2010; and

(II) at least 100,000,000 patients by July 1, 2012; and

(iii) convene a committee of experts, including individuals who are recognized in the field of protecting data privacy and security, to make recommendations to the Secretary on the development of tools and methods for the ethical and scientific

uses for, and communication of, postmarketing data specified under subparagraph (C), including recommendations on the development of effective research methods for the study of drug safety questions.

(C) Establishment of the postmarket risk identification and analysis system

(i) In general

The Secretary shall, not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), establish and maintain procedures--

(I) for risk identification and analysis based on electronic health data, in compliance with the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996, and in a manner that does not disclose individually identifiable health information in violation of paragraph (4)(B);

(II) for the reporting (in a standardized form) of data on all serious adverse drug experiences (as defined in section 355-1(b) of this title) submitted to the Secretary under paragraph (1), and those adverse events submitted by patients, providers, and drug sponsors, when appropriate;

(III) to provide for active adverse event surveillance using the following data sources, as available:

(aa) Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs);

(bb) private sector health-related electronic data (such as pharmaceutical purchase data and health insurance claims data); and

(cc) other data as the Secretary deems necessary to create a robust system to identify adverse events and potential drug safety signals;

(IV) to identify certain trends and patterns with respect to data accessed by the system;

(V) to provide regular reports to the Secretary concerning adverse event trends, adverse event patterns, incidence and prevalence of adverse events, and other information the Secretary determines appropriate, which may include data on comparative national adverse event trends; and

(VI) to enable the program to export data in a form appropriate for further aggregation, statistical analysis, and reporting.

(ii) Timeliness of reporting

The procedures established under clause (i) shall ensure that such data are accessed, analyzed, and reported in a timely, routine, and systematic manner, taking into consideration the need for data completeness, coding, cleansing, and standardized analysis and transmission.

(iii) Private sector resources

To ensure the establishment of the active postmarket risk identification and analysis system under this subsection not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), as required under clause (i), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(iv) Complementary approaches

To the extent the active postmarket risk identification and analysis system under this subsection is not sufficient to gather data and information relevant to a priority drug safety question, the Secretary shall develop, support, and participate in complementary approaches to gather and analyze such data and information, including--

(I) approaches that are complementary with respect to assessing the safety of use of a drug in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children); and

(II) existing approaches such as the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink or successor databases.

(v) Authority for contracts

The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subparagraph.

(4) Advanced analysis of drug safety data

(A) Purpose

The Secretary shall establish collaborations with public, academic, and private entities, which may include the Centers for Education and Research on Therapeutics under section 299b-1 of Title 42, to provide for advanced analysis of drug safety data described in paragraph (3)(C) and other information that is publicly available or is provided by the Secretary, in order to--

(i) improve the quality and efficiency of postmarket drug safety risk-benefit analysis;

(ii) provide the Secretary with routine access to outside expertise to study advanced drug safety questions; and

(iii) enhance the ability of the Secretary to make timely assessments based on drug safety data.

(B) Privacy

Such analysis shall not disclose individually identifiable health information when presenting such drug safety signals and trends or when responding to inquiries regarding such drug safety signals and trends.

(C) Public process for priority questions

At least biannually, the Secretary shall seek recommendations from the Drug Safety and Risk Management Advisory Committee (or any successor committee) and from other advisory committees, as appropriate, to the Food and Drug Administration on--

(i) priority drug safety questions; and

(ii) mechanisms for answering such questions, including through--

(I) active risk identification under paragraph (3); and

(II) when such risk identification is not sufficient, postapproval studies and clinical trials under subsection (o)(3).

(D) Procedures for the development of drug safety collaborations

(i) In general

Not later than 180 days after the date of the establishment of the active postmarket risk identification and analysis system under this subsection, the Secretary shall establish and implement procedures under which the Secretary may routinely contract with one or more qualified entities to--

(I) classify, analyze, or aggregate data described in paragraph (3)(C) and information that is publicly available or is provided by the Secretary;

(II) allow for prompt investigation of priority drug safety questions, including--

(aa) unresolved safety questions for drugs or classes of drugs; and

(bb) for a newly-approved drugs, [2] safety signals from clinical trials used to approve the drug and other preapproval trials; rare, serious drug side effects; and the safety of use in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children);

(III) perform advanced research and analysis on identified drug safety risks;

(IV) focus postapproval studies and clinical trials under subsection (o)(3) more effectively on cases for which reports under paragraph (1) and other safety signal detection is not sufficient to resolve whether there is an elevated risk of a serious adverse event associated with the use of a drug; and

(V) carry out other activities as the Secretary deems necessary to carry out the purposes of this paragraph.

(ii) Request for specific methodology

The procedures described in clause (i) shall permit the Secretary to request that a specific methodology be used by the qualified entity. The qualified entity shall work with the Secretary to finalize the methodology to be used.

(E) Use of analyses

The Secretary shall provide the analyses described in this paragraph, including the methods and results of such analyses, about a drug to the sponsor or sponsors of such drug.

(F) Qualified entities

(i) In general

The Secretary shall enter into contracts with a sufficient number of qualified entities to develop and provide information to the Secretary in a timely manner.

(ii) Qualification

The Secretary shall enter into a contract with an entity under clause (i) only if the Secretary determines that the entity has a significant presence in the United States and has one or more of the following qualifications:

(I) The research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the activities under this paragraph, including the capability and expertise to provide the Secretary de-identified data consistent with the requirements of this subsection.

(II) An information technology infrastructure in place to support electronic data and operational standards to provide security for such data.

(III) Experience with, and expertise on, the development of drug safety and effectiveness research using electronic population data.

(IV) An understanding of drug development or risk/benefit balancing in a clinical setting.

(V) Other expertise which the Secretary deems necessary to fulfill the activities under this paragraph.

(G) Contract requirements

Each contract with a qualified entity under subparagraph (F)(i) shall contain the following requirements:

(i) Ensuring privacy

The qualified entity shall ensure that the entity will not use data under this subsection in a manner that--

(I) violates the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996;

(II) violates sections 552 or 552a of Title 5 with regard to the privacy of individually-identifiable beneficiary health information; or

(III) discloses individually identifiable health information when presenting drug safety signals and trends or when responding to inquiries regarding drug safety signals and trends.

Nothing in this clause prohibits lawful disclosure for other purposes.

(ii) Component of another organization

If a qualified entity is a component of another organization--

(I) the qualified entity shall establish appropriate security measures to maintain the confidentiality and privacy of such data; and

(II) the entity shall not make an unauthorized disclosure of such data to the other components of the organization in breach of such confidentiality and privacy requirement.

(iii) Termination or nonrenewal

If a contract with a qualified entity under this subparagraph is terminated or not renewed, the following requirements shall apply:

(I) Confidentiality and privacy protections

The entity shall continue to comply with the confidentiality and privacy requirements under this paragraph with respect to all data disclosed to the entity.

(II) Disposition of data

The entity shall return any data disclosed to such entity under this subsection to which it would not otherwise have access or, if returning the data is not practicable, destroy the data.

(H) Competitive procedures

The Secretary shall use competitive procedures (as defined in section 132 of Title 41) to enter into contracts under subparagraph (G).

(I) Review of contract in the event of a merger or acquisition

The Secretary shall review the contract with a qualified entity under this paragraph in the event of a merger or acquisition of the entity in order to ensure that the requirements under this paragraph will continue to be met.

(J) Coordination

In carrying out this paragraph, the Secretary shall provide for appropriate communications to the public, scientific, public health, and medical communities, and other key stakeholders, and to the extent practicable shall coordinate with the activities of private entities, professional associations, or other entities that may have sources of drug safety data.

(5) The Secretary shall--

(A) conduct regular screenings of the Adverse Event Reporting System database and post a quarterly report on the Adverse Event Reporting System Web site of any new safety information or potential signal of a serious risk identified by Adverse [3] Event Reporting System within the last quarter; and [4]

(B) on an annual basis, review the entire backlog of postmarket safety commitments to determine which commitments require revision or should be eliminated, report to the Congress on these determinations, and assign start dates and estimated completion dates for such commitments; and

(C) make available on the Internet website of the Food and Drug Administration--

(i) guidelines, developed with input from experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that detail best practices for drug safety surveillance using the Adverse Event Reporting System; and

(ii) criteria for public posting of adverse event signals.

(l) Public disclosure of safety and effectiveness data and action package

(1) Safety and effectiveness data and information which has been submitted in an application under subsection (b) for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown--

(A) if no work is being or will be undertaken to have the application approved,

(B) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(C) if approval of the application under subsection (c) is withdrawn and all legal appeals have been exhausted,

(D) if the Secretary has determined that such drug is not a new drug, or

(E) upon the effective date of the approval of the first application under subsection (j) which refers to such drug or upon the date upon which the approval of an application under subsection (j) which refers to such drug could be made effective if such an application had been submitted.

(2) Action package for approval

(A) Action package

The Secretary shall publish the action package for approval of an application under subsection (b) or section 262 of Title 42 on the Internet Web site of the Food and Drug Administration--

(i) not later than 30 days after the date of approval of such applications--

(I) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under this section; or

(II) for a biological product, no active ingredient of which has been approved in any other application under section 262 of Title 42; and

(ii) not later than 30 days after the third request for such action package for approval received under section 552 of Title 5 for any other drug or biological product.

(B) Immediate publication of summary review

Notwithstanding subparagraph (A), the Secretary shall publish, on the Internet Web site of the Food and Drug Administration, the materials described in subparagraph (C)(iv) not later than 48 hours after the date of approval of the drug, except where such materials require redaction by the Secretary.

(C) Contents

An action package for approval of an application under subparagraph (A) shall be dated and shall include the following:

(i) Documents generated by the Food and Drug Administration related to review of the application.

(ii) Documents pertaining to the format and content of the application generated during drug development.

(iii) Labeling submitted by the applicant.

(iv) A summary review that documents conclusions from all reviewing disciplines about the drug, noting any critical issues and disagreements with the applicant and within the review team and how they were resolved, recommendations for action, and an explanation of any nonconcurrence with review conclusions.

(v) The Division Director and Office Director's decision document which includes--

(I) a brief statement of concurrence with the summary review;

(II) a separate review or addendum to the review if disagreeing with the summary review; and

(III) a separate review or addendum to the review to add further analysis.

(vi) Identification by name of each officer or employee of the Food and Drug Administration who--

(I) participated in the decision to approve the application; and

(II) consents to have his or her name included in the package.

(D) Review

A scientific review of an application is considered the work of the reviewer and shall not be altered by management or the reviewer once final.

(E) Confidential information

This paragraph does not authorize the disclosure of any trade secret, confidential commercial or financial information, or other matter listed in section 552(b) of Title 5.

(m) "Patent" defined

For purposes of this section, the term "patent" means a patent issued by the United States Patent and Trademark Office.

(n) Scientific advisory panels

(1) For the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug under this section or section 262 of Title 42, the Secretary shall establish panels of experts or use panels of experts established before November 21, 1997, or both.

(2) The Secretary may delegate the appointment and oversight authority granted under section 394 of this title to a director of a center or successor entity within the Food and Drug Administration.

(3) The Secretary shall make appointments to each panel established under paragraph (1) so that each panel shall consist of--

(A) members who are qualified by training and experience to evaluate the safety and effectiveness of the drugs to be referred to the panel and who, to the extent feasible, possess skill and experience in the development, manufacture, or utilization of such drugs;

(B) members with diverse expertise in such fields as clinical and administrative medicine, pharmacy, pharmacology, pharmacoeconomics, biological and physical sciences, and other related professions;

(C) a representative of consumer interests, and a representative of interests of the drug manufacturing industry not directly affected by the matter to be brought before the panel; and

(D) two or more members who are specialists or have other expertise in the particular disease or condition for which the drug under review is proposed to be indicated.

Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a voting member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(4) The Secretary shall, as appropriate, provide education and training to each new panel member before such member participates in a panel's activities, including education regarding requirements under this chapter and related regulations of the Secretary, and the administrative processes and procedures related to panel meetings.

(5) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including traveltime, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS-15 of the General Schedule. While serving away from their homes or regular places of business, panel members may

be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of Title 5, for persons in the Government service employed intermittently.

(6) The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such a panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meetings.

(7) Within 90 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the rationale for the decision.

(o) Postmarket studies and clinical trials; labeling

(1) In general

A responsible person may not introduce or deliver for introduction into interstate commerce the new drug involved if the person is in violation of a requirement established under paragraph (3) or (4) with respect to the drug.

(2) Definitions

For purposes of this subsection:

(A) Responsible person

The term “responsible person” means a person who--

(i) has submitted to the Secretary a covered application that is pending; or

(ii) is the holder of an approved covered application.

(B) Covered application

The term “covered application” means--

(i) an application under subsection (b) for a drug that is subject to section 353(b) of this title; and

(ii) an application under section 262 of Title 42.

(C) New safety information; serious risk

The terms "new safety information", "serious risk", and "signal of a serious risk" have the meanings given such terms in section 355-1(b) of this title.

(3) Studies and clinical trials

(A) In general

For any or all of the purposes specified in subparagraph (B), the Secretary may, subject to subparagraph (D), require a responsible person for a drug to conduct a postapproval study or studies of the drug, or a postapproval clinical trial or trials of the drug, on the basis of scientific data deemed appropriate by the Secretary, including information regarding chemically-related or pharmacologically-related drugs.

(B) Purposes of study or clinical trial

The purposes referred to in this subparagraph with respect to a postapproval study or postapproval clinical trial are the following:

(i) To assess a known serious risk related to the use of the drug involved.

(ii) To assess signals of serious risk related to the use of the drug.

(iii) To identify an unexpected serious risk when available data indicates the potential for a serious risk.

(C) Establishment of requirement after approval of covered application

The Secretary may require a postapproval study or studies or postapproval clinical trial or trials for a drug for which an approved covered application is in effect as of the date on which the Secretary seeks to establish such requirement only if the Secretary becomes aware of new safety information.

(D) Determination by Secretary

(i) Postapproval studies

The Secretary may not require the responsible person to conduct a study under this paragraph, unless the Secretary makes a determination that the reports under subsection (k)(1) and the active postmarket risk identification and analysis system as available under subsection (k)(3) will not be sufficient to meet the purposes set forth in subparagraph (B).

(ii) Postapproval clinical trials

The Secretary may not require the responsible person to conduct a clinical trial under this paragraph, unless the Secretary makes a determination that a postapproval study or studies will not be sufficient to meet the purposes set forth in subparagraph (B).

(E) Notification; timetables; periodic reports

(i) Notification

The Secretary shall notify the responsible person regarding a requirement under this paragraph to conduct a postapproval study or clinical trial by the target dates for communication of feedback from the review team to the responsible person regarding proposed labeling and postmarketing study commitments as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

(ii) Timetable; periodic reports

For each study or clinical trial required to be conducted under this paragraph, the Secretary shall require that the responsible person submit a timetable for completion of the study or clinical trial. With respect to each study required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such study including whether any difficulties in completing the study have been encountered. With respect to each clinical trial required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such clinical trial including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to the requirements under section 282(j) of Title 42. If the responsible person fails to comply with such timetable or violates any other requirement of this subparagraph, the responsible person shall be considered in violation of this subsection, unless the responsible person demonstrates good cause for such noncompliance or such other violation. The Secretary shall determine what constitutes good cause under the preceding sentence.

(F) Dispute resolution

The responsible person may appeal a requirement to conduct a study or clinical trial under this paragraph using dispute resolution procedures established by the Secretary in regulation and guidance.

(4) Safety labeling changes requested by Secretary

(A) New safety or new effectiveness information

If the Secretary becomes aware of new information, including any new safety information or information related to reduced effectiveness, that the Secretary determines should be included in the labeling of the drug, the Secretary shall promptly notify the responsible person or, if the same drug approved under subsection (b) is not currently marketed, the holder of an approved application under subsection (j).

(B) Response to notification

Following notification pursuant to subparagraph (A), the responsible person or the holder of the approved application under subsection (j) shall within 30 days--

(i) submit a supplement proposing changes to the approved labeling to reflect the new safety information, including changes to boxed warnings, contraindications, warnings, precautions, or adverse reactions, or new effectiveness information; or

(ii) notify the Secretary that the responsible person or the holder of the approved application under subsection (j) does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

(C) Review

Upon receipt of such supplement, the Secretary shall promptly review and act upon such supplement. If the Secretary disagrees with the proposed changes in the supplement or with the statement setting forth the reasons why no labeling change is necessary, the Secretary shall initiate discussions to reach agreement on whether the labeling for the drug should be modified to reflect the new safety or new effectiveness information, and if so, the contents of such labeling changes.

(D) Discussions

Such discussions shall not extend for more than 30 days after the response to the notification under subparagraph (B), unless the Secretary determines an extension of such discussion period is warranted.

(E) Order

Within 15 days of the conclusion of the discussions under subparagraph (D), the Secretary may issue an order directing the responsible person or the holder of the approved application under subsection (j) to make such a labeling change as the Secretary deems appropriate to address the new safety or new effectiveness information. Within 15 days of such an order, the responsible person or the holder of the approved application under subsection (j) shall submit a supplement containing the labeling change.

(F) Dispute resolution

Within 5 days of receiving an order under subparagraph (E), the responsible person or the holder of the approved application under subsection (j) may appeal using dispute resolution procedures established by the Secretary in regulation and guidance.

(G) Violation

If the responsible person or the holder of the approved application under subsection (j) has not submitted a supplement within 15 days of the date of such order under subparagraph (E), and there is no appeal or dispute resolution proceeding pending, the responsible person or holder shall be considered to be in violation of this subsection. If at the conclusion of any dispute resolution procedures the Secretary determines that a supplement must be submitted and such a supplement is not submitted within 15 days of the date of that determination, the responsible person or holder shall be in violation of this subsection.

(H) Public health threat

Notwithstanding subparagraphs (A) through (F), if the Secretary concludes that such a labeling change is necessary to protect the public health, the Secretary may accelerate the timelines in such subparagraphs.

(I) Rule of construction

This paragraph shall not be construed to affect the responsibility of the responsible person or the holder of the approved application under subsection (j) to maintain its label in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, Code of Federal Regulations (or any successor regulations).

(5) Non-delegation

Determinations by the Secretary under this subsection for a drug shall be made by individuals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

(p) Risk evaluation and mitigation strategy

(1) In general

A person may not introduce or deliver for introduction into interstate commerce a new drug if--

(A)(i) the application for such drug is approved under subsection (b) or (j) and is subject to section 353(b) of this title; or

(ii) the application for such drug is approved under section 262 of Title 42; and

(B) a risk evaluation and mitigation strategy is required under section 355-1 of this title with respect to the drug and the person fails to maintain compliance with the requirements of the approved strategy or with other requirements under section 355-1 of this title, including requirements regarding assessments of approved strategies.

(2) Certain postmarket studies

The failure to conduct a postmarket study under section 356 of this title, subpart H of part 314, or subpart E of part 601 of title 21, Code of Federal Regulations (or any successor regulations), is deemed to be a violation of paragraph (1).

(q) Petitions and civil actions regarding approval of certain applications

(1) In general

(A) Determination

The Secretary shall not delay approval of a pending application submitted under subsection (b)(2) or (j) of this section or section 262(k) of Title 42 because of any request to take any form of action relating to the application, either before or during consideration of the request, unless--

(i) the request is in writing and is a petition submitted to the Secretary pursuant to section 10.30 or 10.35 of title 21, Code of Federal Regulations (or any successor regulations); and

(ii) the Secretary determines, upon reviewing the petition, that a delay is necessary to protect the public health.

Consideration of the petition shall be separate and apart from review and approval of any application.

(B) Notification

If the Secretary determines under subparagraph (A) that a delay is necessary with respect to an application, the Secretary shall provide to the applicant, not later than 30 days after making such determination, the following information:

(i) Notification of the fact that a determination under subparagraph (A) has been made.

(ii) If applicable, any clarification or additional data that the applicant should submit to the docket on the petition to allow the Secretary to review the petition promptly.

(iii) A brief summary of the specific substantive issues raised in the petition which form the basis of the determination.

(C) Format

The information described in subparagraph (B) shall be conveyed via either, at the discretion of the Secretary--

(i) a document; or

(ii) a meeting with the applicant involved.

(D) Public disclosure

Any information conveyed by the Secretary under subparagraph (C) shall be considered part of the application and shall be subject to the disclosure requirements applicable to information in such application.

(E) Denial based on intent to delay

If the Secretary determines that a petition or a supplement to the petition was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues, the Secretary may deny the petition at any point based on such determination. The Secretary may issue guidance to describe

the factors that will be used to determine under this subparagraph whether a petition is submitted with the primary purpose of delaying the approval of an application.

(F) Final agency action

The Secretary shall take final agency action on a petition not later than 150 days after the date on which the petition is submitted. The Secretary shall not extend such period for any reason, including--

(i) any determination made under subparagraph (A);

(ii) the submission of comments relating to the petition or supplemental information supplied by the petitioner; or

(iii) the consent of the petitioner.

(G) Extension of 30-month period

If the filing of an application resulted in first-applicant status under subsection (j)(5)(D)(i)(IV) and approval of the application was delayed because of a petition, the 30-month period under such subsection is deemed to be extended by a period of time equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates), without regard to whether the Secretary grants, in whole or in part, or denies, in whole or in part, the petition.

(H) Certification

The Secretary shall not consider a petition for review unless the party submitting such petition does so in written form and the subject document is signed and contains the following certification: "I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: _____. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.", with the date on which such information first became known to such party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(I) Verification

The Secretary shall not accept for review any supplemental information or comments on a petition unless the party submitting such information or comments does so in written form and the subject document is signed and contains the following verification: "I certify that, to my best knowledge and belief: (a) I have not intentionally delayed submission of this document or its contents; and (b) the information upon which I have based the action requested herein first became known to me on or about _____. If I received or expect to receive payments, including cash and other forms of

consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.", with the date on which such information first became known to the party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(2) Exhaustion of administrative remedies

(A) Final agency action within 150 days

The Secretary shall be considered to have taken final agency action on a petition if--

(i) during the 150-day period referred to in paragraph (1)(F), the Secretary makes a final decision within the meaning of section 10.45(d) of title 21, Code of Federal Regulations (or any successor regulation); or

(ii) such period expires without the Secretary having made such a final decision.

(B) Dismissal of certain civil actions

If a civil action is filed against the Secretary with respect to any issue raised in the petition before the Secretary has taken final agency action on the petition within the meaning of subparagraph (A), the court shall dismiss without prejudice the action for failure to exhaust administrative remedies.

(C) Administrative record

For purposes of judicial review related to the approval of an application for which a petition under paragraph (1) was submitted, the administrative record regarding any issue raised by the petition shall include--

(i) the petition filed under paragraph (1) and any supplements and comments thereto;

(ii) the Secretary's response to such petition, if issued; and

(iii) other information, as designated by the Secretary, related to the Secretary's determinations regarding the issues raised in such petition, as long as the information was considered by the agency no later than the date of final agency action as defined under subparagraph (2)(A), and regardless of whether the Secretary responded to the petition at or before the approval of the application at issue in the petition.

(3) Annual report on delays in approvals per petitions

The Secretary shall annually submit to the Congress a report that specifies--

(A) the number of applications that were approved during the preceding 12-month period;

(B) the number of such applications whose effective dates were delayed by petitions referred to in paragraph (1) during such period;

(C) the number of days by which such applications were so delayed; and

(D) the number of such petitions that were submitted during such period.

(4) Exceptions

(A) This subsection does not apply to--

(i) a petition that relates solely to the timing of the approval of an application pursuant to subsection (j)(5)(B)(iv); or

(ii) a petition that is made by the sponsor of an application and that seeks only to have the Secretary take or refrain from taking any form of action with respect to that application.

(B) Paragraph (2) does not apply to a petition addressing issues concerning an application submitted pursuant to section 262(k) of Title 42.

(5) Definitions

(A) Application

For purposes of this subsection, the term "application" means an application submitted under subsection (b)(2) or (j) of this section or section 262(k) of Title 42.

(B) Petition

For purposes of this subsection, other than paragraph (1)(A)(i), the term "petition" means a request described in paragraph (1)(A)(i).

(r) Postmarket drug safety information for patients and providers

(1) Establishment

Not later than 1 year after September 27, 2007, the Secretary shall improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site that--

(A) provides links to drug safety information listed in paragraph (2) for prescription drugs that are approved under this section or licensed under section 262 of Title 42; and

(B) improves communication of drug safety information to patients and providers.

(2) Internet Web site

The Secretary shall carry out paragraph (1) by--

(A) developing and maintaining an accessible, consolidated Internet Web site with easily searchable drug safety information, including the information found on United States Government Internet Web sites, such as the United States National Library of Medicine's Daily Med and Medline Plus Web sites, in addition to other such Web sites maintained by the Secretary;

(B) ensuring that the information provided on the Internet Web site is comprehensive and includes, when available and appropriate--

(i) patient labeling and patient packaging inserts;

(ii) a link to a list of each drug, whether approved under this section or licensed under such section 262, for which a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations), is required;

(iii) a link to the registry and results data bank provided for under subsections (i) and (j) of section 282 of Title 42;

(iv) the most recent safety information and alerts issued by the Food and Drug Administration for drugs approved by the Secretary under this section, such as product recalls, warning letters, and import alerts;

(v) publicly available information about implemented RiskMAPs and risk evaluation and mitigation strategies under subsection (o);

(vi) guidance documents and regulations related to drug safety; and

(vii) other material determined appropriate by the Secretary;

(C) providing access to summaries of the assessed and aggregated data collected from the active surveillance infrastructure under subsection (k)(3) to provide information of known and serious side-effects for drugs approved under this section or licensed under such section 262;

(D) preparing and making publicly available on the Internet website established under paragraph (1) best practices for drug safety surveillance activities for drugs approved under this section or section 262 of Title 42;

(E) enabling patients, providers, and drug sponsors to submit adverse event reports through the Internet Web site;

(F) providing educational materials for patients and providers about the appropriate means of disposing of expired, damaged, or unusable medications; and

(G) supporting initiatives that the Secretary determines to be useful to fulfill the purposes of the Internet Web site.

(3) Posting of drug labeling

The Secretary shall post on the Internet Web site established under paragraph (1) the approved professional labeling and any required patient labeling of a drug approved under this section or licensed under such section 262 not later than 21 days after the date the drug is approved or licensed, including in a supplemental application with respect to a labeling change.

(4) Private sector resources

To ensure development of the Internet Web site by the date described in paragraph (1), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(5) Authority for contracts

The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subsection.

(6) Review

The Advisory Committee on Risk Communication under section 360bbb-6 of this title shall, on a regular basis, perform a comprehensive review and evaluation of the types of risk communication information provided on the Internet Web site established under paragraph (1) and, through other means, shall identify, clarify, and define the purposes and types of information available to facilitate the efficient flow of information to patients and providers, and shall recommend ways for the Food and Drug Administration to work with outside entities to help facilitate the dispensing of risk communication information to patients and providers.

(s) Referral to advisory committee

The Secretary shall--

(1) refer a drug or biological product to a Food and Drug Administration advisory committee for review at a meeting of such advisory committee prior to the approval of such drug or biological if it is--

(A) a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under this section; or

(B) a biological product, no active ingredient of which has been approved in any other application under section 262 of Title 42; or

(2) if the Secretary does not refer a drug or biological product described in paragraph (1) to a Food and Drug Administration advisory committee prior to such approval, provide in the action letter on the application for the drug or biological product a summary of the reasons why the Secretary did not refer the drug or biological product to an advisory committee prior to approval.

(t) Database for authorized generic drugs

(1) In general

(A) Publication

The Commissioner shall--

(i) not later than 9 months after September 27, 2007, publish a complete list on the Internet Web site of the Food and Drug Administration of all authorized generic drugs (including drug trade name, brand company manufacturer, and the date the authorized generic drug entered the market); and

(ii) update the list quarterly to include each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug during the preceding 3-month period.

(B) Notification

The Commissioner shall notify relevant Federal agencies, including the Centers for Medicare & Medicaid Services and the Federal Trade Commission, when the Commissioner first publishes the information described in subparagraph (A) that the information has been published and that the information will be updated quarterly.

(2) Inclusion

The Commissioner shall include in the list described in paragraph (1) each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug after January 1, 1999.

(3) Authorized generic drug

In this section, the term “authorized generic drug” means a listed drug (as that term is used in subsection (j)) that--

(A) has been approved under subsection (c); and

(B) is marketed, sold, or distributed directly or indirectly to retail class of trade under a different labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trade mark than the listed drug.

(u) Certain drugs containing single enantiomers

(1) In general

For purposes of subsections (c)(3)(E)(ii) and (j)(5)(F)(ii), if an application is submitted under subsection (b) for a non-racemic drug containing as an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) a single enantiomer that is contained in a racemic drug approved in another application under subsection (b), the applicant may, in the application for such non-racemic drug, elect to have the single enantiomer not be considered the same active moiety as that contained in the approved racemic drug, if--

(A)(i) the single enantiomer has not been previously approved except in the approved racemic drug; and

(ii) the application submitted under subsection (b) for such non-racemic drug--

(I) includes full reports of new clinical investigations (other than bioavailability studies)--

(aa) necessary for the approval of the application under subsections (c) and (d); and

(bb) conducted or sponsored by the applicant; and

(II) does not rely on any clinical investigations that are part of an application submitted under subsection (b) for approval of the approved racemic drug; and

(B) the application submitted under subsection (b) for such non-racemic drug is not submitted for approval of a condition of use--

(i) in a therapeutic category in which the approved racemic drug has been approved; or

(ii) for which any other enantiomer of the racemic drug has been approved.

(2) Limitation

(A) No approval in certain therapeutic categories

Until the date that is 10 years after the date of approval of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph, the Secretary shall not approve such non-racemic drug for any condition of use in the therapeutic category in which the racemic drug has been approved.

(B) Labeling

If applicable, the labeling of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph shall include a statement that the non-racemic drug is not approved, and has not been shown to be safe and effective, for any condition of use of the racemic drug.

(3) Definition

(A) In general

For purposes of this subsection, the term "therapeutic category" means a therapeutic category identified in the list developed by the United States Pharmacopeia pursuant to section 1395w-104(b)(3)(C)(ii) of Title 42 and as in effect on September 27, 2007.

(B) Publication by Secretary

The Secretary shall publish the list described in subparagraph (A) and may amend such list by regulation.

(4) Availability

The election referred to in paragraph (1) may be made only in an application that is submitted to the Secretary after September 27, 2007, and before October 1, 2022.

(v) Antibiotic drugs submitted before November 21, 1997

(1) Antibiotic drugs approved before November 21, 1997

(A) In general

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) shall be eligible for, with respect to the drug, the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable.

(B) Application; antibiotic drug described

(i) Application

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) Antibiotic drug

An antibiotic drug described in this clause is an antibiotic drug that was the subject of an application approved by the Secretary under section 357 of this title (as in effect before November 21, 1997).

(2) Antibiotic drugs submitted before November 21, 1997, but not approved

(A) In general

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) may elect to be eligible for, with respect to the drug--

(i)(I) the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; and

(II) the 5-year exclusivity period referred to under clause (ii) of subsection (c)(3)(E) and under clause (ii) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; or

(ii) a patent term extension under section 156 of Title 35, subject to the requirements of such section.

(B) Application; antibiotic drug described

(i) Application

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) Antibiotic drug

An antibiotic drug described in this clause is an antibiotic drug that was the subject of 1 or more applications received by the Secretary under section 357 of this title (as in effect before November 21, 1997), none of which was approved by the Secretary under such section.

(3) Limitations

(A) Exclusivities and extensions

Paragraphs (1)(A) and (2)(A) shall not be construed to entitle a drug that is the subject of an approved application described in subparagraphs [5] (1)(B)(i) or (2)(B)(i), as applicable, to any market exclusivities or patent extensions other than those exclusivities or extensions described in paragraph (1)(A) or (2)(A).

(B) Conditions of use

Paragraphs (1)(A) and (2)(A)(i) shall not apply to any condition of use for which the drug referred to in subparagraph (1)(B)(i) or (2)(B)(i), as applicable, was approved before October 8, 2008.

(4) Application of certain provisions

Notwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law, and subject to the limitations in paragraphs (1), (2), and (3), the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 shall apply to any drug subject to paragraph (1) or any drug with respect to which an election is made under paragraph (2)(A).

(w) Deadline for determination on certain petitions

The Secretary shall issue a final, substantive determination on a petition submitted pursuant to subsection (b) of section 314.161 of title 21, Code of Federal Regulations (or any successor regulations), no later than 270 days after the date the petition is submitted.

(x) Date of approval in the case of recommended controls under the CSA

(1) In general

In the case of an application under subsection (b) with respect to a drug for which the Secretary provides notice to the sponsor that the Secretary intends to issue a scientific and medical evaluation and recommend controls under the Controlled Substances Act, approval of such application shall not take effect until the interim final rule controlling the drug is issued in accordance with section 201(j) of the Controlled Substances Act.

(2) Date of approval

For purposes of this section, with respect to an application described in paragraph (1), the term “date of approval” shall mean the later of--

(A) the date an application under subsection (b) is approved under subsection (c); or

(B) the date of issuance of the interim final rule controlling the drug.

(y) Contrast agents intended for use with applicable medical imaging devices

(1) In general

The sponsor of a contrast agent for which an application has been approved under this section may submit a supplement to the application seeking approval for a new use following the authorization of a premarket submission for an applicable medical imaging device for that use with the contrast agent pursuant to section 360j(p)(1) of this title.

(2) Review of supplement

In reviewing a supplement submitted under this subsection, the agency center charged with the premarket review of drugs may--

(A) consult with the center charged with the premarket review of devices; and

(B) review information and data submitted to the Secretary by the sponsor of an applicable medical imaging device pursuant to section 360e, 360(k), or 360c(f)(2) of this title so long as the sponsor of such applicable medical imaging device has provided to the sponsor of the contrast agent a right of reference.

(3) Definitions

For purposes of this subsection--

(A) the term "new use" means a use of a contrast agent that is described in the approved labeling of an applicable medical imaging device described in section 360j(p) of this title, but that is not described in the approved labeling of the contrast agent; and

(B) the terms "applicable medical imaging device" and "contrast agent" have the meanings given such terms in section 360j(p) of this title.

CREDIT(S)

(June 25, 1938, c. 675, § 505, 52 Stat. 1052; Pub.L. 86-507, § 1(18), June 11, 1960, 74 Stat. 201; Pub.L. 87-781, Title I, §§ 102(b) to (d), 103(a), (b), 104(a) to (d)(2), Oct. 10, 1962, 76 Stat. 781, 784, 785; Pub.L. 92-387, § 4(d), Aug. 16, 1972, 86 Stat. 562; Pub.L. 98-417, Title I, §§ 101, 102(a) to (b)(5), 103, 104, Sept. 24, 1984, 98 Stat. 1585, 1592, 1593, 1597; Pub.L. 102-282, § 5, May 13, 1992, 106 Stat. 161; Pub.L. 103-80, § 3(n), Aug. 13, 1993, 107 Stat. 777; Pub.L. 105-115, Title I, §§ 115, 117, 119, 120, 124(a), Nov. 21, 1997, 111 Stat. 2313, 2315, 2316, 2318, 2324; Pub.L. 106-113, Div. B, § 1000(a)(9) [Title IV, § 4732(b)(11)], Nov. 29, 1999, 113 Stat. 1536, 1501A-584; Pub.L. 107-109, § 15(c)(1), Jan. 4, 2002, 115 Stat. 1420; Pub.L. 108-155, § 2(b)(1), Dec. 3, 2003, 117 Stat. 1941; Pub.L. 108-173, Title XI, §§ 1101(a), (b), 1102(a), 1103(a), Dec. 8, 2003, 117 Stat. 2448, 2452, 2457, 2460; Pub.L. 110-85, Title VII, § 701(b), Title VIII, § 801(b)(3)(A), (B), Title IX, §§ 901(a), 903, 905(a), 914(a), 915, 916, 918, 920, 921, Title XI, § 1113, Sept. 27, 2007, 121 Stat. 903, 921, 922, 943, 944, 953, 957, 960, 961, 976; Pub.L. 110-316, Title III, § 301, Aug. 14, 2008, 122 Stat. 3524; Pub.L. 110-379, § 4(a), Oct. 8, 2008, 122 Stat. 4076; Pub.L. 111-31, Div. A, Title I, § 103(e), June 22, 2009, 123 Stat. 1837; Pub.L. 111-148, Title VII, § 7002(d)(1), Title X, § 10609, Mar. 23,

2010, 124 Stat. 816, 1014; Pub.L. 112-144, Title IX, § 905, Title XI, §§ 1101, 1134(a), 1135, July 9, 2012, 126 Stat. 1092, 1108, 1123; Pub.L. 113-5, Title III, § 301, Mar. 13, 2013, 127 Stat. 179; Pub.L. 114-89, § 2(a)(1), Nov. 25, 2015, 129 Stat. 698; Pub.L. 114-255, Div. A, Title III, §§ 3024(b), 3031(a), 3075(a), (b), 3101(a)(2)(B), 3102(1), Dec. 13, 2016, 130 Stat. 1099, 1138, 1152, 1156; Pub.L. 115-52, Title VI, § 601, Title VII, § 706(b), Title VIII, §§ 801, 802, 808, Title IX, § 901(a), Aug. 18, 2017, 131 Stat. 1048, 1059, 1068, 1069, 1074, 1076; Pub.L. 115-271, Title III, § 3041(b), Oct. 24, 2018, 132 Stat. 3942; Pub.L. 116-290, § 2(a) to (d)(1), (g), Jan. 5, 2021, 134 Stat. 4889, 4892; Pub.L. 117-9, § 1(a)(1), (b)(1), Apr. 23, 2021, 135 Stat. 256, 258.)

Notes of Decisions (623)

Footnotes

1 So in original. Probably should be “bioavailability”.
2 So in original. Probably should be “drug,”.
3 So in original. Probably should be preceded by “the”.
4 So in original. The word “and” probably should not appear.
5 So in original. Probably should be “subparagraph”.

21 U.S.C.A. § 355, 21 USCA § 355
Current through PL 117-12 with the exception of PL 116-283. Incorporation of changes from PL 116-283 are in progress. See credits for details.

End of Document

United States Code Annotated
Title 21. Food and Drugs (Refs & Annos)
Chapter 13. Drug Abuse Prevention and Control (Refs & Annos)
Subchapter I. Control and Enforcement
Part F. General Provisions (Refs & Annos)

21 U.S.C.A. § 902

§ 902. Savings provisions

Currentness

Nothing in this chapter, except this part and, to the extent of any inconsistency, sections 827(e) and 829 of this title, shall be construed as in any way affecting, modifying, repealing, or superseding the provisions of the Federal Food, Drug, and Cosmetic Act.

CREDIT(S)

(Pub.L. 91-513, Title II, § 707, Oct. 27, 1970, 84 Stat. 1284.)

Notes of Decisions (1)

21 U.S.C.A. § 902, 21 USCA § 902
Current through PL 117-12 with the exception of PL 116-283. Incorporation of changes from PL 116-283 are in progress. See credits for details.

End of Document

United States Code Annotated
Title 21. Food and Drugs (Refs & Annos)
Chapter 13. Drug Abuse Prevention and Control (Refs & Annos)
Subchapter I. Control and Enforcement
Part C. Registration of Manufacturers, Distributors, and Dispensers of Controlled Substances

21 U.S.C.A. § 822

§ 822. Persons required to register

Effective: October 24, 2018
Currentness

(a) Period of registration

(1) Every person who manufactures or distributes any controlled substance or list I chemical, or who proposes to engage in the manufacture or distribution of any controlled substance or list I chemical, shall obtain annually a registration issued by the Attorney General in accordance with the rules and regulations promulgated by him.

(2) Every person who dispenses, or who proposes to dispense, any controlled substance, shall obtain from the Attorney General a registration issued in accordance with the rules and regulations promulgated by him. The Attorney General shall, by regulation, determine the period of such registrations. In no event, however, shall such registrations be issued for less than one year nor for more than three years.

(b) Authorized activities

Persons registered by the Attorney General under this subchapter to manufacture, distribute, or dispense controlled substances or list I chemicals are authorized to possess, manufacture, distribute, or dispense such substances or chemicals (including any such activity in the conduct of research) to the extent authorized by their registration and in conformity with the other provisions of this subchapter.

(c) Exceptions

The following persons shall not be required to register and may lawfully possess any controlled substance or list I chemical under this subchapter:

(1) An agent or employee of any registered manufacturer, distributor, or dispenser of any controlled substance or list I chemical if such agent or employee is acting in the usual course of his business or employment.

(2) A common or contract carrier or warehouseman, or an employee thereof, whose possession of the controlled substance or list I chemical is in the usual course of his business or employment.

(3) An ultimate user who possesses such substance for a purpose specified in section 802(25) [1] of this title.

(d) Waiver

The Attorney General may, by regulation, waive the requirement for registration of certain manufacturers, distributors, or dispensers if he finds it consistent with the public health and safety.

(e) Separate registration

(1) A separate registration shall be required at each principal place of business or professional practice where the applicant manufactures, distributes, or dispenses controlled substances or list I chemicals.

(2) Notwithstanding paragraph (1), a registrant who is a veterinarian shall not be required to have a separate registration in order to transport and dispense controlled substances in the usual course of veterinary practice at a site other than the registrant's registered principal place of business or professional practice, so long as the site of transporting and dispensing is located in a State where the veterinarian is licensed to practice veterinary medicine and is not a principal place of business or professional practice.

(f) Inspection

The Attorney General is authorized to inspect the establishment of a registrant or applicant for registration in accordance with the rules and regulations promulgated by him.

(g) Delivery of controlled substances by ultimate users for disposal

(1) An ultimate user who has lawfully obtained a controlled substance in accordance with this subchapter may, without being registered, deliver the controlled substance to another person for the purpose of disposal of the controlled substance if--

(A) the person receiving the controlled substance is authorized under this subchapter to engage in such activity; and

(B) the disposal takes place in accordance with regulations issued by the Attorney General to prevent diversion of controlled substances.

(2) In developing regulations under this subsection, the Attorney General shall take into consideration the public health and safety, as well as the ease and cost of program implementation and participation by various communities. Such regulations may not require any entity to establish or operate a delivery or disposal program.

(3) The Attorney General may, by regulation, authorize long-term care facilities, as defined by the Attorney General by regulation, to dispose of controlled substances on behalf of ultimate users who reside, or have resided, at such long-term care

facilities in a manner that the Attorney General determines will provide effective controls against diversion and be consistent with the public health and safety.

(4) If a person dies while lawfully in possession of a controlled substance for personal use, any person lawfully entitled to dispose of the decedent's property may deliver the controlled substance to another person for the purpose of disposal under the same conditions as provided in paragraph (1) for an ultimate user.

(5)(A) In the case of a person receiving hospice care, an employee of a qualified hospice program, acting within the scope of employment, may handle, without being registered under this section, any controlled substance that was lawfully dispensed to the person receiving hospice care, for the purpose of disposal of the controlled substance so long as such disposal occurs onsite in accordance with all applicable Federal, State, Tribal, and local law and--

(i) the disposal occurs after the death of a person receiving hospice care;

(ii) the controlled substance is expired; or

(iii)(I) the employee is--

(aa) the physician of the person receiving hospice care; and

(bb) registered under section 823(f) of this title; and

(II) the hospice patient no longer requires the controlled substance because the plan of care of the hospice patient has been modified.

(B) For the purposes of this paragraph:

(i) The terms “hospice care” and “hospice program” have the meanings given to those terms in section 1395x(dd) of Title 42.

(ii) The term “employee of a qualified hospice program” means a physician, physician assistant, nurse, or other person who--

(I) is employed by, or pursuant to arrangements made by, a qualified hospice program;

(II)(aa) is licensed to perform medical or nursing services by the jurisdiction in which the person receiving hospice care was located; and

(bb) is acting within the scope of such employment in accordance with applicable State law; and

(III) has completed training through the qualified hospice program regarding the disposal of controlled substances in a secure and responsible manner so as to discourage abuse, misuse, or diversion.

(iii) The term "qualified hospice program" means a hospice program that--

(I) has written policies and procedures for assisting in the disposal of the controlled substances of a person receiving hospice care after the person's death;

(II) at the time when the controlled substances are first ordered--

(aa) provides a copy of the written policies and procedures to the patient or patient representative and family;

(bb) discusses the policies and procedures with the patient or representative and the family in a language and manner that they understand to ensure that these parties are educated regarding the safe disposal of controlled substances; and

(cc) documents in the patient's clinical record that the written policies and procedures were provided and discussed; and

(III) at the time following the disposal of the controlled substances--

(aa) documents in the patient's clinical record the type of controlled substance, dosage, route of administration, and quantity so disposed; and

(bb) the time, date, and manner in which that disposal occurred.

CREDIT(S)

(Pub.L. 91-513, Title II, § 302, Oct. 27, 1970, 84 Stat. 1253; Pub.L. 98-473, Title II, § 510, Oct. 12, 1984, 98 Stat. 2072; Pub.L. 103-200, § 3(b), Dec. 17, 1993, 107 Stat. 2336; Pub.L. 111-273, § 3(a), Oct. 12, 2010, 124 Stat. 2859; Pub.L. 113-143, § 2, Aug. 1, 2014, 128 Stat. 1750; Pub.L. 115-271, Title III, § 3222(a), Oct. 24, 2018, 132 Stat. 3948.)

Notes of Decisions (25)

Footnotes

1 Redesignated as 21 U.S.C.A. § 802(27) by Pub.L. 99-570, Title I, § 1003(b)(2), see References in Text note set out under this section.

21 U.S.C.A. § 822, 21 USCA § 822

Current through PL 117-12 with the exception of PL 116-283. Incorporation of changes from PL 116-283 are in progress. See credits for details.

End of Document

Code of Federal Regulations
Title 21. Food and Drugs
Chapter II. Drug Enforcement Administration, Department of Justice
Part 1307. Miscellaneous (Refs & Annos)
General Information

21 C.F.R. § 1307.03

§ 1307.03 Exceptions to regulations.

Effective: March 9, 2010
Currentness

Any person may apply for an exception to the application of any provision of this chapter by filing a written request with the Office of Diversion Control, Drug Enforcement Administration, stating the reasons for such exception. See the Table of DEA Mailing Addresses in § 1321.01 of this chapter for the current mailing address. The Administrator may grant an exception in his discretion, but in no case shall he/she be required to grant an exception to any person which is otherwise required by law or the regulations cited in this section.

Credits
[60 FR 32454, June 22, 1995; 62 FR 13966, March 24, 1997; 75 FR 10678, March 9, 2010]

SOURCE: 36 FR 7801, Apr. 24, 1971. Redesignated at 38 FR 26609, Sept. 24, 1973; 50 FR 31588, Aug. 5, 1985, unless otherwise noted.

AUTHORITY: 21 U.S.C. 821, 822(d), 871(b).

Current through May 13, 2021; 86 FR 26336.

End of Document

57 FR 10499-02, 1992 WL 57777(F.R.)
NOTICES
DEPARTMENT OF JUSTICE
Drug Enforcement Administration
(Docket No. 86-22)

Marijuana Scheduling Petition; Denial of Petition; Remand

Thursday, March 26, 1992

AGENCY: Drug Enforcement Administration, Justice.

ACTION: Final order.

SUMMARY: This is a final order of the Administrator of the Drug Enforcement Administration (DEA) concluding the plant material marijuana has no currently accepted medical use and denying the petition of the National Organization for Reform of Marijuana Laws (NORML) to reschedule marijuana from Schedule I to Schedule II of the Controlled Substances Act.
EFFECTIVE DATE: March 26, 1992.

FOR FURTHER INFORMATION CONTACT: Office of Congressional and Public Affairs, 202-307-7363.

SUPPLEMENTARY INFORMATION:

Background

On December 21, 1989, the former Administrator of DEA, following rulemaking on the record, which included a hearing before an administrative law judge, issued a final order concluding the plant material marijuana has no currently accepted medical use, and denying the petition of NORML to reschedule marijuana from Schedule I to Schedule II of the Controlled Substances Act. 54 FR 63767. On April 26, 1991, the United States Court of Appeals for the District of Columbia Circuit remanded the matter to the Administrator for clarification of DEA's interpretation of the term "currently accepted medical use in treatment in the United States." Alliance for Cannabis Therapeutics v. DEA, 930 F.2d 936.

Following a review of the entire record in this matter, and a comprehensive re-examination of the relevant statutory standard, I conclude that marijuana has no currently accepted medical use and must remain in Schedule I. Further hearings are unnecessary since the record is extraordinarily complete, all parties had ample opportunity and wide latitude to present evidence and to brief all relevant issues, and the narrow question on remand centers exclusively on this Agency's legal interpretation of a statutorily-created standard.

Summary of the Decision

Does the marijuana plant have any currently accepted medical use in treatment in the United States, within the meaning of the Federal Controlled Substances Act, 21 U.S.C. 801, et seq.? Put simply, is marijuana good medicine for illnesses we all fear, such as multiple sclerosis (MS), glaucoma and cancer?

The answer might seem obvious based simply on common sense. Smoking causes lung cancer and other deadly diseases. Americans take their medicines in pills, solutions, sprays, shots, drops, creams and sometimes in suppositories, but never by smoking. No medicine prescribed for us today is smoked.

With a little homework, one can learn that marijuana has been rejected as medicine by the American Medical Association, the National Multiple Sclerosis Society, the American Glaucoma Society, the American Academy of Ophthalmology the American Cancer Society. Not one American health association accepts marijuana as medicine.

For the last half century, drug evaluation experts at the United States Food and Drug Administration (FDA) have been responsible for protecting Americans from unsafe and ineffective new medicines. Relying on the same scientific standards used to judge all other drugs, FDA experts repeatedly have rejected marijuana for medical use.

Yet claims persist that marijuana has medical value. Are these claims true, What are the facts?

Between 1987 and 1988, DEA and NORML, under the guidance of an administrative law judge, collected all relevant information on this subject. Stacked together it stands nearly five feet high. Is there reliable scientific evidence that marijuana is medically ***10500** effective, If it has medical value, do its benefits outweight its risks? What do America's top medical and scientific experts say? Would they prescribe it for their patients, their families, their friends?

As the current Administrator of Drug Enforcement, and as a former United States District Judge, I have made a detailed review of the evidence in this record to find the answers.

There are significant short-term side effects and long-term risks linked to smoking marijuana. Marijuana is likely to be more cancer-causing than tobacco; damages brain cells; causes lung problems, such as bronchitis and emphysema; may weaken the body's antibacterial defenses in the lungs; lowers overall blood pressure, which could adversely affect the supply of blood to the head; causes sudden drops in blood pressure (orthostatic hypotension), rapid heart beat (tachycardia), and heart palpitations; suppresses luteinizing hormone secretion in women, which affects the production of progesterone, an important female hormone; causes anxiety and panic in some users because of its mind-altering effects; produces dizziness, trouble with thinking, trougle with concentrating, fatigue, and sleepiness; and impairs motor skills.

As a plant, marijuana can contain bacteria capable of causing serious infections in humans, such as salmonella enteritidis, Klebsiella pneumoniae, group D Streptoccoccus and pathogenic aspergillus.

Several of these risk stand out. The immune systems of cancer patients are weakened by radiation and chemotherapy, leaving them susceptible to infection. If they experiment with marijuana to control nausea, they risk weakening their immune systems further and exposing themselves to the infection-causing bacteria in the plant. It is estimated, for example, that at Memorial Sloan-Kettering Cancer Center 60 patients die each year from pathogenic aspergillus infections.

Glaucoma patients face possible blindness caused by very high fluid pressures within their eyes. If they experiment with marijuana to lower their eye fluid pressure, it can cause dramatic drops in their blood pressure and reduce the blood supply to their heads. Glaucoma experts testified this reduced the blood supply to the optic nerves and could speed up, rather than slow down, their loss of eyesight.

MS, glaucoma and cancer patients who have undiagnosed heart problems risk heart palpitations, very rapid heart beats and sudden dramatic drops in blood pressure if they experiment with marijuana. For MS and glaucoma patients who must take medications for the rest of their lives, experimenting with marijuana poses the additional risks of lung cancer, emphysema, bladder cancer and leukemia.

Many risks remain unknown. Marijuana contains over 400 separately identified chemicals. No one knows all the effects of burning these chemicals together and inhaling the burnt mix. Are these risks outweighed by medical benefits?

There are scientific studies showing pure THC (Delta-9-Tetrahydrocannabinol), one of the many chemicals found in marijuana, has some effect in controlling nausea and vomiting. Pure THC is pharmaceutically made in a clean capsule form, called Marinol,

and is available for use by the medical community. More information on Marinol can be found in the "Physicians' Desk Reference," available in most libraries.

Since marijuana contains THC, you might think marijuana also would be effective. However, the effect of taking a drug in combination with other chemicals is seldom the same as taking just the pure drug. As already noted, marijuana contains over 400 other chemicals, not just THC. There are no reliable scientific studies that show marijuana to be significantly effective in controlling nausea and vomiting. People refer to the Sallan study as proving marijuana's effectiveness. They are mistaken. The Sallan study involved pure THC, not marijuana. People refer to the Chang study to support marijuana's effectiveness. They also are mistaken. Doctor Chang tested the combination of pure THC and marijuana to treat nausea and vomiting. The preliminary results he got were probably due to the THC, not the marijuana. Because he tested the combination, we cannot tell just what effects can be attributed to marijuana alone. People cite a third study, done by Doctor Levitt, as proof marijuana is effective. They are mistaken. Doctor Levitt compared marijuana to THC in controlling nausea and vomiting, and he concluded that THC was the more effective drug.

A librarian can help locate copies of thes studies should you want to see them for yourself. Sallan, et al., "Antiemetic Effect of Delta-9-Tetrahydrocannibinol in Patients Receiving Cancer Chemotherapy," 293 New England Journal of Medicine 795-797 (1975); Chang, et al., "Delta-9-Tetrahydrocannabinol as an Antiemetic in Cancer Patients Receiving High-Dose Methotrexate," 91 Annals of Internal Medicine 819-824 (1979); Levitt, et al., "Randomized Double Blind Comparison of Delta-9-Tetrahydrocannabinol (THC) and Marijuana As Chemotherapy Antiemetics," (Meeting Abstract) 3 Proceedings of the Annual Meeting of the American Society of Clinical Oncology 91 (1984).

During the 1970's and 1980's, a number of states set up research programs to give marijuana to cancer and glaucoma patients, on the chance it might help. Some people point to these programs as proof of marijuana's usefulness. Unfortunately, all research is not necessarily good scientific research. These state programs failed to follow responsible scientific methods. Patients took marijuana together with their regular medicines, so it is impossible to say whether marijuana helped them. Observations or results were not scientifically measured. Procedures were so poor that much critical research data were lost or never recorded. Although these programs were well-intentioned, they are not scientific proof of anything.

Some people refer to a study by Doctor Thomas Ungerleider as proof marijuana reduced nausea in bone marrow transplant patients. Unfortunately, Doctor Ungerleider neglected to follow responsible scientific methods in his study. Like the state programs, it proves nothing. Doctor Ungerleider chose not to publish his study evidently because of its serious weaknesses. He admitted as much when questioned under oath.

Those who say there are reliable scientific studies showing marijuana is an effective drug for teating nausea and vomiting are wrong. No such studies exist.

Our nation's top cancer experts reject marijuana for medical use. Doctor David S. Ettinger, a professor of oncology at the Johns Hopkins University School of Medicine, an author of over 100 scholarly articles on cancer treatment, and a nationally respected cancer expert, testified:

There is no indication that marijuana is effective in treating nausea and vomiting resulting from radiation treatment or other causes. No legitimate studies have been conducted which make such conclusions.

Doctor Richard J. Gralla, a professor of medicine at Cornell University Medical College, an associate attending physician at the Memorial Sloan-Kettering Cancer Center, and an expert in cancer research, testified:

Most experts would say, and our studies support, that the cannabinoids in general are not very effective against the major causes of nausea and vomiting.

***10501** Doctor Gralla added:

I have found that because of the negative side effects and problems associated with marijuana * * *, most medical oncologists and researchers have little interest in marijuana for the treatment of nausea and vomiting in their patients.

Doctor John Laszlo, Vice President of Research for the American Cancer Society, an expert who has spent 37 years researching cancer treatments, and who has written a leading textbook on the subject, "Antiemetics and Cancer Chemotherapy," testified there is not enough scientific evidence to justify using marijuana to treat nausea and vomiting. Not one nationally-recognized cancer expert could be found to testify on marijuana's behalf.

To be an effective treatment for glaucoma, a drug must: (i) Lower the pressure within the eye (intraocular pressure), (ii) for prolonged periods of time, and (iii) actually preserve sight (visual fields). Five scientific studies are cited as evidence marijuana is an effective glaucoma treatment. Those who cite these studies are mistaken. These studies tested pure THC, not marijuana. W.D. Purnell and J.M. Gregg, "Delta-9-Tetrahydorcannabinol, Euphoria and Intraocular Pressure in Man," 7 Annals of Ophthalmology 921-923 (1975); M. Perez-Reyes, D. Wagner, M.E. Wall, and K.H. Davis, "Intravenous Administration of Cannabinoids on Intraocular Pressure," The Pharmacology of Marijuana 829-832 (M.C. Braude and S. Szara eds. 1976); J.C. Merritt, S.M. McKinnon, J.R. Armstrong, G. Hatem, and L.A. Reid, "Oral Delta-9-Tetrahydrocannabinol in Hyperogeneous Glaucomas," 12 Annals of Ophthalmology 947 (1980); K. Green and M. Roth, "Ocular Effects of Topical Administration of Delta-9-Tetrahydrocannabinol in Man," 100 Archives of Ophthalmology 265-267 (1982); and W.M. Jay and K. Green, "Multiple-Drop Study of Topically Applied 1% Delta-9-Tetrahydrocannabinol in Human Eyes," 101 Archives of Ophthalmology 591-593 (1983).

Threee studies show very heavy doses of marijuana, taken for short periods of time, can reduce eye pressure. R.S. Hepler, I.M. Frank, and T.J. Ungerleider, "Pupillary Constriction After Marijuana Smoking," 74 American Journal of Ophthalmology 1185-1190 (1972); R.S. Hepler, I.M. Frank, and R. Petrus, "Ocular Effects of Marijuana Smoking," The Pharmacology of Marijuana 815-824 (1976); and J.C. Merritt, W.J. Crawford, P.C. Alexander, A.L. Anduze and S.S. Gelbart, "Effect of Marijuana on Intraocular and Blood Pressure in Glaucoma," 87 Ophthalmology 222-228 (1980)

Unusally large doses or marijuana were needed in these three studies to achieve the desired effect. Heavy marijuana use produces dizziness, trouble with thinking, impaired motor skills, fatigue and sleepiness. The 1976 study by Doctors Hepler, Frank and Petrus emphasized "Our subjects were sometimes too sleepy to permit measurement of intraocular pressures * * * 3 hours after intoxication." If a glaucoma patient were to smoke marijuana 8 to 10 times every day for the rest of his life, would he be alert and energetic enough to live a relatively normal life? Would he develop other diseases? No scientific studies exist to answer these questions. Robert Randall claims to have saved his sight by smoking 8 to 10 marijuana cigarettes every day. Under oath he admits he stays at home most days, follows no daily schedule or routine, and has not held a regular job in over 15 years. He also has avoided having a comprehensive medical examination since 1975.

No scientific studies have shown marijuana can reduce eye pressure over long periods of time.

No scientific studies have shown marijuana can save eyesight.

America's top glaucoma experts reject marijuana as medicine. Doctor Keith Green is a professor of Ophthalmology who serves, or has served, on the editorial boards of eight prestigious eye journals (Ophthalmic Research, Oftalmo Abstracto, Current Eye Research, Experimental Eye Research, Investigative Opthalmology, American Journal of Ophthalmology, Archives of Ophthalmology, and Survey of Ophthalmology). Doctor Green has conducted extensive basic and clinical research using marijuana and THC to treat glaucoma patients. He has authored over 200 books or research articles in ophthalmology and is a highly respected expert on this subject. Doctor Green testified:

There is no scientific evidence * * * that indicates that marijuana is effective in regulating the progression of symptoms associated with glaucoma. * * * It is clear that there is no evidence that marijuana use prevents the progression of visual loss in glaucoma. * * * The quantities of the drug required to reduce intraocular pressure in glaucoma sufferers are large, and would require the inhalation of at least six marijuana cigarettes each day. * * * Smoking is not a desirable form of treatment for many reasons * * * (M)arijuana . . . has little potential future as a glaucoma medication.

Doctor George Spaeth is the Director of the Glaucoma Service at Wills Eye Hospital in Philadelphia, the largest service in the United States devoted to researching and treating glaucoma and to teaching other doctors about this disease. Doctor Spaeth is President of the American Glaucoma Society. He is a professor of ophthalmology, the editor of a scholarly eye journal (Ophthalmic Surgery), and the author of over 200 research articles on glaucoma. He testified:

I have not found any documentary evidence which indicates that a single patient has had his or her natural history of the disease altered by smoking marijuana.

Amputees and victims of MS can suffer from extreme muscle spasms. It is claimed marijuana is useful in treating spasticity. Three unusually small, inconclusive studies have tried using pure THC, not marijuana, to treat spasticity. D.J. Petro and C. Ellenberger, "Treatment of Human Spasticity with Delta-9-Tetrahydro-cannabinol," 21 Journal of Clinical Pharmacology 413S-416S (1981) (included only nine patients). Two of the studies are mere abstracts, or short digests, without much detail. Hanigan, Destee & Troung Abstr. B45, Clin. Pharmacol. Ther. 198 (1986) (included only five patients), and Sandyk, Cannoe, Stern and Snider Abstr. PP 331, 36 Neurology 342 (1986) (included only three patients).

No scientific studies exist which test marijuana to relieve spasticity.

National experts on MS reject marijuana as medicine. Doctor Kenneth P. Johnson is Chariman of the Department of Neurology at the University of Maryland School of Medicine. He manages that Maryland Center for MS, one of the most active MS research and treatment centers in the United States. He sits on the editiorial boards of noted medical journals related to MS (Neurology and Journal of Neuroimmunology). He is the author of over 100 scientific and medical articles on MS. Doctor Johnson has spent most of his long career researching MS and has diagnosed and treated more than 6,000 patients with MS. Doctor Johnson testified:

At this time, I am not aware of * * * any legitimate medical research in which marijuana was used to treat the symptoms of multiple sclerosis. * * * To conclude that marijuana is therapeutically effective without conducting rigorous testing would be professionally irresponsible.

Doctor Stephen Reingold is Assistant Vice President of Research for the National Multiple Sclerosis Society, which spends over $7 million each year ***10502** on MS research. Only the Federal Government spends more. Doctor Reingold testified:

I could find no actual published research which has used marijuana * * * In the existing research using THC, the results were inconclusive * * * In the absence of any well-designed, well-controlled research * * *, the National Multiple Sclerosis Society * * * does not endorse or advocate its use * * *.

Doctor Donald H. Silberberg is Chairman of the Department of Neurology at the University of Pennsylvania School of Medicine and Chief of the Neurology Service at the Hospital of Pennsylvania. Doctor Silberberg is on the editorial board of Annals of Neurology and is President of the National Medical Advisory Board for the National Multiple Sclerosis Society. He has been actively researching and treating MS for most of his career, has written over 130 medical articles on MS and is Co-Director of a large MS research center at the University of Pennsylvania. Doctor Silberberg testified:

I have not found any legitimate medical or scientific works which show that marijuana * * * is medically effective in treating multiple sclerosis or spasticity. * * * The long-term treatment of the symptoms of multiple sclerosis through the use of marijuana

could be devastating. * * * (T)he use of (marijuana), especially for long-term treatment * * * would be worse than the original disease itself.

The only favorable evidence that could be found by NORML and DEA consists of stories by marijuana users who claim to have been helped by the drug. Scientists call these stories anecdotes. They do not accept them as reliable proofs. The FDA's regulations, for example, provide that in deciding whether a new drug is a safe and effective medicine, "isolated case reports * * * will not be considered." 21 CFR 314.126(e). Why do scientists consider stories from patients and their doctors to be unreliable?

First, sick people are not objective scientific observers, especially when it comes to their own health. We all have heard of the placebo effect. Patients have a tendency to respond to drugs as they believe is expected of them. Imagine how magnified this placebo effect can be when a suffering person experiments on himself, praying for some relief. Many stories no doubt are due to the placebo effect, not to any real medical effects of marijuana.

Second, most of the stories come from people who took marijuana at the same time they took prescription drugs for their symptoms. For example, Robert Randall claims marijuana has saved his sight, yet he has taken standard glaucoma drugs continuously since 1972. There is no objective way to tell from these stories whether it is marijuana that is helpful, or the proven, traditional medicines. Even these users can never know for sure.

Third, any mind-altering drug that produces euphoria can make a sick person think he feels better. Stories from patients who claim marijuana helps them may be the result of the mind-altering effects of the drug, not the results of improvements in their conditions.

Fourth, long-time abusers of marijuana are not immune to illness. Many eventually get cancer, glaucoma, MS and other diseases. People who become dependent on mind-altering drugs tend to rationalize their behavior. They invent excuses, which they can come to believe, to justify their drug dependence. Stories of marijuana's benefits from sick people with a prior history of marijuana abuse may be based on rationalizations caused by drug dependence, not on any medical benefits caused by the drug. Robert Randall, for example, admits under oath to becoming a regular user in 1968, four years before he showed the first signs of, and was diagnosed as having, glaucoma. Since then he has smoked marijuana 8 to 10 times every day.

A century ago many Americans relied on stories to pick their medicines, especially from snake oil salesmen. Thanks to scientific advances and to the passage of the Federal Food, Drug and Cosmetic Act (FDCA) in 1906, 21 U.S.C. 301 et seq., we now rely on rigorous scientific proof to assure the safety and effectiveness of new drugs. Mere stories are not considered an acceptable way to judge whether dangerous drugs should be used as medicines.

There are doctors willing to testify that marijuana has medical uses. NORML found over a dozen to testify in this case. We have a natural tendency to believe doctors. We assume their opinions are entitled to respect. But what if a doctor is giving an opinion beyond his professional competence? Evaluating the safety and effectiveness of drugs is a specialized area. Does the doctor have this specialized expertise? Is he familiar with all the published scientific studies? Or is he improperly basing his opinion on mere stories or anecdotal evidence? Does he really know what he is talking about? Does he have a personal motive to exaggerate or lie? Questions like these led the United States Supreme Court, in 1973, to warn about the opinions of doctors concerning the value of drugs as medicine, when not supported by rigorous scientific testing, Weinberger v. Hynson, Etc., 412 U.S. 609, 639:

(I)mpressions or beliefs of physicians, no matter how fervently held, are treacherous.

Nearly half the doctors who testified for NORML are psychiatrists. They do not specialize in treating or researching cancer, glaucoma or MS. One is a general practitioner who works as a wellness counselor at a health spa. Under oath he admits to using every illegal, mind-altering drug he has ever studied, and he prides himself on recommending drugs that would never be recommended by medical schools or reputable physicians. Another is a general practitioner who quit practicing in 1974. He admits he has not kept up on new medical and scientific information about marijuana for 18 years.

Only one of the doctors called by NORML is a nationally-recognized expert. Doctor John C. Merritt is a board-certified ophthalmologist and researcher who has authored articles on the use of marijuana and cannabinoids to reduce eye pressure. He is in private practice and sees mostly children who suffer from glaucoma. Doctor Merritt testified, "(M)arijuana is a highly effective IOP-lowering drug which may be of critical value to some glaucoma patients who, without marijuana, would progressively go blind." The last scientific study using marijuana in glaucoma patients, published by Doctor Merritt in 1979, concluded:

It is because of the frequency and severity with which the untoward events occurred that marijuana inhalation is not an ideal therapeutic modality for glaucoma patients.

One year later, in 1980, Doctor Merritt gave the following testimony, under oath, before the United States Congress, House Select Committee on Narcotics Abuse and Control:

For me to sit here and say that the lowering pressure effects occurred repeatedly, day in and day out, I have no data, and neither does anyone else, and that is the real crux of the matter. When we are talking about treating a disease like glaucoma, which is a chronic disease, the real issue is, does the marijuana repeatedly lower the intraocular pressure? I have shown you no * * * studies, and to my knowledge there is no data to that effect.

Doctor Merritt was unable to explain, under oath, the contradictory positions he has taken on this subject.

Each of NORML's doctors testified his opinion is based on the published scientific studies. With one exception, none of them could identify under oath the scientific studies they swore they relied on. Only one had enough knowledge to discuss the scientific technicalities involved. Eventually, each ***10503** one admitted he was basing his opinion on anecdotal evidence, on stories he heard from patients, and on his impressions about the drug.

Sadly, Doctor Ivan Silverberg, an oncologist from San Francisco, exaggerated while on the witness stand. At first he swore "there is voluminous medical research which shows marijuana is effective in easing nausea and vomiting." Pushed on cross-examination to identify this voluminous research, Doctor Silverberg replied, "Well * * *, I'm going to have to back off a little bit from that." How far would Doctor Silverberg back off? Was he aware, at least, of the approximate number of scientific studies that have been done using marijuana to treat nausea? Under oath, he replied, "I would doubt very few. But, no, I'm not."

Beyond doubt, the claims that marijuana is medicine are false, dangerous and cruel.

Sick men, women and children can be fooled by these claims and experiment with the drug. Instead of being helped, they risk serious side effects. If they neglect their regular medicines while trying marijuana, the damage could be irreversible. It is a cruel hoax to offer false hope to desperately ill people.

Those who insist marijuana has medical uses would serve society better by promoting or sponsoring more legitimate scientific research, rather than throwing their time, money and rhetoric into lobbying, public relations campaigns and perennial litigation.

Clarification of Currently Accepted Medical Use

The Controlled Substances Act of 1970 divides the universe of all durgs of abuse into five sets or schedules. Drugs in Schedule I are subject to the most severe controls, because they have a high potential for abuse and no currently accepted medical use in treatment in the United States. 21 U.S.C. 812 (b)(1). Drugs of abuse which have currently accepted medical use in treatment in the United States are placed in Schedules II, III, IV and V. Regrettably, the Controlled Substances Act does not speak directly to what is meant by "currently accepted medical use."

A century before the Controlled Substances Act was enacted, the determination of what drugs to accept as medicine was totally democratic and totally standardless. Each patient and each physician was free to decide for himself, often based on no more

than anecdotal evidence. This state of affairs became unsatisfactory to a majority of the American people. In 1906, Congress intervened with the passage of the Food, Drug and Cosmetic Act (FDCA). A shift began away from anecdotal evidence to objectively conducted scientific research, away from uninformed opinions of lay persons and local doctors to expert opinions of specialists trained to evaluate the safety and effectiveness of drugs, and away from totally democratic decision-making to oversight by the Federal Government.

By 1969, Congress had developed detailed Federal statutory criteria under the FDCA to determine whether drugs are acceptable for medical use. Those deemed acceptable can be marketed nationally. Those deemed unacceptable are subject to Federal seizure if marketed interstate. The FDCA is a very complex regulatory scheme not easily summarized. However, it is fair to say that drugs falling into one of four FDCA categories were accepted by Congress for medical use.

First, Congress accepted new drugs which have been approved by FDA's experts as safe and effective for use in treatment, based on substantial scientific evidence. 21 U.S.C. 321(p) and 355 (so-called “NDA-approved drugs”).

Second, Congress accepted those drugs “generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective,” based on substantial scientific evidence. 21 U.S.C. 321(p) and 355; Weinberger v. Bentex Pharmaceuticals, Inc., 412 U.S. 645 (1973). An acronym for this category is “human GRASE drugs” (Generally Recognized As Safe and Effective). These drugs achieve acceptance through rigorous scientific proof, through a past history of widespread use in treatment in the United States, and through recognition by a consensus of drug experts outside the FDA.

Third, Congress accepted for use in veterinary medicine those drugs “generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective,” based on substantial scientific evidence. 21 U.S.C. 321(w) and 355. An acronym for these is “animal GRASE drugs.” They achieve acceptance through rigorous scientific evidence and through recognition by a consensus of drug experts outside the FDA. Unlike human GRASE drugs, animal GRASE drugs need not have a past history of widespread use.

Finally, Congress accepted those drugs marketed prior to 1938 which had been subject to the 1906 provisions of the FDCA, provided these very old drugs retain their exact formulations and are never promoted for new uses. 21 U.S.C. 321(p) and (w). These are politically “grandfathered” drugs. They need not meet modern standards for safety and effectiveness.

A fifth group of drugs was accepted for research use only, not for use in treatment of patients. 21 U.S.C. 355(i) (so-called “IND or approved investigational new drugs”).

Drugs intended for medical use and shipped interstate are subject to Federal seizure under the FDCA if they do not fit within one of the above accepted sets or groupings. It seems fair to say that seizable drugs were rejected by Congress for medical uses.

In enacting the Controlled Substances Act in 1970, could Congress have intended to create a totally new Federal standard for determining whether drugs have accepted medical uses? Or did Congress intend to rely on standards it had developed over the prior 64 years under the FDCA? There is nothing in the Controlled Substances Act, its legislative history, or its purposes that would indicate Congress intended to depart radically from existing Federal law.

Indeed, it seems likely that the core standards developed under the FDCA represent a long-term consensus of expert medical and scientific opinion concerning when a drug should be accepted by anyone as safe and effective for medical use.

Fortunately, there is a way to corroborate what Congress intended. Congress did more than just announce criteria for scheduling drugs of abuse under the Controlled Substances Act; Congress applied those criteria to an initial listing of drugs that it placed into the original five schedules of the Act.

NDA-approved drugs were placed by Congress into Schedules II, III, IV and V of the Act. For example, pethidine (also known as meperidine) received New Drug Application (NDA) approval in 1942. Congress put it into Schedule II(b)(14). Methamphetamine had an approved NDA. Congress put it into Schedule III(a)(3). I am not aware of any drug with an approved NDA that Congress originally put into Schedule I.

Drugs with medical uses, but without approved NDA's also were placed by Congress into Schedules II, III, IV and V. For example, cocaine was put into Schedule II(a)(4). Codeine combinations were put into Schedules III(d)(1) and V. Morphine combinations were put into Schedule III(d)(8). Phenobarbital was put into Schedule IV(11). Barbiturates were put into Schedule III(b)(1). Amphetamines were put into Schedule III(a)(1).

The Court of Appeals for the First Circuit was correct when it decided in ***10504** Grinspoon v. DEA, 828 F.2d 881 (1987) that NDA approval is not the only method by which drugs can achieve Federal recognition as having medical uses. Congress put both GRASE drugs and pre-1938-grandfathered drugs into Schedules II, III, IV and V of the CSA.

Drugs recognized under the FDCA for research use only, not for use in treatment, such as alphacetylmethadol and marijuana, were placed by Congress into Schedule I.

Unfortunately, Federal records are not complete enough to do a comprehensive mathematical mapping, tracing every drug in the initial Controlled Substances Act schedules back to its legal status under the FDCA. Nevertheless, determining legislative intent does not require mathematical certainty. Probability based on circumstantial evidence, on samplings, and on inductive reasoning can suffice, especially when there is nowhere else to turn.

The pattern of initial scheduling of drugs in the Controlled Substance Act, viewed in light of the prior legal status of these drugs under the FDCA, convinces me that Congress equated the term “currently accepted medical use in treatment in the United States” as used in the Controlled Substances Act with the core FDCA standards for acceptance of drugs for medical use.

This is not to say that every FDCA requirement for GRASE status, or for NDA approval, is pertinent to scheduling determinations under the Controlled Substances Act. There are differences. But the core FDCA criteria appear to have guided the Congress in the decisions it made concerning the initial scheduling of drugs in the Act.

These same core FDCA criteria served as the basis for an eight-point test used by my predecessor as Administrator to describe drugs with currently accepted medical uses. 54 FR 53783 (December 29, 1989):

1. Scientifically determined and accepted knowledge of its chemistry;

2. The toxicology and pharmacology of the substance in animals;

3. Establishment of its effectiveness in humans through scientifically designed clinical trials;

4. General availability of the substance and information regarding the substance and its use;

5. Recognition of its clinical use in generally accepted pharmacopeia, medical references, jounals or textbooks;

6. Specific indications for the treatment of recognized disorders;

7. Recognition of the use of the substance by organizations or associations of physicians; and

8. Recognition and use of the substance by a substantial segment of the medical practitioners in the United States.

Some uncertainty remains over the precise meaning and application of parts of this test. Therefore, the Court of Appeals for the District of Columbia Circuit remanded these proceedings for a further explanation. In addition to addressing those parts of the test that concerned the Court of Appeals, it would be useful to clarify the entire test, pinpoint its origins, and identify which elements are both necessary and sufficient to establish a prima facie case of currently accepted medical use. This is not an effort to change the substantive law. The statutory meaning of currently accepted medical use remains the same as enacted by Congress in 1970. My purpose simply is to clarify this Agency's understanding of the law.

A. The Drug's Chemistry Must Be Known and Reproducible

The ability to recreate a drug in standardized dosages is fundamental to testing that drug and to using it as a medicine. Knowing the composition, properties, methods of production, and methods of analysis of a drug is essential to reproducing it in standardized dosages. To be GRASE or to receive NDA approval, a drug's chemistry must be known and reproducible. See e.q., 21 CFR 314.50(d)(1) and 314.126(b)(7)(d); Dorovic v. Richardson, 749 F.2d 242, 251 (7th Cir. 1973). The listing of a drug in a current edition of one of the official compendia normally satisfies this requirement. 21 U.S.C. 321(j); 21 CFR 314.50(d)(1).

The first element of our eight-point test, namely, “scientifically determined and acccepted knowledge of its chemistry,” should be clarified to read:

The substance's chemistry must be scientifically established to permit it to be reproduced into dosages which can be standardized. The listing of the substance in a current edition of one of the official compendia, as defined by section 201(j) of the Food, Drug and Cosmetic Act, 21 U.S.C. 321(j), is sufficient generally to meet this requirement.

Acceptance of this knowledge will be discussed elsewhere.

B. There Must Be Adequate Safety Studies

No drug can be considered safe in the abstract. Safety has meaning only when judged against the intended use of the drug, its known effectiveness, its known and potential risks, the severity of the illness to be treated, and the availability of alternative therapies. Hess & Clark Division of Rhodia, Inc. v. FDA, 495 F.2d 975, 993 (D.C. Cir. 1974). To know the risks, there must be adequate studies, by all methods reasonably applicable, to show the pharmacological and toxicological effects of the drug. 21 CFR 314.125(b)(2). This includes animal studies and clinical trials in large numbers of humans. 21 CFR 312.21. The studies need not be well-controlled, but they must be adequate. Edison Pharmaceuticals Co. v. FDA, 600 F.2d 831 (D.C. Cir. 1979). Short term (acute) studies of a drug intended to treat long-term (chronic) illnesses, such as glaucoma or MS, are clearly inadequate. United States v. Naremco, Inc., 553 F.2d 1138, 1143 (8th Cir. 1977). The second element of our eight-point test, namely, “the toxicology and pharmacology of the substance in animals,” should be clarified as follows:

There must be adequate pharmacological and toxicological studies, done by all methods reasonably applicable, on the basis of which it could fairly and responsibly be concluded, by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that the substance is safe for treating a specific, recognized disorder.

It must be emphasized that while the existence of adequate safety tests is a separate analytical question, the ultimate determination of whether a drug is safe for a specific use is not a distinct issue. Safety and effectiveness are inextricably linked in a risks-benefits calculation. A determination that a drug is ineffective is tantamount to a determination that it is unsafe. United States v. Rutherford, 442 U.S. 544 (1970).

The scheduling criteria of the Controlled Substances Act appear to treat the lack of medical use and lack of safety as separate considerations. Prior rulings of this Agency purported to treat safety as a distinct factor. 53 FR 5156 (February 22, 1988). In retrospect, this is inconsistent with scientific reality. Safety cannot be treated as a separate analytical question.

C. There Must Be Adequate and Well-Controlled Studies Proving Efficacy

Since 1962, Congress has prohibited the FDA to approve an NDA unless the applicant submits adequate, well-contolled, well-designed, well-conducted, and well-documented studies, performed by qualified investigators, which prove the efficacy of a drug for its intended use. 21 U.S.C. 355(d); 21 CFR 314.126. Similarly, a drug cannot be considered GRASE unless it is supported by this same quantity and quality of scienfitic proof. 21 CFR 314.200(e)(i); Weinberger v. Hynson, Etc., 412 U.S. 609, 629 (1973).

***10505** Studies involving related, but not identical, drugs are irrelevant. United States v. Articles of Food & Drug, 518 F.2d 743, 747 (5th Cir. 1975). Studies involving the same drug combined with other drugs are irrelevant. United States v. Articles of Drug * * * Promise Toothpaste, 826 F.2d 564, 570 (7th Cir. 1987). Incomplete studies are insufficient. United States v. Articles of Food & Drug, supra. Uncontrolled studies are insufficient. 21 U.S.C. 355(d); Cooper Labs v. FDA, 501 F.2d 772, 778 (D.C. Cir. 1974). Statistically insignificant studies are insufficient. 21 CFR 312.21, 314.50(d)(6) and 314.126(b)(7). Poorly designed studies are insufficient. 21 CFR 314.126(b)(2). Poorly conducted studies are insufficient. 21 CFR part 58—Good Laboratory Practices. Poorly documented studies are insufficient. 21 CFR 312.58 and 314.200(e)(4). Studies by investigators who are not qualified, both to conduct and to evaluate them are insufficient. 21 U.S.C. 355(d). Moreover, since scientific reliability requires a double examination with similar results, one valid study is insufficient. There must be two or more valid studies which corroborate each other. See 1 J. O'Reilley "Food and Drug Administration" 13-55 n.12 (1985).

Lay testimonials, impressions of physicians, isolated case studies, random clinical experience, reports so lacking in details they cannot be scientifically evaluated, and all other forms of anecdotal proof are entirely irrelevant. 21 CFR 314.126(e); Weingerger v. Hynson, Etc., 412 U.S. 609, 630 (1973).

Element three of our eight-point test, namely, "establishment of its effectiveness in humans through scientifically designed clinical trials," should be restated as:

There must be adequate, well-controlled, well-designed, well-conducted and well-documented studies, including clinical investigations, by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, on the basis of which it could fairly and responsibly be concluded by such experts that the substance will have the intended effect in treating a specific, recognized disorder.

D. Acceptance by Qualified Experts Is Required

The opinions of lay persons are totally irrelevant to whether a drug is GRASE or meets NDA requirements. The observations and opinions of medical practioners who are not experts in evaluating drugs also are irrelevant to whether a drug is GRASE or meets NDA requirements. Weinberger v. Hynson, Etc., 412 U.S. 609, 619 (1973). By explicit requirements in the FDCA since 1938, the only body of opinion that counts is that of experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs. 21 U.S.C. 321 (p) and (w).

From this, one would conclude that expert acceptance of a drug as safe and effective for its intended use is essential to a drug having a currently accepted medical use under the CSA. How widespread must this expert acceptance be?

To be GRASE, a drug must be "generally recognized" among experts as safe and effective for its intended use. The drug must be known or familiar to the national community of relevant experts. United States v. Articles of Drug* * * Furestrol Vaginal Suppositories, 294 F. Supp. 1307, 1309 (N.D. Ga. 1968) aff'd, 415 F.2d 390 (5th Cir. 1969). To determine if a drug is known to the community of experts, courts have looked to whether there is widely available scientific literature about the drug, Premo Pharmaceutical Laboratories, Inc. v. United States, 629 F.2d 795, 803 (2d Cir. 1980), whether it is widely taught in medical schools, Lemmon Pharmaceuticals Co. v. Richardson, 319 F. Sup. 375, 378 (E.D. Pa. 1970), and whether it is widely discussed by experts. United States v. Bentex Ulcerine, 469 F. 2d 875, 880 (5th Cir. 1972).

The recognition of a drug as GRASE need not be universal. General recognition is sufficient. United States v. 41 Cartons* * *Ferro-Lac, 420 F.2d 1126, 1132 (5th Cir. 1970). The Supreme Court has interpreted this to mean a consensus of experts is familiar with and accepts a drug as safe and effective. Weinberger v. Hynson, Etc., 412 U.S. 609, 629 (1973). However, if there is a serious dispute among the experts, a drug cannot be considered GRASE. United States v. An Article of Food***Coco Rico, 752 F.2d 11, 15 (1st Cir. 1985); Merrit Corp. v. Folsom, 165 F. Supp. 418, 421 (D.D.C. 1958).

During the NDA process, the FDA may reach out to the expert community for its views. 21 CFR 314.103(c)(3). The FDA need not determine that a drug is generally known and accepted by the expert community. Nor must the FDA develop a consensus of opinion among outside experts. The FDA has both the experts and the statutory mandate to resolve conflicts over the safety and efficacy of new drugs. Weinberger v. Bentex Pharmaceuticals, Inc., 412 U.S.C 638, 653 (1973).

In drafting the Controlled Substances Act, Congress appears to have accommodated, rather than chosen from these different FDCA standards. Clearly, the Controlled Substances Act does not authorize the Attorney General, nor by delegation the DEA Administrator, to make the ultimate medical and policy decision as to whether a drug should be used as medicine. Instead, he is limited to determing whether others accept a drug for medical use. Any other construction would have the efect of reading the word “accepted” out of the statutory standard. Since Congress recognized NDA-approved drugs as having currently accepted medical uses, without any need for a national consensus of experts, FDA acceptance of a drug through the NDA process would seem to satisfy the Controlled Substances Act. And, since Congress recognized GRASE drugs as having currently accepted medical uses, without the need for NDA approval, acceptance of a drug by a national consensus of experts also would seem to satisfy the Act.

When a drug lacks NDA approval and is not accepted by a consensus of experts outside FDA, it cannot be found by the Attorney General or his delegate to have a currently accepted medical use. To do so would require the Attorney Genral to resolve complex scientific and medical disputes among experts, to decide the ultimate medical policy question, rather than merely determine whether the drug is accepted by others.

Because the recognition of a drug by non-experts is irrelevant to GRASE status, to NDA approval, and to currently accepted medical use under the Controlled Substances Act, points seven and eight of our eight-point test should be combined and restated as follows:

The drug has a New Drug Application (NDA) approved by the Food and Drug Administration pursuant to the Food, Drug and Cosmetic Act, 21 U.S.C. 355. Or, a consensus of the national community of experts, qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, accepts the safety and effectiveness of the substance for use in treating a specific, recognized disorder. A material conflict of opinion among experts precludes a finding of consensus.

This restatement also incorporates the component of part one of our eight-point test concerning “accepted knowledge of its chemistry.”

E. The Scientific Evidence Must Be Widely Available

Nothing in the FDCA, nor in FDA's regulations, requires that scientific evidence supporting an NDA be published. This stems from the fact that a consensus of experts outside FDA is ***10506** not required for NDA approval. In contrast, most courts have held that a drug cannot be considered GRASE unless the supporting scientific evidence appears in the published scientific and medical literature. Without published studies, it would be difficult for the community of experts outside FDA to develop an informed acceptance of a drug for medical use. Cooper Labs Inc. v. FDA, 501 F.2d 772, 786 (D.C. Cir. 1974).

Point four of the eight-point test focuses, in part, on the “general availability of information regarding the substance and its use.” This should be clarified to read:

In the absence of NDA approval, information concerning the chemistry, pharmacology, toxicology and effectiveness of the substance must be reported, published, or otherwise widely available, in sufficient detail to permit experts, qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, to fairly and responsibly conclude the substance is safe and effective for use in treating a specific, recognized disorder.

F. General Availability of a Drug Is Irrelevant

The second component of point four of the eight--point test involves the "general availability of the substance" for use in treatment. The second component of point eight focuses on "use of the substance by a substantial segment of the medical practitioners in the United States." These elements justifiably concerned the Court of Appeals, leading to the remand in this case.

Under the FDCA, a human GRASE drug must have a material history of past use in treatment in the United States. 21 U.S.C. 321(p)(2) (which has * * *, otherwise than in such investigations, been used to a material extent or a material time); Weinberger v. Hynson, Etc., 412 U.S. 609, 631 (1973). Rigorous scientific proofs and current unanimous acceptance by the medical and scientific community are not enough for a human drug to be GRASE. Tri-Bio Labs, Inc. v. United States, 836 F.2d 135, 142 n.8 (3d Cir. 1987). The general availability of a drug for use in treatment is a factor courts have considered to determine if a human drug is GRASE.

In contrast, a drug can achieve current acceptance for human medical use through the NDA process without a past history of use in treatment. Also, animal drugs can become accepted as GRASE without any past history of medical use. Given this conflict in FDCA standards, which did Congress choose when drafting the CSA?

As the Court of Appeals points out, requiring a material history of past use in treatment before recognizing a drug as having a currently accepted medical use, would permanently freeze all Schedule I drugs into Schedule I. 930 F.2d at 940. Clearly, Congress did not intend this result. Moreover, the use of the word "currently" before the term "accepted medical use" would indicate Congress rejected the human GRASE requirement of past material use in treatment. I conclude that the general availability of a drug is irrelevant to whether it has a currently accepted medical use in treatment within the meaning of the Controlled Substances Act.

G. Recognition in Generally Accepted Texts Is Irrelevant

Point five of the eight-point test deals with "recognition of its clinical use in generally accepted pharmacopeia, medical references, journals or textbooks." The listing of a drug in an official compendium is sufficient to show its chemistry is scientifically established. This appears in my clarification to point one. The requirement that information concerning the chemistry, pharmacology, toxicology and effectiveness of the substance be reported, published or otherwise widely available, is explained adequately in revised point four. To the extent the scheduling of a drug directly influences its recognition in publications, this element is subject to the same criticism identified by the Court of Appeals concerning point four. Therefore, this should not be treated as a distinct requirement.

H. Specific, Recognized Disorders Are the Referent

It is impossible to judge the safety and effectiveness of a drug except in relation to a specific intended use. A drug cannot obtain NDA approval or GRASE status except in relation to the treatment of a specific, recognized disorder. This is an essential aspect of whether a drug has currently accepted medical use. Rather than standing alone, this requirement will be more clearly understood by incorporating it into the other critical elements.

To summarize, the five necessary elements of a drug with currently accepted medical use in treatment in the United States are:

(i) The Drug's Chemistry Must Be Known and Reproducible

The substance's chemistry must be scientifically established to permit it to be reproduced into dosages which can be standardized. The listing of the substance in a current edition of one of the official compendia, as defined by section 201(j) of the Food, Drug and Cosmetic Act, 21 U.S.C. 321(j), is sufficient generally to meet this requirement.

(ii) There Must Be Adequate Safety Studies

There must be adequate pharmacological and toxicological studies done by all methods reasonably applicable on the basis of which it could fairly and responsibly be concluded, by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that the substance is safe for treating a specific, recognized disorder.

(iii) There Must Be Adequate and Well-Controlled Studies Proving Efficacy

There must be adequate, well-controlled, well-designed, well-conducted and well-documented studies, including clinical investigations, by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs on the basis of which it could fairly and responsibly be concluded by such experts, that the substance will have its intended effect in treating a specific, recognized disorder.

(iv) The Drug Must Be Accepted by Qualified Experts

The drug must have a New Drug Application (NDA) approved by the Food and Drug Administration, pursuant to the Food, Drug and Cosmetic Act. 21 U.S.C. 355. Or, a consensus of the national community of experts, qualified by scientific training and experience to evaluate the safety and effectivenss of drugs, must accept the safety and effectiveness of the substance of use in treating a specific, recognized disorder. A material conflict of opinion among experts precludes a finding of consensus.

(v) The Scientific Evidence Must Be Widely Available

In the absence of NDA approval, information concerning the chemistry, pharmacology, toxicology and effectiveness of the substance must be reported, published, or otherwise widely available in sufficient detail to permit experts, qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, to fairly and responsibly conclude the substance is safe and effective for use in treating a specific, recognized disorder.

Together these five elements constitute prima facie evidence that a drug has currently accepted medical use in treatment in the United States. In the interest of total clarity, let me emphasize those proofs that are irrelevant to the determination of currently accepted medical use, and that will not be considered by the Administrator:

(i) Isolated case reports;

(ii) Clinical impressions of practitioners;

(iii) Opinions of persons not qualified by scientific training and experience to evaluate the safety and effectiveness of the substance at issue;

(iv) Studies or reports so lacking in detail as to preclude responsible scientific evaluation;

***10507** (v) Studies or reports involving drug substances other than the precise substance at issue;

(vi) Studies or reports involving the substance at issue combined with other drug substances;

(vii) Studies conducted by persons not qualified by scientific training and experience to evaluate the safety and effectivness of the substance at issue;

(viii) Opinions of experts based entirely on unrevealed or unspecified information;

(ix) Opinions of experts based entirely on theoretical evaluations of safety or effectiveness.

Bad Medicine By Any Standard

My predecessor as DEA Adminstrator developed and relied upon an eight-point test to determine whether marijuana has accepted medical uses. 54 FR 53783 (December 29, 1989):

1. Scientifically determined and accepted knowledge of its chemistry;

2. the toxicology and pharmacology of the substance in animals;

3. Establishment of its effectiveness in humans through scientifically designed clinical trials;

4. General availability of the substance and information regarding the substance and its use;

5. Recognition of its clincial use in generally accepted pharmacopeia, medical references, journals or textbooks;

6. Specific indications for the treatment of recognized disorders;

7. Recognition of the use of the substance by organizations or associations of physicians; and

8. Recognition and use of the substance by a substantial segment of the medical practitioners in the United States.

The Court of Appeals remanded the decision of my predecessor for clarification of what role factors (4), (5) and (8) of the initial eight-point test played in his reasoning. For ease of discussion, these factors can be divided as follows:

(4)(a) General availability of the substance * * *;

(4)(b) General availability of * * * information regarding the substance and its use;

(5) Recognition of its clinical use in generally accepted pharmacopeia, medical references, journals or textbooks;

(8)(a) Recognition * * * of the substance by a substantial segment of the medical practitioners in the United States; and

(8)(b) (U)use of the substance by a substantial segment of the medical practitioners in the United States.

I have found no evidence indicating initial factors (4)(a) or (8)(b) played any role in my predecessor's decision. In light of my understanding of the legal standard involved, these factors are irrelevant to whether marijuana has a currently accepted medical use.

My predecessor emphasized the lack of scientific evidence of marijuana's effectiveness, and the limited data available on its risks, as reflected in the published scientific studies. He also emphasized the importance of this data to the conclusions reached by experts concerning the drug. 54 FR 53783. I take this to mean that, under initial factor (4)(b), he believed the information available to experts is insufficient for them responsibly and fairly to conclude the marijuana is safe and effective for use as medicine.

Marijuana is not recognized as medicine in generally accepted pharmacopeia, medical references and textbooks, as noted by my predecessor. 54 FR 53784. I take this to mean, under initial factor (5), that he determined that marijuana's chemistry is neither known, nor reproducible, as evidenced by its absence from the official pharmacopeia. Finally, my predecessor concluded, under initial factor (8)(a), that the vast majority of physicians does not accept marijuana as having medical use. 54 FR 53784. Along the way, he found that highly respected oncologists and antiemetic researchers reject marijuana for use in controlling nausea and vomiting, 54 FR 53777, that experts experienced in researching glaucoma medications reject marijuana for use in treating glaucoma, 54 FR 53779, and that noted neurologists who specialize in treating and conducting research in spasticity reject marijuana for use by MS patients, 54 FR 53780. I take this to mean my predecessor found no national consensus of qualified experts accepts marijuana's value as medicine.

Certainly I cannot know my predecessor's unstated reasoning. However, I have reviewed the entire record de novo, and I am convinced that his application of the initial eight-point test to this record correctly resulted in the conclusion that marijuana has no currently accepted medical use in treatment in the United States. Therefore, I adopt in their entirety the findings of facts and conclusions of law reached by the former Administrator in his final order of December 21, 1989, 54 FR 53767.

Pursuant to the remand of the Court of Appeals, I have condensed and clarified the initial standard into a five-point test. My application of the refined, five-point test to this record is set out briefly below.

First, marijuana's chemistry is neither fully known, nor reproducible. Thus far, over 400 different chemicals have been identified in the plant. The proportions and concentrations differ from plant to plant, depending on growing conditions, age of the plant, harvesting and storage factors. THC levels can vary from less than 0.2% to over 10%. It is not known how smoking or burning the plant material affects the composition of all these chemicals. It is not possible to reproduce the drug in dosages which can be considered standardized by any currently accepted scientific criteria. Marijuana is not recognized in any current edition of the official compendia. 21 U.S.C. 321(j).

Second, adequate safety studies have not been done. All reasonably applicable pharmacological and toxicological studies have not been carried out. Most of the chronic animal studies have been conducted with oral or intravenous THC, not with marijuana. Pharmacological data on marijuana's bioavailability, metabolic pathways and pharmacokinetics in inadequate. Studies in humans are too small and too few. Sophisticated epidemiological studies of marijuana use in large populations are required, similar to those done for tobacco use. Far too many questions remain unknown for experts fairly and responsibly to conclude marijuana is safe for any use.

Third, there are no adequate, well-controlled scientific studies proving marijuana is effective for anything.

Fourth, marijuana is not accepted for medical use in treatment by even a respectable minority, much less a consenus, of experts trained to evaluate drugs. The FDA's expert drug evaluators have rejected marijuana for medical use. No NDA has been approved by FDA for marijuana. The testimony of nationally recognized experts overwhelmingly rejects marijuana as medicine, compared to the scientifically empty testimony of the psychiatrists, a wellness counselor and general practitioners presented by NORML.

Fifth, given my conclusions on points one, two and three, it follows that the published scientific evidence is not adequate to permit experts to fairly and responsibly conclude that marijuana is safe and effective for use in humans.

A failure to meet just one of the five points precludes a drug from having a currently accepted medical use. Marijuana fails all five points of the test.

NORML has argued, unsuccessfully, that the legal standard for currently accepted medical use should be whether a respectable minority of physicians accepts the drug. The key to this medical malpractice defense is that the minority opinion must be recognized as respectable, as competent, by members of the profession.

In the absence of reliable evidence adequately establishing marijuana's chemistry, pharmacology, toxicology and effectiveness, no responsible physician could conclude that marijuana ***10508** is safe and effective for medical use. To quote Doctor Kenneth P. Johnson, Chairman of the Department of Neurology at the University of Maryland, and the author of over 100 scientific and medical articles on MS: "To conclude that marijuana is therapeutically effective without conducting rigorous testing would be professionally irresponsible."

By any modern scientific standard, marijuana is no medicine.

Under the authority vested in the Attorney General by section 201(a) of the Controlled Substances Act, 21 U.S.C. 811(a), and delegated to the Administrator of the Drug Enforcement Administration by regulations of the Department of Justice, 28 CFR 0.100(b), the Administrator hereby orders that marijuana remain in Schedule I as listed in 21 CFR 1308.11(d)(14).

Dated: March 18, 1992.

Robert C. Bonner,

Administrator.

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