



# Researcher's Manual

## AN INFORMATIONAL OUTLINE OF THE CONTROLLED SUBSTANCES ACT

Revised 2022

Drug Enforcement Administration  
**Researcher's Manual**

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This Researcher's Manual has been prepared by the Drug Enforcement Administration (DEA), Diversion Control Division, as a guide to assist researchers, who are authorized to conduct research with schedules I-V controlled substances, in their understanding of the Federal Controlled Substances Act and its implementing regulations as they pertain to their profession.

The 2022 edition replaces all previous editions of the Researcher's Manual issued by DEA, both hard copy and electronic.

Guidance documents, like this document, are not binding and lack the force and effect of law, unless expressly authorized by statute or expressly incorporated into a contract, grant, or cooperative agreement.

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**SECTION I - INTRODUCTION**

**Disclaimer**

This Researcher's Manual is intended to summarize and explain the basic requirements for prescribing, administering, and dispensing controlled substances under the Controlled Substances Act (CSA), [U.S.C. 801-904](#); the Controlled Substances Import and Export Act (CSIEA), [21 U.S.C. 951-971](#); and DEA regulations, [CFR parts 1300 to end](#). Pertinent citations to the law and regulations are included in this manual.

This Researcher's Manual is a guidance document that provides statutory and regulatory requirements as well as recommended practices. Statutory and regulatory requirements use language such as "must," "shall," or "required" and include the statutory and/or regulatory citation(s). Recommended practices in this Researcher's Manual are voluntary and use language such as "should" or "recommend" to identify these suggestions. Readers should refer to the most current copy of the laws (CSA and CSIEA), regulations (CFR), and [Federal Register \(FR\) notices](#) to obtain the most complete and accurate up-to-date statutory and regulatory information.

Printed copies of the complete regulations implementing the CSA (21 CFR parts 1300 to End) can be obtained from:

Superintendent of Documents  
U.S. Government Printing Office  
Washington, DC 20402  
1-866-512-1800

Both the CFR and the FR (which includes proposed and final rules implementing the CSA) are available on the Internet through the U.S. Government Printing Office (GPO) website. This website, which provides information by section, citation, and keywords, can be accessed at:

[www.govinfo.gov](http://www.govinfo.gov)

Unofficial copies of pertinent CFR citations and this researcher's manual can be found on the Internet within DEA's Diversion Control Division website:

<https://www.deadiversion.usdoj.gov/>.

Should any pertinent provisions of the law or regulations be modified in the future, DEA will issue a revised electronic version of this document, which will be posted on DEA's Diversion Control Division website.

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If there are errors in this document, please notify the following: [ODLP@dea.gov](mailto:ODLP@dea.gov) or

Diversion Control Division  
Attn: Policy Section/DPY  
Drug Enforcement Administration  
8701 Morrissette Drive  
Springfield, VA 22152

Inquiries regarding topics within this document can be addressed to [your local DEA Diversion Field Office](#) or the address above.

**Authorized for Public Dissemination**

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**Message from the Assistant Administrator**

The DEA Diversion Control Division is pleased to provide you with the 2022 edition of the Researcher's Manual to assist you in understanding the provisions of the CSA and its implementing regulations. This Researcher's Manual will answer questions you may encounter in your practice and provide guidance in complying with CSA regulations.

There is a legitimate need for conducting research with controlled substances. However, the diversion and abuse of pharmaceutical controlled substances remains a public health concern in the United States. Your role in the proper use of controlled substances in your research helps protect society against drug abuse and diversion. Your compliance with the CSA and its objectives is a powerful resource for protecting the public health, assuring patient safety, and preventing the diversion of controlled substances.

Sincerely,

 Digitally signed by  
KRISTI O'MALLEY  
Date: 2022.06.16  
17:26:44 -04'00'

Kristi N. O'Malley  
Assistant Administrator  
Diversion Control Division  
Drug Enforcement Administration

# Drug Enforcement Administration Researcher's Manual

## Preface

In October 1970, Congress passed the Comprehensive Drug Abuse Prevention and Control Act, PL 91-513, October 27, 1970, 84 Stat. 1236, better known as the [CSA](#), to consolidate and replace more than 50 pieces of national drug legislation. The CSA went into effect on May 1, 1971. DEA was established in 1973 to serve as the single federal agency to coordinate the Federal Government's drug control activities. The CSA and its implementing regulations establish federal requirements regarding both illicit and licit controlled substances. Subsequent laws added regulated chemicals and certain equipment under the purview of the CSA. With respect to pharmaceutical controlled substances, DEA's responsibility is twofold: to prevent diversion and abuse of these substances while ensuring an adequate and uninterrupted supply is available to meet the country's legitimate medical, scientific, and research needs. In carrying out this mission, DEA works closely with state and local authorities and other federal agencies.

Under the framework of the CSA, all controlled substance transactions take place within a "closed system" of distribution established by Congress. Within this closed system, all legitimate handlers of controlled substances -- manufacturers, distributors, practitioners pharmacies, researchers, and others, must be registered with DEA (unless exempt) and maintain strict accounting for all controlled substance transactions.

To carry out this mission effectively, DEA seeks to educate its registrants regarding their legal rights and obligations. It is DEA's goal to maintain a positive working relationship with all of its registrants, including researchers. DEA understands that it can best serve the public interest by working with the researcher community to prevent the diversion of controlled substances into the illicit market.

Federal controlled substance laws are designed to function in tandem with state controlled substance laws. DEA works in cooperation with state professional licensing boards and state and local law enforcement officials to make certain that pharmaceutical controlled substances are prescribed, administered, and dispensed for a legitimate medical purpose in the usual course of professional practice. Within this framework, the majority of investigations into possible violations of controlled substance laws are carried out by state authorities. DEA focuses its investigations on cases involving violators of the highest level or most significant impact.

DEA and researchers have a common interest in the appropriate use of controlled substances. An effective working relationship to ensure compliance with federal requirements will continue to produce lasting benefits on a national scale.



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## SECTION II - SCHEDULES OF CONTROLLED SUBSTANCES

Drugs and other substances that are considered controlled substances under the CSA are divided into five schedules. A listing of the substances and their schedules is found in DEA regulations at [21 CFR 1308.11-15](#). Except where control is required by United States obligations under an international treaty, convention, or protocol, in effect on October 27, 1970, and except in the case of an immediate precursor, a controlled substance is placed in its respective schedule based on whether it has a currently accepted medical use in treatment in the United States, its relative abuse potential, and likelihood of causing dependence. [21 U.S.C. 812](#). Some examples of controlled substances in each schedule are listed below.

**NOTE:** Drugs listed in schedule I have no currently accepted medical use in treatment in the United States and, therefore, may not be prescribed, administered, or dispensed for medical use. [21 U.S.C. 812](#). In contrast, drugs listed in schedules II-V have some accepted medical use and may be prescribed, administered, or dispensed for medical use. [21 U.S.C. 812](#).

### Schedule I Controlled Substances

Substances in this schedule have a high potential for abuse, have no currently accepted medical use in treatment in the United States, and there is a lack of accepted safety for use of the drug or other substance under medical supervision. [21 U.S.C. 812\(b\)\(1\)](#).

Some examples of substances listed in schedule I are heroin, lysergic acid diethylamide, marihuana, peyote, methaqualone, and 3,4-methylenedioxymethamphetamine. [21 U.S.C. 812\(c\)](#), [Schedule I](#) and [21 CFR 1308.11](#).

### Schedule II Controlled Substances

Substances in this schedule have a high potential for abuse which may lead to severe psychological or physical dependence, and have a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions. [21 U.S.C. 812\(b\)\(2\)](#).

Examples of schedule II narcotics include morphine, codeine, and opium, except in certain formulations scheduled elsewhere. Other schedule II narcotic substances and their common name brand products include: any combination products containing hydrocodone (Maxidone, Zydone, Vicodin, Lortab, Vicoprofen, Reprexain, and hydromorphone (Dilaudid), methadone (Dolophine), meperidine (Demerol), oxycodone (OxyContin), and fentanyl (Sublimaze or Duragesic).

Examples of schedule II stimulants include amphetamine (Dexedrine, Adderall), methamphetamine (Desoxyn), methylphenidate (Ritalin), and lisdexamfetamine (Vyvanse). Other schedule II substances include: cocaine, amobarbital, and glutethimide. [21 U.S.C. 812\(c\)](#), [Schedule II](#), [21 CFR 1308.12](#).

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## Schedule III Controlled Substances

Substances in this schedule have a potential for abuse less than substances in schedules I or II, have a currently accepted medical use in treatment in the United States, and abuse may lead to moderate or low physical dependence or high psychological dependence. [21 U.S.C. 812\(b\)\(3\)](#).

Examples of schedule III narcotics include morphine combination products containing not more than 50 milligrams of morphine per 100 milliliters or per 100 grams, with one or more active, non-narcotic ingredients in recognized therapeutic amounts, and products containing not more than 90 milligrams of codeine per dosage unit with an equal or greater quantity of an isoquinoline alkaloid of opium (Tylenol with codeine). Also included are buprenorphine products used to treat opioid addiction.

Examples of schedule III non-narcotics include benzphetamine (Didrex), phendimetrazine, ketamine, and anabolic steroids such as oxandrolone (Oxandrin). [21 U.S.C. 812](#) and [21 CFR 1308.13](#).

## Schedule IV Controlled Substances

Substances in this schedule have a low potential for abuse relative to substances in schedule III, have a currently accepted medical use in treatment in the United States, and abuse may lead to limited physical dependence or psychological dependence relative to substances in schedule III. [21 U.S.C. 812\(b\)\(4\)](#).

An example of a schedule IV narcotic is tramadol (Ultram).

Other schedule IV substances include alprazolam (Xanax), carisoprodol (Soma), clonazepam (Klonopin), clorazepate (Tranxene), diazepam (Valium), lorazepam (Ativan), midazolam (Versed), temazepam (Restoril), and triazolam (Halcion). [21 U.S.C. 812\(c\)](#), [Schedule IV](#), [21 CFR 1308.14](#).

## Schedule V Controlled Substances

Substances in this schedule have a low potential for abuse relative to substances listed in schedule IV, have a currently accepted medical use in treatment in the United States, and abuse may lead to limited physical dependence or psychological dependence relative to substances in schedule IV. [21 U.S.C. 812\(b\)\(5\)](#). They consist primarily of preparations containing limited quantities of certain narcotics. These are generally used for antitussive, antidiarrheal, and analgesic purposes. [21 U.S.C. 812\(c\)](#), [Schedule V](#), [21 CFR 1308.15](#).

Examples include cough preparations containing not more than 200 milligrams of codeine per 100 milliliters or per 100 grams (Robitussin AC, Phenergan with Codeine).

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## SECTION III - REGISTRATION REQUIREMENTS

There are two separate categories for researcher registration which are based on controlled substance schedules, the first is *schedule I researcher*, and the second is *schedule II-V researcher*. If a researcher wishes to conduct research in schedules I and schedules II-V, they must obtain two separate registrations, a researcher may not have schedules I-V on one DEA registration. [21 CFR 1301.13\(e\)](#).

### New Researcher Registration

Unless otherwise exempted, as explained in the subsections below, every researcher who intends to conduct research with schedule I controlled substances or schedule II-V controlled substances must be registered with DEA. [21 U.S.C. 823\(f\)](#), [21 CFR 1301.11\(a\)](#). A state license to conduct research and/or a state controlled substance registration, if applicable, must be obtained. [21 U.S.C. 823\(f\)](#).

To register as a new researcher, the DEA Form 225 must be completed. [21 CFR 1301.13\(e\)\(1\)\(v\)](#), [\(vi\)](#). If a person conducts research at more than one location, each place must be separately registered with DEA. [21 CFR 1301.12\(a\)](#).

The DEA Form 225 should be completed [online](#).

A paper version of the DEA Form 225 can be requested by writing to:

Drug Enforcement Administration  
Diversion Control Division  
Attn: Registration & Program Support Section/DRR  
P.O. Box 2639  
Springfield, VA 22152-2639

### Certificate of Registration

A researcher must maintain the Certificate of Registration (DEA Form 223) at the registered location in a readily retrievable manner and available for official inspection. [21 CFR 1301.35\(c\)](#).

A Certificate of Registration for a researcher is valid for 12 months. However, a researcher may receive an initial registration period of a minimum of nine months or a maximum of 15 months. A detailed explanation for this occurrence can be found at [21 CFR 1301.13](#).

If a researcher needs a duplicate Certificate of Registration, a copy can be requested online, or by contacting DEA Headquarters at 1-800-882-9539, or via e-mail at [DEA.Registration.Help@dea.gov](mailto:DEA.Registration.Help@dea.gov).

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## Registration Application Fee

The annual application fee for a researcher registration is listed on the Application for Registration (DEA Form 225). Instructions for methods of payment and additional information can be found online. If paying by check, make checks payable to "Drug Enforcement Administration."

## Application Fee Exemption

Applies to federal, state, and local employees for their **official duties only**. [21 CFR 1301.21](#). Contract employees working at government institutions **do not** qualify. The following also do not qualify as fee exempt:

Non-profit clinics/organizations  
501(c)(3) facilities and organizations  
Federally-qualified health centers

Volunteer positions  
Faith-based organizations  
Tax-exempt organizations

Federal, state, and local law enforcement agency laboratories that receive and transfer controlled substances for use as standards in chemical analysis shall annually obtain a DEA registration to conduct such chemical analysis, but are exempt from the registration fee. [21 CFR 1301.24\(c\)](#).

To claim exemption from the registration fee, the applicant's supervisor (if the applicant is an individual) or agency officer (if the applicant is an agency) must certify exempt status by providing their signature, authority title, telephone number, and certify to the status and business address of the individual applicant or institution and to the authority of the applicant to acquire, possess or handle controlled substances in section 1 of the registration application (DEA Form 225). [21 CFR 1301.21\(b\)](#).

## Registration Exemption

The requirement of registration is waived for the following persons under the following conditions:

- An individual researcher who is an agent or employee of another practitioner (other than a mid-level practitioner) registered to dispense controlled substances may, when acting in the normal course of business or employment, administer or dispense (other than by issuance of prescription) controlled substances if and to the extent that such individual practitioner is authorized or permitted to do so by the jurisdiction in which they practice, under the registration of the employer or principal practitioner in lieu of being registered themselves. [21 CFR 1301.22\(b\)](#).
- An individual researcher who is an agent or employee of a DEA-registered hospital or other institution, may, when acting in the normal course or business or employment and in the usual course of their professional practice, administer, dispense, or prescribe controlled substances under the registration of the hospital or other institution, if the institution has verified that the employee or agent is permitted to dispense, administer or prescribe drugs within its jurisdiction. [21 CFR 1301.22\(c\)](#). The hospital or other institution must designate a specific internal code number for each individual

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practitioner consisting of numbers, letters, or a combination thereof as a suffix to the institution's DEA registration number, preceded by a hyphen (e.g., APO123456-10 or APO123456-A12). A current list of internal codes and the corresponding individual practitioners must be kept by the hospital or other institution and made available at all times to other registrants and law enforcement agencies upon request for the purpose of verifying the authority of the prescribing individual practitioner. [21 CFR 1301.22\(c\)](#).

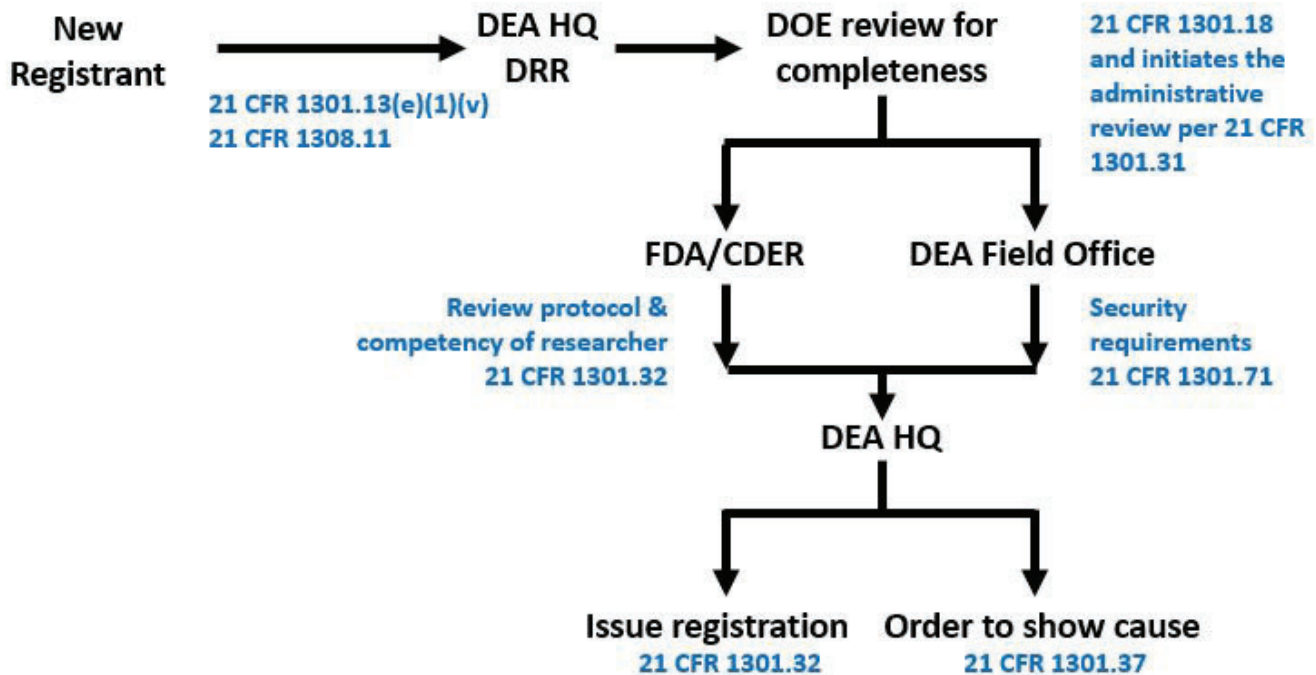
- Any official of the U.S. Army, Navy, Marine Corps, Air Force, Coast Guard, Public Health Service, or Bureau of Prisons who is authorized to prescribe, dispense, or administer, but not to procure or purchase, controlled substances in the course of their official duties. [21 CFR 1301.23\(a\)](#). If an official exempted from registration under this provision engages as a private individual in any activity or group of activities for which registration is required, such official shall obtain a separate registration before participating in those private activities. [21 CFR 1301.23\(c\)](#). This separate registration is not fee exempt.

### Registration Requirements for Multiple Locations

A separate registration must be obtained for each principal place of business or professional practice where controlled substances are stored, administered, or dispensed. [21 CFR 1301.12\(a\)](#).

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## Schedule I Researchers



### New Schedule I Researcher Application Addendums

In addition to completing the application itself, a schedule I researcher must file and receive approval for a research protocol. [21 CFR 1301.13\(e\), 1301.18, 1301.32](#). An applicant can upload supporting documentation at the time of application. The following “Pre-Application Checklist for Schedule I Researchers” outlines what documents are required:

### Pre-Application Checklist for Schedule I Researcher Applications

This checklist is for **new** applicants who intend to handle schedule I controlled substances for research purposes. Additional information on renewing a DEA registration is found towards the end of this chapter.

1. If an application is found to involve manufacturing activities not permitted under a researcher registration, the application may be denied. Some examples of impermissible manufacturing activities include the following:

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- a. Activities to satisfy regulatory requirements such as Food and Drug Administration (FDA) submissions or good manufacturing practice;
- b. Activities related to production of material used for pilot, scale-up, and reformulation studies; or
- c. Activities related to product development including bioavailability, dosage formulation, stability, and validation studies.

For additional questions or clarification related to manufacturing activities please email [DPEScheduleIResearch@dea.gov](mailto:DPEScheduleIResearch@dea.gov).

2. Registering as a researcher requires a non-refundable fee noted on the application. There is no prorated application fee and the subsequent withdrawal of an application does not qualify for a return of an application fee.
3. The applicant must be the only individual completing and certifying by e-signature that the information provided is accurate for purposes of the DEA application. There is an exception to this requirement if the applicant files a power of attorney with DEA. [21 CFR 1301.13\(j\)](#).
4. A schedule I researcher must currently possess all required state authority to handle controlled substances for the state of the researcher's registered business/office address. It is recommended that applicants contact the local [Diversion Field Office](#) for clarification on state law/regulations before completing the application. A lack of state authorization does not entitle a return of the application fee.
5. A schedule I researcher must currently possess appropriate institutional authority to conduct research with schedule I controlled substances. [21 CFR 1301.18\(a\)\(1\)\(ii\)](#).
6. A schedule I researcher must separately identify each of the studies/projects, by project name, that are covered by this application. If the research involves one or multiple studies/projects, the researcher must provide information specific for each of these studies/projects. [21 CFR 1301.18\(a\)\(2\)\(i\)](#). For a given study/project:
  - a. If a schedule I researcher is conducting human research, the schedule I researcher must:
    - i. Have Institutional Review Board (IRB) approval for clinical studies (PDF file upload required);
    - ii. Have an approved active Notice of Claimed Investigational Exemption for a New Drug (IND) (number) for clinical studies. (PDF file upload required); and

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- iii. Have a protocol.\* See [21 CFR 1301.18](#) and [21 CFR 1301.32](#) for the protocol requirements. (PDF file upload required).
- b. If a schedule I researcher is conducting animal research, the schedule I researcher must:
  - i. Have approval from Institutional Animal Care and Use Committee (IACUC) for animal studies. (PDF file upload required); and
  - ii. Have a protocol.\* See [21 CFR 1301.18](#) and [21 CFR 1301.32](#) for the protocol requirements. (PDF file upload required).
- c. If the schedule I research does not use animals or humans (e.g., In-Vitro laboratory research that doesn't require institutional approval, research to develop analytical methods, and research to develop chemical synthesis procedures, etc.) the schedule I researcher must:
  - i. Have a protocol.\* See [21 CFR 1301.18](#) and [21 CFR 1301.32](#) for the protocol requirements. (PDF file upload required).

\*Protocols: If a given study/project has a consolidated research protocol which covers all of the types of research being performed, then a schedule I researcher only needs to upload the consolidated research protocol once for that study/project. If study/project's research protocols have not been consolidated, then a schedule I researcher must upload a dedicated research protocol for each type of research being performed.

A schedule I researcher must submit a curriculum vitae and research protocol as part of the application process. See [21 CFR 1301.18](#) and [21 CFR 1301.32](#) for the protocol requirements. (PDF file upload required).

If schedule I controlled substances mentioned in the research protocol are procured from external sources, then the schedule I researcher must provide the DEA registration number(s) of the source(s) and validate the supplier's name and address.

- 7. A schedule I researcher may be exempt from the application fee if the applicant is a current direct hire employee for a federal, state, or local government institution, or of a public university. The fee exemption is not applicable for future employment. The exemption will restrict the use of a DEA registration to government or university duties only. In accordance with [21 CFR 1301.21\(b\)](#), a schedule I researcher must certify their status on the application. A schedule I researcher may forfeit the fee exemption by not complying with this regulation. A schedule I researcher must include an email address that is associated with the fee-exempt location. An applicant can be required to provide evidence of government or public university employment.
- 8. An applicant should not submit an online application if the applicant mailed a paper application. Duplicate submissions may result in a duplicate collection of non-refundable application fees.



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9. For additional questions or clarification, the following services are available:

- Contact a customer service representative at 1-800-882-9539.
- Email [DEA.Registration.help@dea.gov](mailto:DEA.Registration.help@dea.gov).
- Contact a [Registration Program Specialist](#) specific to your state.

*Note: Size limit for file uploads when submitting supporting application information is 10 MB.*

**IND Certificate:** the IND certificate must be included in a schedule I researcher's application for planned research on investigational new drugs.

I hereby certify that on \_\_\_\_\_, pursuant to 21 U.S.C. 355(i) and  
Date

21 CFR 312.2 \_\_\_\_\_  
Name and Address of IND Sponsor

Submitted a Notice of Claimed IND to the Food and Drug Administration for:

\_\_\_\_\_  
Name of Investigational Drug

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of Applicant

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**Schedule I Research Protocols**

A schedule I research protocol shall contain the following information (in accordance with [21 CFR 1301.18, 1301.32](#)):

1. Investigator
  - a) Name, address, and DEA registration number, if any
  - b) Institutional (or company) affiliation
  - c) Qualifications, including curriculum vitae with list of publications
  
2. Research Project
  - a) Title of project
  - b) Statement of purpose of research
  - c) Name of controlled substances (CS) involved, amount (with justification) of each CS needed and source of CS
  - d) Detailed description of procedures, including number and species of research subjects
  - e) Dosage to be administered, route and method of administration, duration of project
  - f) Location where research will be conducted
  - g) Statement of security provisions for storing the CS (in accordance with [21 CFR 1301.75](#)) and dispensing the CS in order to prevent diversion
  - h) Manufacturing or import statement

**Note:** For an approved research protocol, an increase in the quantity of controlled substances utilized for the research project does not require the submission of a new research protocol. However, per [21 CFR 1301.18\(c\)](#), if the researcher requires an increase in quantity of controlled substances, they must submit a request for approval to the DEA Drug and Chemical Evaluation Section. The request can be made via registered mail, return receipt requested or via email at; [DPEScheduleIResearch@dea.gov](mailto:DPEScheduleIResearch@dea.gov). The request shall contain the following information: DEA registration number; name of the controlled substance or substances and the quantity of each authorized in the approved protocol; and the additional quantity of each desired. Upon verification of receipt of the request by DEA, either by registered mail return receipt or email verification by DEA, the registrant shall be authorized to purchase the additional quantity of controlled substance or substances specified in the request.

**Supplemental Protocol (for Schedule I Researcher Applications Only)**

A supplemental protocol may include adding new controlled substances and any procedural changes affecting inventory, security, record keeping, and disposal of the controlled substances. In accordance to [21 CFR 1301.18\(d\)](#), in the event the registrant desires to conduct research beyond the variations provided in the registrant's approved protocol (excluding any increase in the quantity of the controlled substance requested for their research project), they shall submit via an online submission on Diversion Control's website a copy of a supplemental protocol in accordance with [21 CFR 1301.18\(a\)](#) describing the new research and procedural changes and omitting the information provided in the original protocol. Supplemental protocols shall be processed and approved or denied in the same manner as original research protocols.

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The request for a protocol change should be submitted via email to [DPEScheduleIResearch@dea.gov](mailto:DPEScheduleIResearch@dea.gov)

When the researcher is notified by DEA that the supplemental protocol has been approved, the researcher is then authorized to conduct research as described in the approved supplemental protocol.

### Examples of Activities that may be Authorized for a Schedule I Researcher

- Preclinical studies
  - *In vitro* studies (cell)
  - *In vivo* studies (animal)
- Clinical studies (human)
- Chemical synthesis, methods development
- Devices for detection of controlled substances
- Agricultural studies
- Plant research
- Environmental studies
- Pharmaceutical drug development not to include manufacturing

### Other Research

Researchers applying for DEA registrations to use schedule I controlled substances for other types of research must indicate institutional approval.

### Authorized Coincident Activities (for Schedule I Researchers) [21 CFR 1301.13 \(e\)\(1\)\(v\)](#)

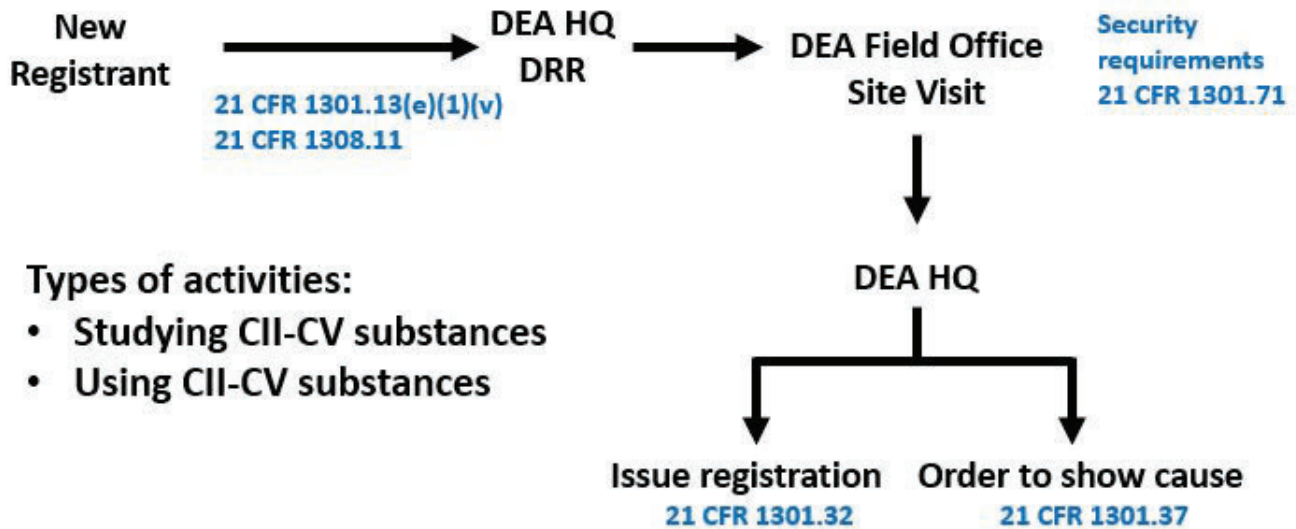
A schedule I researcher may, as a coincidental activity to their researcher registration:

- Manufacture or import the basic class of controlled substance for which registration was issued, provided that such manufacture or import is set forth in the protocol required in [21 CFR 1301.18](#)
- Distribute the basic class of controlled substance for which registration was issued to persons registered or authorized to conduct research with such class of substance or registered or authorized to conduct chemical analysis with controlled substances.

\* The manufacture or import of controlled substances authorized by this coincident activity must be for research purposes.

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## Schedule II-V Researchers



## Schedule II-V Research Protocols

Schedule II-V researchers are not required to report drug codes or submit a research protocol with their application. The local DEA Field Office may conduct an on-site inspection prior to approving the new application for registration. DEA can require an applicant to submit additional documents or written statements of fact relevant to the application as DEA deems necessary to determine whether the application should be granted. [21 CFR 1301.15](#).

## Authorized Coincident Activities (for Schedule II-V Researchers) [21 CFR 1301.13 \(e\)\(1\)\(vi\)](#)

Schedule II-V researchers may conduct the following coincident activities with their DEA schedule II-V researcher registration, i.e., they may conduct these activities without having to obtain a separate DEA registration as an analytical lab, manufacturer, importer, etc.:

- Conduct chemical analysis with controlled substances in those schedules for which registration was issued;
- Manufacture controlled substances if and to the extent that such manufacture is set forth in a manufacturing statement filed with the researcher's registration application, provided that the manufacture is not for purposes of dosage form development;
- Import controlled substances in those schedules for which registration was issued for research purposes;

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- Distribute controlled substances in those schedules for which registration was issued to persons registered or authorized to conduct chemical analysis, instructional activities, or research with such substances, and to persons exempted from registration pursuant to [21 CFR 1301.24](#) such as law enforcement; and
- Conduct instructional activities with controlled substances.

Note: The manufacture or import of controlled substances authorized by this coincident activity must be for research purposes.

### Manufacturing Statement

A schedule II-V researcher can obtain authorization to manufacture small amounts of bulk controlled substances by submitting with their registration application a manufacturing statement which includes:

- The Administration Controlled Substances Code Number, as set forth in [21 CFR part 1308](#), for each basic class to be manufactured as a coincident activity of that registration;
- The quantities of controlled substances the researcher intends to manufacture;
- A description of the purpose for manufacturing these controlled substances (e.g., to develop synthesis procedures or other research not related to dosage form development); and
- The purpose for which these manufactured controlled substances will be distributed to other persons registered to conduct chemical analysis, instructional activities or research, and the quantities of controlled substances distributed. [21 CFR 1301.13\(h\)](#).

### Research vs. Manufacturing

The exemption from separate registrations for certain research coincident activities is intended to facilitate research by allowing for the limited manufacture of controlled substances for those activities related directly to research set forth in the manufacture statement filed with the application for researcher registration.

However, once the manufacture of controlled substances for research moves beyond the scope of research and becomes product development (as described in the Clarification of Coincident Activities for Researchers Policy Statement, [60 FR 55310](#), (October 31, 1995)), those activities are no longer considered to be coincident research activities, but rather manufacturing activities, permissible only under a manufacturer registration. Any person seeking to manufacture controlled substances for such purposes must meet the primary requirements for registration as a manufacturer as set forth in [21 U.S.C. 823](#).

Some examples of manufacturing activities that are **not** considered research and can only be conducted under a DEA manufacturer registration include the following:

- Satisfying FDA requirements or good manufacturing practices;
- Production of material used for pilot, scale-up, and reformulation studies; or

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- Product development including bioavailability, dosage formulation, stability, and validation studies.

DEA cannot predict when an individual's activities may shift from researcher to manufacturer. Therefore, it is imperative that a person who is conducting research, whose activities move from bench type to scale-up and development, be aware and alert for the requirements of [21 CFR 1301.13](#). For questions or guidance on this area, contact your local DEA office for specific clarification.

### Renewal of Registration

A researcher's registration must be renewed annually using the DEA Form 225a (Renewal Application for DEA Registration). [21 CFR 1301.13\(e\)\(1\)\(v\), \(vi\)](#). The most expeditious method to renew a DEA registration is online, but it can be completed by paper application no earlier than 60 days prior to the current expiration date. [21 CFR 1301.13\(b\)](#). The information from the existing DEA Form 223 is needed to login to initiate the renewal process. The application fee is indicated on the application.

Registrants will begin to receive renewal notifications approximately 60 days prior to the registration expiration date. [21 CFR 1301.13\(e\)\(3\)](#). DEA no longer sends renewal notifications by U.S. Postal Service. Instead, an electronic reminder to renew will be sent at 60, 45, 30, 15, and 5 days prior to the expiration date of the registration to the associated email address. All registrants should ensure that the email address listed on their registration is correct and active. See [Registration](#) (usdoj.gov) for more information. Researchers can request a paper DEA Form 225a, via email to [DEA.Registration.Help@dea.gov](mailto:DEA.Registration.Help@dea.gov) or call 1-800-882-9539.

The completed renewal application should be mailed to the following address:

Drug Enforcement Administration  
Diversion Control Division  
Attn: Registration & Program Support Section/DRR  
P.O. Box 2639  
Springfield, VA 22152-2639

For additional information or questions, contact DEA's Registration Section at 1-800-882-9539 or [DEA.Registration.Help@dea.gov](mailto:DEA.Registration.Help@dea.gov).

### Schedule I Research Registration Renewals

Schedule I researchers should renew their registration online at [DEAdiversion.usdoj.gov](https://DEAdiversion.usdoj.gov).

When submitting a renewal application for a "Schedule I Researcher" registration, researchers must certify with a signed and dated statement that there are no changes to their approved research protocol, drug codes, or amount of controlled substances listed on the registration renewal application.

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If the researcher intends to change a previously approved protocol in their renewal application, the researcher must submit a supplemental protocol online at [DEAdiversion.usdoj.gov](https://DEAdiversion.usdoj.gov). Click on "Registration" at the top of the home page, then click on "Make Changes to my DEA Registration." The supplemental protocol can also be emailed to [DPEScheduleIResearch@dea.gov](mailto:DPEScheduleIResearch@dea.gov) or can be mailed to DEA via registered mail, return receipt requested, to:

Drug Enforcement Administration  
Attn: Drug and Chemical Evaluation Section (DPE)  
Schedule I Research Coordinator  
8701 Morrissette Drive  
Springfield, VA 22152-2639

### Modification of Registration

A researcher may apply to modify a DEA registration at any time. Modifications can include change of business and/or mailing address, name change, addition of new drug codes, or change of drug schedules. There is no fee for a modification of registration. Modifications are handled in the same manner as applications and must be approved by DEA. [21 CFR 1301.51\(a\)](#). Request a [modification of registration](#) on DEA's website or contact the local [DEA Registration Specialist](#). If the modification is approved, DEA issues a new Certificate of Registration and, if requested, new schedule I and II order forms (DEA Form 222). A researcher should maintain the new certificate with the old certificate until expiration.

### Change of Business Address

Every registrant under [21 U.S.C. 801-904](#) shall be required to report any change of professional or business address in accordance with DEA regulations. [21 U.S.C. 827\(h\)](#). A researcher that moves to a new physical location must first request a modification of registration. The request must contain the registrant's name, address, and registration number as printed on the Certificate of Registration; the new name or address; and a signature in accordance with [21 CFR 1301.13\(j\)](#). If the registrant's change of address involves changing the registrant's state, then the registrant must first provide the proper state-issued license in that new state and, if applicable, the proper state-issued controlled substances registration in that new state, prior to DEA's approval of any modification of the federal registration. [21 U.S.C. 823\(f\)](#). If the modification is approved, DEA issues an updated Certificate of Registration and, if requested, new schedule II order forms (DEA Form 222). The registrant should maintain the new certificate with the old certificate until expiration. A Renewal Application for Registration (DEA Form 225a) will only be sent to the registrant's mailing address on file with DEA. It will not be forwarded.

### Termination of Registration

A researcher's registration shall terminate, without any further action by DEA, if and when a researcher dies, if a business ceases legal existence, if a researcher discontinues business or professional practice, or when a researcher surrenders a DEA registration. [21 CFR 1301.52\(a\)](#).

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If a researcher discontinues business activities either completely or only regarding controlled substances, the researcher must promptly notify the local [Special Agent in Charge](#) and seek authority and instructions to dispose of any controlled substances obtained under the authority of that registration. A researcher that discontinues business must return their DEA registration certificate to the local DEA Registration Program Specialist ([Appendix F](#)). [21 CFR 1301.52\(c\)](#).

In the event a state board revokes a researcher's license or registration, DEA will request a voluntary surrender of that DEA registration. If a researcher surrenders their DEA registration for cause, it shall be terminated when a duly executed DEA Form 104, Voluntary Surrender of Controlled Substances Privileges, or any signed writing indicating a desire to surrender a registration is received by any DEA employee. [21 CFR 1301.52\(a\)](#). If a researcher refuses to surrender their registration, DEA will pursue administrative action to revoke the DEA registration based on lack of state authorization. DEA may also pursue civil or criminal sanctions if there is sufficient evidence to justify a prosecution. All such actions are designed to protect the public health and safety.

Unwanted controlled substances in the researcher's possession must be disposed of in accordance with DEA regulations (See [Section VIII, Disposal of Controlled Substances](#)).

### Denial, Suspension, or Revocation of Registration

Under [21 U.S.C. 824\(a\)](#), DEA has the authority to deny, suspend, or revoke a DEA registration upon a finding that a researcher has done any of the following:

1. Materially falsified the application.
2. Been convicted of a felony relating to a controlled substance or a List I chemical.
3. Had a state license or registration suspended, revoked, or denied by a competent state authority and is no longer authorized by state law to engage in the manufacturing, distribution, or dispensing of controlled substances or List I chemicals, or has had a suspension, revocation, or denial of a registration recommended by a competent state authority.
4. Committed an act which would render the DEA registration inconsistent with the public interest.
5. Been excluded (or directed to be excluded) from participation in a Medicare or state health care program.

### Denial of Registration in the Public Interest

In determining the public interest, [21 U.S.C. 823\(f\)](#) provides that the following factors are to be considered:

1. The recommendation of the appropriate state licensing board or professional disciplinary authority.
2. A researcher's experience in dispensing or conducting research with respect to controlled substances.
3. A researcher's conviction record under federal or state laws relating to the manufacture, distribution, or dispensing of controlled substances.
4. Compliance with applicable state, federal, or local laws relating to controlled substances.



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5. Such other conduct which may threaten the public health and safety.

## SECTION IV - ORDERING CONTROLLED SUBSTANCES

On September 30, 2019, DEA issued a final rule entitled *New Single-Sheet Format for U.S. Official Order Form for Schedule I and II Controlled Substances (DEA Form 222)*, which implemented a single-sheet format for DEA Form 222, used by DEA registrants to order schedule I and II controlled substances. [84 FR 51368](#). The rule became effective on October 30, 2019.

### Ordering Schedule I and II Controlled Substances

Only schedule I and II controlled substances are ordered with an official paper order form, [DEA Form 222](#), or the electronic equivalent (See below, [Controlled Substance Ordering System \(CSOS\) - Electronic Order Forms](#)). A DEA Form 222 is required for each distribution or transfer of a schedule I or schedule II controlled substance unless exempted. [21 CFR 1305.03](#), [1307.11\(a\)\(1\)\(iii\)](#), [1301.52\(e\)\(1\)](#).

When a controlled substance has been moved by DEA from schedule I or schedule II to another schedule at the federal level, in many states it may remain a schedule I or schedule II controlled substance pending any legislative or administrative action that may result from the federal action. States may require transactions that involve substances they classify as schedule I or schedule II to be made via DEA Form 222 or the electronic equivalent.

### Requesting DEA Forms 222

DEA Forms 222 are issued in mailing envelopes containing a predetermined number of forms based on the business activity of the registrant, each form consisting of a single sheet. A limit, which is based on the business activity of the registrant, is imposed on the number of DEA Forms 222 that are furnished upon a requisition for order forms unless additional forms are specifically requested and a reasonable need for such additional forms is shown. [21 CFR 1305.11\(a\)](#).

Unexecuted DEA Forms 222 can be requested initially by checking the block in "Section 3" on the DEA Form 225, which can be found [online](#).

Any person with an active registration that is authorized to order schedule I and II controlled substances is entitled to obtain a DEA Form 222, which will be supplied at any time after the DEA registration is granted. Any person holding a registration authorizing the person to obtain a DEA Form 222 can requisition the forms through a [DEA secured network](#) connection or by contacting either a local [DEA Diversion Field Office](#) or the [Registration Section](#) of the Administration through the customer service center. [21 CFR 1305.11\(b\)](#).

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DEA Forms 222 have an order form number and are issued with the name, address, and registration number of the registrant, the authorized activity, and schedules of the registrant. This information cannot be altered or changed by the registrant; the registrant must report any errors to the local [DEA Diversion Field Office](#) or the Registration Section of the Administration to modify the registration. [21 CFR 1305.11\(d\)](#).

## Completing DEA Forms 222

A purchaser must prepare and execute a DEA Form 222 by use of a typewriter, computer printer, pen, or indelible pencil. [21 CFR 1305.12\(a\)](#). Only one item can be entered on each numbered line. An item must consist of one or more commercial or bulk containers of the same finished or bulk form and quantity of the same substance. The number of lines completed must be noted on that form at the bottom of the form, in the space provided. [21 CFR 1305.12\(b\)](#). The purchaser should record the name and address from whom the controlled substances were ordered on the form. [21 CFR 1305.12\(c\)](#). If the purchaser does not have this information then the supplier should ensure it is on the form.

The purchaser must make a copy of the original DEA Form 222 for its records and then submit the original to the supplier. [21 CFR 1305.13\(a\)](#). The purchaser does not have the option of retaining the original. The copy retained by the purchaser may be in paper or electronic form. [21 CFR 1305.13\(a\)](#).

Each DEA Form 222 must be signed and dated by a person authorized to sign a registration application or a person granted power of attorney. (See below, [Power of Attorney to Sign an Official Order Form](#).) [21 CFR 1305.12\(d\)](#). When the items are received, the purchaser must document on the purchaser's copy the actual number of commercial or bulk containers received and the date received. [21 CFR 1305.13\(e\)](#).

The purchaser must retain a copy of each executed DEA Form 222 and all copies of unaccepted or defective forms with each statement attached. [21 CFR 1305.17\(a\)](#). The supplier must retain the original DEA Form 222 for the supplier's files in accordance with [21 CFR 1305.17\(b\)](#). Any supplier who is not required to report acquisition/disposition transactions to the Automation of Reports and Consolidated Orders System (ARCOS) under [21 CFR 1304.33\(c\)](#) (such as a practitioner) must make and submit a copy of the original DEA Form 222 to DEA, either by mail to the Registration Section, or by email to [DEA.Orderforms@usdoj.gov](mailto:DEA.Orderforms@usdoj.gov). [21 CFR 1305.13\(d\)](#). The copy must be forwarded at the close of the month during which the order is filled. If an order is filled by partial shipments, the copy must be forwarded at the close of the month during which the final shipment is made or the 60-day validity period expires. [21 CFR 1305.13\(d\)](#).

DEA Forms 222 must be maintained separately from all other records of the registrant. [21 CFR 1305.17\(c\)](#). DEA Forms 222 are required to be kept available for inspection for a period of two years. [21 CFR 1305.17\(c\)](#). If a purchaser has several registered locations, the purchaser must retain a copy of the executed DEA Form 222 and any attached statements or other related documents (not including unexecuted DEA Forms 222, which may be kept elsewhere under [21 CFR 1305.12\(e\)](#)), at the registered location printed on the DEA Form 222. [21 CFR 1305.17\(c\)](#).

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Electronic copies of DEA Forms 222 do not need to be stored on a different server or electronic system from a registrant's other records. The requirement to store DEA Forms 222 separately from all other records may be met, for electronic copies, by storing them in such a way that they can be readily retrieved separately from all other records. [21 CFR 1305.17\(e\)](#). Electronic copies of DEA Forms 222 may be stored on a system at a location different from the registered location, provided such copies are readily retrievable at the registered location. [21 CFR 1305.17\(e\)](#). Purchasers must be able, during an inspection or upon other DEA requests, to readily retrieve their electronic copies of DEA Forms 222, with any related statements or other documents, and without any other records.

Under [21 CFR 1305.15\(a\)\(1\)](#), an order must not be filled if the DEA Form 222 is not complete, legible, or properly prepared, executed, or endorsed, or if the DEA Form 222 shows any alteration, erasure, or change of any description. For a discussion of the circumstances in which an electronic order must not be filled, see below, [CSOS - Electronic Order Forms](#).

If a DEA Form 222 cannot be filled for any reason, the supplier must return the original DEA Form 222 to the purchaser with a statement explaining the reason the order could not be filled (e.g., illegible or altered). [21 CFR 1305.15\(b\)](#). A supplier may refuse to accept an order for any reason. [21 CFR 1305.15\(c\)](#). If a supplier refuses to accept an order, a statement that the order is not accepted is sufficient. [21 CFR 1305.15\(c\)](#). For electronic orders, if the order cannot be filled, the supplier must notify the purchaser and provide a statement as to the reason; if the order is refused, a statement that the order is not accepted is sufficient (See below, [CSOS - Electronic Order Forms](#)). [21 CFR 1305.25\(b\)](#).

### Power of Attorney to Sign DEA Forms 222

Any registrant (researcher) may authorize one or more individuals, whether or not they are located at the registered location, to obtain and execute DEA Forms 222 by granting a power of attorney to each such individual. [21 CFR 1305.05\(a\)](#). Pursuant to [21 CFR 1305.05\(d\)](#), the power of attorney must be signed by:

1. The registrant, if an individual; a partner of the registrant, if a partnership; or an officer of the registrant, if a corporation, corporate division, association, trust or other entity;
2. The person to whom the power of attorney is being granted; and
3. Two witnesses.

A power of attorney executed under this section may be signed electronically, by any or all of the persons required to sign. [21 CFR 1305.05\(f\)](#).

The power of attorney may be revoked at any time by the person who signed the most recent application for DEA registration or reregistration and two witnesses. [21 CFR 1305.05\(e\)](#). Only if the renewal application is signed by a different person is it necessary to grant a new power of attorney when the pharmacy completes a renewal registration. The power of attorney should be filed with

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executed DEA Forms 222 if applicable, and must be available for inspection. [21 CFR 1305.05\(a\)](#).  
The power of attorney is not submitted to DEA.

**Suggested formats for granting and revoking a power of attorney follow:**

Forms granting or revoking a power of attorney must be similar to the following formats. [21 CFR 1305.05\(c\)](#).

Power of Attorney for DEA Forms 222 and Electronic Orders

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

(Name of registrant)  
(Address of registrant)  
(DEA registration number)

I, \_\_\_\_\_(name of person granting power), the undersigned, who am authorized to sign the current application for registration of the above named registrant under the Controlled Substances Act or Controlled Substances Import and Export Act, have made, constituted, and appointed, and by these presents, do make, constitute, and appoint \_\_\_\_\_(name of attorney-in-fact), my true and lawful attorney for me in my name, place, and stead, to execute applications for books of official order forms and to sign such order forms in requisition for schedule II controlled substances, in accordance with 21 U.S.C. 828 and part 1305 of Title 21 of the Code of Federal Regulations. I hereby ratify and confirm all that said attorney shall lawfully do or cause to be done by virtue hereof.

\_\_\_\_\_  
(Signature of person granting power)

I, \_\_\_\_\_(name of attorney-in-fact), hereby affirm that I am the person named herein as attorney-in-fact and that the signature affixed hereto is my signature.

\_\_\_\_\_  
(Signature of attorney-in-fact)

Witnesses:

1. \_\_\_\_\_
2. \_\_\_\_\_

Signed and dated on the \_\_\_\_ day of \_\_\_\_\_ in the year \_\_\_\_ at \_\_\_\_\_.

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Notice of Revocation

The foregoing power of attorney is hereby revoked by the undersigned, who is authorized to sign the current application for registration of the above-named registrant under the Controlled Substances Act. Written notice of this revocation has been given to the attorney-in-fact \_\_\_\_\_ this same day.

\_\_\_\_\_  
(Signature of person revoking power)

Witnesses:

1. \_\_\_\_\_
2. \_\_\_\_\_

Signed and dated on the \_\_\_\_ day of \_\_\_\_\_ in the year \_\_\_\_ at \_\_\_\_\_.

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### Cancellation and Voiding DEA Forms 222

A purchaser may cancel part or all of an order on a DEA Form 222 by notifying the supplier in writing of the cancellation. [21 CFR 1305.19\(a\)](#). The supplier must indicate the cancellation on the original DEA Form 222 sent by the purchaser by drawing a line through the canceled items and printing "canceled" in the space provided for the number of items shipped. [21 CFR 1305.19\(a\)](#).

A supplier may void part or all of an order on a DEA Form 222 by notifying the purchaser in writing of the voiding. [21 CFR 1305.19\(b\)](#). The supplier must indicate the voiding on the original DEA Form 222 sent by the purchaser by drawing a line through the canceled items and printing "voided" in the space provided for the number of items shipped. [21 CFR 1305.19\(b\)](#).

For information regarding canceled electronic orders, see below, [CSOS - Electronic Order Forms](#).

### Lost or Stolen DEA Forms 222

If a purchaser ascertains that an unfilled DEA Form 222 has been lost, the purchaser must execute another and attach a statement containing the order form number and date of the lost form, and stating that the goods covered by the first DEA Form 222 were not received through loss of that DEA Form 222. [21 CFR 1305.16\(a\)](#). A copy of the second form and a copy of the statement must be retained with a copy of the DEA Form 222 first executed. [21 CFR 1305.16\(a\)](#). A copy of the statement must be attached to a copy of the second DEA Form 222 sent to the supplier. [21 CFR 1305.16\(a\)](#). If the first DEA Form 222 is subsequently received by the supplier to whom it was directed, the supplier must mark upon the face "Not Accepted" and return the original DEA Form 222 to the purchaser, who must attach it to the statement. [21 CFR 1305.16\(a\)](#).

A researcher, upon discovery of the loss or theft of used or unused order forms, must immediately report the loss or theft to the local DEA Diversion Field Office ([Appendix F](#)) and provide the serial numbers of each lost or stolen order form. [21 CFR 1305.16\(b\)](#).

If any DEA Forms 222 are lost or stolen, and the purchaser is unable to provide the order form numbers of DEA Forms 222, the purchaser must report, in lieu of numbers of the forms, the date or approximate date of issuance. [21 CFR 1305.16\(d\)](#).

If an unused order form reported stolen or lost is later recovered or found, the researcher must immediately notify the local DEA Diversion Field Office ([Appendix F](#)). [21 CFR 1305.16\(e\)](#).

### Return of Unused DEA Forms 222

If the registration of any purchaser terminates (because the purchaser dies, ceases legal existence, discontinues business or professional practice, or changes the name or address as shown on the purchaser's registration) or is suspended or revoked under [21 CFR 1301.36](#) for all schedule I and II controlled substances for which the purchaser is registered, the purchaser must return all unused DEA Forms 222 to the Registration Section. [21 CFR 1305.18](#).

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### Controlled Substance Ordering System (CSOS) - Electronic Order Forms

Any registrant permitted to order schedule I and II controlled substances may do so electronically via the DEA CSOS and maintain the records of these orders electronically for two years. [21 CFR 1311.10\(a\)&\(b\)](#). The use of electronic orders is optional; registrants may continue to issue orders on a paper DEA Form 222. CSOS allows for secure electronic transmission of controlled substance orders without the supporting paper DEA Form 222. The adoption of the CSOS standards is the only allowance for the electronic transmission of schedule II controlled substance orders between controlled substance manufacturers, distributors, researchers, and other DEA authorized entities. CSOS uses Public Key Infrastructure (PKI) technology, which requires CSOS users to obtain a CSOS digital certificate for electronic ordering. The electronic orders must be signed using a digital signature issued by the Certification Authority (CA) run by DEA. [21 CFR 1305.21\(a\)](#).

Digital certificates can be obtained only by the person who signed the most recent DEA registration application or renewal application, a person authorized to sign a registration application, or a person granted power of attorney by a DEA registrant to sign orders for one or more schedules of controlled substances. [21 CFR 1311.10\(a\), \(b\)](#). A registrant must appoint a CSOS coordinator who will serve as that registrant's recognized agent regarding issues pertaining to issuance of, revocation of, and changes to, digital certificates issued under that registrant's DEA registration. [21 CFR 1311.20\(a\)](#). A CSOS digital certificate is valid until the DEA registration under which it is issued expires or until the CSOS CA is notified that the certificate should be revoked. [21 CFR 1311.30\(e\), 1311.40\(a\)](#). Certificates will be revoked if the certificate holder is no longer authorized to sign schedule II orders for the registrant, if the information on which the certificate is based changes, or if the digital certificate used to sign electronic orders has been compromised, stolen, or lost. [21 CFR 1311.30\(e\), 1311.40\(a\)](#).

A "Questions and Answers" page about the CSOS certificate is available on the DEA E-Commerce Program website at [www.DEAecom.gov](http://www.DEAecom.gov). Applicants can download the Diversion PKI CSOS Enrollment document and the CSOS Subscriber's Manual for assistance on the enrollment process. DEA maintains a support line to assist applicants and subscribers with issues pertaining to certificate enrollment, issuance, revocation, and renewal. Staff is available from 8:00 a.m. to 5:50 p.m. (Eastern Time), Monday through Friday at 1-877-332-3266 if further assistance is needed.

### Unaccepted and Defective Electronic Orders

Under [21 CFR 1305.25\(a\)](#), an electronic order for controlled substances may not be filled if any of the following occurs:

1. The required data fields have not been completed.
2. The order is not signed using a digital certificate issued by the DEA.
3. The digital certificate used has expired or been revoked prior to signature.
4. The purchaser's public key will not validate the digital certificate.

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5. The validation of the order shows that the order is invalid for any reason.

When a purchaser receives an unaccepted electronic order from the supplier, the purchaser must electronically link the statement of non-acceptance to the original order. The original statement and all linked records for that order must be retained for two years. [21 CFR 1305.25\(c\)](#), [1305.27\(a\)](#). Neither a purchaser nor a supplier may correct a defective order. The purchaser must issue a new order for the order to be filled. [21 CFR 1305.25\(d\)](#).

### Cancellation and Voiding of Electronic Orders

A supplier may void all (or part) of an electronic order by notifying the purchaser of the voiding. If the entire order is voided, the supplier must make an electronic copy of the order and indicate “void” on the copy and return it to the purchaser. The supplier is not required to retain a record of orders that are not filled. [21 CFR 1305.28\(a\)](#). The purchaser must retain an electronic copy of the voided order. [21 CFR 1305.28\(b\)](#). Should a supplier partially void an order, the supplier must indicate in the linked record that nothing was shipped for each item voided. [21 CFR 1305.28\(c\)](#).

### Lost Electronic Orders

If a purchaser determines that an unfilled electronic order has been lost before or after receipt, the purchaser must provide, to the supplier, a signed statement. This statement must include the unique tracking number and date of the lost order and state that the goods covered by the first order were not received through loss of that order. [21 CFR 1305.26\(a\)](#). If the purchaser executes a new order to replace the lost order, the purchaser must electronically link an electronic record of the second order and a copy of the statement with the record of the first order and retain them both. [21 CFR 1305.26\(b\)](#). If the supplier to whom the order was directed subsequently receives the first order, the supplier must indicate that it is “Not Accepted” and return it to the purchaser. The purchaser must link the returned order to the record of that order and the statement. [21 CFR 1305.26\(c\)](#).

### Clinical Trials Involving Schedules I-II Controlled Substances

Due to the unique nature of double-blind studies, including the impact on required recordkeeping and DEA's desire to avoid any confusion on behalf of the manufacturer or DEA registrants participating in these studies, DEA would like to reiterate the proper procedure for the use of DEA Form 222 in blind clinical studies where schedule I or II controlled substances may be involved. This guidance is not an exception to regulations, but an application of DEA's existing policy regarding blind clinical studies. Below is guidance for completing the DEA Form 222 in a double-blind clinical trial:

1. Each DEA registrant participating in this study submits the original paper copy of their DEA Form 222 to the controlled substance supplier and retains a copy (paper or electronic) for the registrant's records. The DEA Form 222 indicates the total quantity of each test material



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requested. Test materials may consist of active ingredient dosage units, placebo, or some combination thereof. The registrant will not know if the test materials received actually contain a controlled substance until the end of the study.

2. The controlled substance supplier must record its DEA registration number and the actual quantity of controlled substance(s) (active dosage units) distributed and the date on which the containers are shipped on each original DEA Form 222. [21 CFR 1305.13\(b\)](#). The supplier must retain each original DEA Form 222 separately from all other records in accordance with [21 CFR 1305.17\(c\)](#). ARCOS reporting suppliers are not required to provide DEA a copy of each filled original DEA Form 222.
3. The DEA registered researcher participating in this study physically receives their shipment and records the date of receipt, but they do not fill in the true name of the controlled substance received, or the amount of controlled substance received, on the retained copy of the original DEA Form 222 until after the completion of the blind clinical study. Upon completion of the study, the supplier notifies the registrant of the actual name and quantity of the controlled substance(s) involved, if any, that the supplier provided. The registrant then attaches documentation denoting the actual amount of each test material received to their retained copy of the original DEA Form 222, and records the name and quantity of each controlled substance received on their retained copy of the original DEA Form 222. The purchaser must record on its copy of the DEA Form 222 the actual amount of each test material received.

### Marihuana (Cannabis) Research

On December 20, 2018, the Agriculture Improvement Act of 2018 (2018 Farm Bill) was signed into law by the President of the United States. Pub. L. No. 115-334, 132 Stat. 4490, (2018). As enacted, the 2018 Farm Bill removes hemp from the CSA and defines it as "the plant *Cannabis sativa* L. and any part of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or not, with a delta-9-tetrahydrocannabinol (THC) concentration of not more than 0.3 percent on a dry weight basis." [21 U.S.C. 802\(16\)\(B\)](#), [7 U.S.C. 1639o\(1\)](#). Therefore, hemp, which meets this definition, is not regulated by DEA, and a DEA registration would not be required to conduct research with such material. However, any such product with a THC concentration of **more** than 0.3 percent on a dry weight basis is considered to be marihuana, a schedule I controlled substance under federal law, and all federal controlled substance laws and regulations would apply, including the requirement to be registered with DEA to conduct research with any such material. [21 U.S.C. 802\(16\)\(A\)-\(B\)](#).

On December 18, 2020, DEA published a final rule in the FR titled "Controls to Enhance the Cultivation of Marihuana for Research in the United States" to (1) facilitate the cultivation of marihuana for research and licit purposes in compliance with the CSA, including a provision requiring consistency with the 1961 Single Convention on Narcotic Drugs (Single Convention); (2) amend DEA regulations pertaining to applications by persons seeking to become registered with DEA to grow marihuana as bulk manufacturers; and (3) establish regulations related to the purchase and sale of this marihuana by DEA. [85 FR 82333](#). The purpose of the final rule is to increase the number and variety of marihuana growers in order to diversify the supply available to researchers. The final rule became effective on January 19, 2021. For clarification, the Single Convention used the terms

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“cannabis,” “cannabis plant,” and “cannabis resin”—all of which are generally encompassed by the CSA definitions of “marihuana” in [21 U.S.C. 802\(16\)](#). Therefore, for purposes of this manual, the terms “cannabis” and “marihuana” are interchangeable.

As of January 19, 2021, the effective date of the final rule, and in compliance with the CSA and the Single Convention, DEA has the exclusive right of importing, exporting, wholesale trading, and maintaining cannabis stocks other than those held by registered manufacturers of medicinal cannabis or cannabis preparations. “Medicinal cannabis” means a drug product made from the cannabis plant, or derivatives thereof that can be legally marketed under the Federal Food, Drug, and Cosmetic Act. However, such term does not include any material, compound, mixture, or preparation that falls outside the CSA definition of marihuana. “Cannabis preparation” means cannabis that was delivered to DEA and subsequently converted by a registered manufacturer into a mixture (solid or liquid) containing cannabis, cannabis resin, or extracts of cannabis. However, such term does not include any material, compound, mixture, or preparation that falls outside the CSA definition of marihuana.

Over the last several decades, the National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health (NIH), has administered a contract to produce high quality marihuana for use by researchers who had obtained federal funding (grants) for such research. This contract was awarded to the National Center for Natural Products Research at the University of Mississippi (National Center). The National Center was the sole DEA registrant in the United States authorized to grow marihuana for the purposes of supplying researchers. The National Center was authorized to grow marihuana up to the limit established by their DEA-issued quota. At the time of harvest, some of the material was held in inventory at the National Center, while some of it was distributed to another DEA registrant, Research Triangle Institute (RTI). At the direction of NIDA, via NIDA's Drug Supply Program (DSP), the National Center and RTI prepared marihuana in a manner suitable for research studies and then shipped it to researchers. Marihuana held in inventory at the National Center was the property of NIDA.

The final rule has instituted changes to the scheme described above. Although NIDA can and will continue to administer the contract in support of its DSP, and the National Center (or other NIDA contract holder) can continue to grow and produce marihuana in support of research pursuant to that contract, the marihuana grown at the National Center will not be the property of NIDA, as was previously the case, rather, DEA takes title and possession of the crop, and the material is maintained, under seal, at the National Center until such time distribution to another DEA registrant is authorized.

Under the new regulations contained within the final rule, there are changes related to the availability of cannabis for research and to DEA's role in all transactions involving cannabis, to comply with DEA's statutory and treaty obligations. As previously stated, effective January 19, 2021, DEA has the exclusive right of importing, exporting, wholesale trading, and maintaining stocks of cannabis, other than those held by registered manufacturers and distributors of medicinal cannabis or cannabis preparations.

DEA reviews pending bulk manufacturers of marihuana with the goal of approving multiple bulk manufacturers so as to increase the number and variety of cannabis growers in order to diversify the

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supply available to researchers. The number of manufacturers approved by DEA is limited, as required by the CSA, to the number necessary to produce an adequate and uninterrupted supply under adequately competitive conditions. [21 U.S.C. 823\(a\)\(1\)](#). All registered manufacturers who cultivate cannabis are required to transfer ownership of their total crops of cannabis to DEA. DEA purchases the cannabis grown by DEA-registered manufacturers and subsequently sells the marijuana to DEA registrants who seek to acquire it for research, product development, or other lawful purposes under the CSA.

Although DEA takes title to the cannabis from DEA registered manufacturers, and sells it to researchers, the price of the cannabis is negotiated between the grower and the purchaser. In addition to the negotiated price, DEA includes an administrative fee (per kilogram) which is added on to the sales price of the marijuana it sells to researchers. The purpose of the administrative fee is to ensure the full recovery by DEA of the costs of administering the program as required by law. [21 U.S.C. 886a\(1\)\(C\)](#). The administrative fee is adjusted annually and is posted on the Diversion Control Division website no later than December 15<sup>th</sup> preceding the year in which the administrative fee is collected. Under the final rule, the administrative fee is considered part of the price of the cannabis DEA sells to the purchasing researcher. However, the rule requires the “parties” to pay the fee to DEA upon entering into a contract for the provision of cannabis, but before the cannabis is actually delivered to the researcher. In other words, DEA is not charging the administrative fee to either party in particular, but to the parties jointly as part of the transaction. The parties are free to apportion the fee among themselves in any way they choose. Additionally, nothing in the final rule prohibits the National Institutes of Health, or any other third-party funder of research grants, from funding marijuana research by covering the cost of marijuana materials used in research, including the administrative fees, via grants to researchers. Additional information on the marijuana growers program, to include a list of approved growers, can be found on our website at [Marijuana Growers Information \(usdoj.gov\)](#).

### Impact of the final rule on marijuana researchers

DEA anticipates minimal procedural change for authorized researchers who plan to acquire bulk marijuana for research. The only anticipated procedural change is that some researchers will acquire the bulk marijuana from DEA, rather than from NIDA. Also, as discussed above, the purchaser of marijuana from DEA includes an administrative fee, in addition to the negotiated price of the marijuana. It should be noted that while the purchaser of marijuana purchases marijuana from DEA, the final rule does not in any way affect the purchaser's source of funds to purchase from DEA. If marijuana for research is funded by a third party, the researcher may not experience any cost increase. In particular, NIH has long served as a third-party funder for research through grants to researchers studying marijuana. Nothing in the final rule prohibits NIH from continuing to fund such research by continuing to cover the cost of marijuana research materials via grants to researchers. Researchers may obtain marijuana for use in research through NIDA's DSP. Bulk marijuana plant material produced under the NIDA DSP is available at no cost to research investigators who are supported by an NIH grant. Marijuana is also available to research investigators who are funded through non-federal sources.

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## Ordering Schedules III-V Controlled Substances

The researcher must keep a receipt (invoice or packing slip) on which it records the date the drugs were received and confirm that the order is accurate. [21 CFR 1304.21\(a\), \(d\)](#). Pursuant to [21 CFR 1304.22\(a\)\(2\) and \(c\)](#), such receipts must also contain the following information:

1. The name of the substance;
2. Each finished form (e.g., 10-milligram tablet or 10-milligram concentration per fluid ounce or milliliter) and the number of units or volume of finished form in each commercial container (e.g., 100-tablet bottle or 3-milliliter vial);
3. The number of units of finished forms and/or commercial containers acquired from other persons, including the date of and number of units and/or commercial containers in each acquisition to inventory and the name, address, and registration number of the person from whom the units were acquired;
4. The number of commercial containers distributed to other persons, including the date of and number of containers in each reduction from inventory, and the name, address, and registration number of the person to whom the containers were distributed; and
5. The number of units of finished forms and/or commercial containers distributed or disposed of in any other manner by the registrant (e.g., by distribution of complimentary samples or by destruction), including the date and manner of distribution or disposal, the name, address, and registration number of the person to whom distributed, and the quantity in finished form distributed or disposed.

In addition, these receipts must be maintained either separately from all other records of the registrant or in such form that the information required is readily retrievable from the ordinary business records of the registrant. [21 CFR 1304.04\(f\)\(2\)](#).

## SECTION V - RECORDKEEPING REQUIREMENTS

Researchers must maintain complete and accurate records on a current basis for each controlled substance manufactured, imported, purchased, received, stored, delivered, distributed, dispensed, or otherwise disposed of. [21 CFR 1304.21\(a\)](#). These records are required to provide accountability of all controlled substances to help reduce the potential for diversion.

DEA requires that all records concerning controlled substances be maintained for at least two years, in a readily retrievable manner, for inspection and copying by duly authorized DEA officials. [21 CFR 1304.04\(a\), 1316.02\(c\), 21 U.S.C. 827\(b\)](#).

Pursuant to [21 CFR. 1300.01\(b\)](#), readily retrievable is defined as:

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1. Records kept by automatic data processing systems or other electronic or mechanized recordkeeping systems in such a manner that they can be separated out from all other records in a reasonable time, and/or
2. Records kept in such a manner that certain items are asterisked, redlined, or in some other manner visually identifiable apart from other items appearing on the records.

### Required Records

The controlled substance records researchers must maintain are:

- Executed official order forms (DEA Form 222) or the electronic equivalent.
- Unexecuted official order forms (DEA Form 222).
- Power of Attorney authorization to sign order forms, if applicable.
- Receipts and/or invoices for schedules III, IV, and V controlled substances.
- Records of controlled substances distributed (i.e., sales to other registrants, returns to vendors, distributions to reverse distributors).
- Records of dispensing (dispensing log).
- All inventory records of controlled substances, including the initial and biennial inventories, dated as of beginning or close of business.
- Reports of Theft or Significant Loss (DEA Form 106), if applicable.
- Inventory of Drugs Surrendered for Disposal (DEA Form 41), if applicable. [21 CFR 1304.22\(c\)](#).

The required records must contain the information listed below for each controlled substance:

1. The name of the substance;
2. Each finished form (e.g., 10-milligram tablet or 10-milligram concentration per fluid ounce or milliliter) and the number of units or volume of finished form in each commercial container (e.g., 100-tablet bottle or 3-milliliter vial).
3. The number of units of finished forms and/or commercial containers acquired from other persons, including the date of and number of units and/or commercial containers in each acquisition to inventory and the name, address, and registration number of the supplier.
4. The number of commercial containers distributed to other persons, including the date of and number of containers in each reduction from inventory, and the name, address, and registration number of the person to whom the containers were distributed.
5. The number of units of finished forms and/or commercial containers distributed or disposed of in any other manner by the researcher, including the date and manner of distribution or disposal, the name, address, and registration number of the person to whom distributed, and the quantity in finished form distributed or disposed.
6. In addition, dispensers using a dispensing log must record the number of units or volume of such finished form dispensed, including the name and address of the person to whom it was

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dispensed, the date of dispensing, the number of units or volume dispensed, and the written or typewritten name or initials of the individual who dispensed or administered the substance on behalf of the dispenser. [21 CFR 1304.22\(c\)](#).

## SECTION VI - INVENTORY REQUIREMENTS

An "inventory" is a complete and accurate list of all stocks and forms of controlled substances in the possession of the registrant as determined by an actual physical count for schedule I-V controlled substances. The CSA requires that all inventory records be maintained at the registered location for at least two years for copying and inspection. [21 CFR 1304.04\(a\)](#), [21 U.S.C. 827\(b\)](#). In addition, the inventory records of schedule I and II controlled substances must be kept separate from all other records of the researcher. [21 CFR. 1304.04\(g\)](#). The inventory records of schedules III, IV, and V controlled substances shall be maintained either separately from all other records of the researcher or in such form that the information required is readily retrievable from ordinary business records of the researcher. [21 CFR 1304.04\(g\)](#).

### Initial Inventory

When issued a DEA registration, a registrant must take an initial inventory, which is an actual physical count of all controlled substances in their possession. [21 U.S.C. 827\(a\)\(1\)](#); [21 CFR 1304.11\(b\)](#). In the event there are no stocks of controlled substances on hand, when the registrant commences business, the registrant should make a record showing a zero inventory. [21 CFR 1304.11\(b\)](#). There is no requirement to submit a copy of the inventory to DEA. Pursuant to [21 CFR 1304.11\(a\)](#), [\(b\)](#) and [\(e\)\(6\)](#), the inventory shall include:

1. The date of the inventory.
2. Whether the inventory was taken at the beginning or close of business.
3. The name of each controlled substance inventoried.
4. The finished form of each of the substances (e.g., 10 milligram tablet).
5. The number of dosage units or volume of each finished form in the commercial container (e.g., 100 tablet bottle or 3 milliliter vial).
6. The number of commercial containers of each finished form (e.g., four 100 tablet bottles).
7. The total count of the substance.
8. For damaged, defective or impure substances awaiting disposal, substances held for quality control purposes, or substances maintained for extemporaneous compounding, the inventories shall include the name of the substance, the total quantity of the substance to the nearest metric unit weight or the total number of units of finished form, and the reason for the

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substance being maintained by the registrant and whether such substance is capable of use in the manufacture of any controlled substance in finished form.

DEA recommends, but does not require, an inventory record that includes the name, address, and DEA registration number of the registrant, and the signature of the person or persons responsible for taking the inventory.

### Biennial Inventory

After the initial inventory, the registrant is required to take a new inventory at least every two years, which requires the same information as the initial inventory (see list above) of all controlled substances on hand. [21 CFR 1304.11\(c\)](#). There is no requirement to submit a copy of the inventory to DEA.

### Newly Scheduled Controlled Substance Inventory

When a drug not previously listed as a controlled substance is scheduled, the drug must be inventoried as of the effective date of scheduling, if possessed by the registrant. [21 CFR 1304.11\(d\)](#).

### Inventory for Damaged, Defective, Impure, and Other Substances

For damaged, defective, or impure substances awaiting disposal, substances held for quality control purposes, or substances maintained for extemporaneous compounding, the inventories, pursuant to [21 CFR 1304.11\(e\)\(1\)\(iv\)](#), shall include:

1. The name of the substance.
2. The total quantity of the substance to the nearest metric unit weight or the total number of units of finished form.
3. The reason for the substance being maintained by the registrant and whether such substance is capable of use in the manufacture of any controlled substance in finished form.

## SECTION VII - SECURITY

### Storage of Controlled Substances

Researchers shall store schedules I-V controlled substances in a securely locked, substantially constructed cabinet. [21 CFR 1301.75\(a\), \(b\)](#).

Note: Researchers can contact their local DEA Field Office with questions regarding proposed controlled substance storage receptacles. A researcher's local DEA office may conduct an on-site

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inspection as part of the registration approval process. If a controlled substance storage receptacle does not meet the security standards listed above, it may delay the processing new applications.

**Controlled Substance Theft or Significant Loss**

A researcher must notify the local DEA Diversion Field Office ([Appendix F](#)) in writing within one business day of the discovery of a theft or significant loss of any controlled substance. [21 CFR 1301.76\(b\)](#). The researcher should also complete the following steps:

A. Notify DEA and Local Police

The theft of controlled substances from a registrant is a criminal act and a source of diversion that requires notification to DEA. A researcher must notify the local DEA Diversion Field Office ([Appendix F](#)) in writing within one business day of discovery of a theft or significant loss of a controlled substance. [21 CFR 1301.76\(b\)](#). Although not specifically required by federal law or regulations, the registrant should also notify local law enforcement and state regulatory agencies. Prompt notification to law enforcement agencies will allow them to investigate the incident and prosecute those responsible for the diversion. If there is a question as to whether a theft has occurred or a loss is significant, a registrant should err on the side of caution and report it to DEA and local law enforcement authorities. (See below, D. Registrant's Responsibility for Identifying "Significant Loss".)

DEA must be notified directly. This requirement is not satisfied by reporting the theft or significant loss in any other manner. For example, a corporation which owns or operates multiple registered sites, and wishes to channel all notifications through corporate management or any other internal department responsible for security, must still provide notice directly to the local DEA Diversion Field Office in writing within one business day of discovery and keep a copy of that notice for its records.

B. Complete a DEA Form 106

A researcher must also complete a [DEA Form 106](#) (Report of Theft or Loss of Controlled Substances) which can be found online at [www.DEAdiversion.usdoj.gov](http://www.DEAdiversion.usdoj.gov) under the Quick Links section. [21 CFR 1301.76\(b\)](#). The DEA Form 106 is used to document the actual circumstances of the theft or significant loss and the quantities of controlled substances involved. A paper version of the form can be obtained by writing to:

Drug Enforcement Administration  
Diversion Control Division  
Attn: Registration & Program Support Section/DRR  
P.O. Box 2639  
Springfield, VA 22152-2639



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If completing the paper version, the researcher should send the original DEA Form 106 to the local DEA Diversion Field Office ([Appendix F](#)) and keep a copy for its records. Please see the *Guidelines for Completing the DEA Form 106* ([Appendix B](#)) for additional guidance.

The DEA Form 106 must include the following information:

1. Name and address of the firm (researcher).
2. DEA registration number.
3. Date of theft or loss (or when discovered if not known).
4. Name and telephone number of local police department (if notified).
5. Type of theft (e.g., night break-in, armed robbery).
6. List of identifying marks or symbols (if any) used by the researcher on the labels of the containers.
7. A listing of controlled substances missing, including the strength, dosage form, and size of container (in milliliters if liquid form) or corresponding National Drug Code numbers.

### C. If Investigation Finds No Theft or Loss

If, after the initial notification to DEA, the investigation of the theft or loss determines no such theft or loss of controlled substances occurred, a DEA Form 106 does not need to be filed. However, for complete and accurate records, the registrant must notify DEA in writing of this fact in order to resolve the initial report and explain why no DEA Form 106 was filed regarding the incident. [21 CFR 1304.21\(a\)](#), [21 U.S.C. 827\(a\)\(3\)](#).

### D. Registrant's Responsibility for Identifying "Significant Loss"

Although the CSA and the regulations do not define the term "significant loss," it is the responsibility of the registrant to use their best judgment to take appropriate action. Whether a "significant loss" has occurred depends, in large part, on the business of the researcher and the likelihood of a rational explanation for a particular occurrence. For example, what would constitute a significant loss for a researcher may be viewed as comparatively insignificant for a hospital or manufacturer.

Further, the loss of a small quantity of controlled substances, repeated over a period of time, may indicate a significant problem for a registrant, which must be reported. Pursuant to [21 CFR 1301.76\(b\)](#), the burden of responsibility is on the registrant to identify what is a significant loss and make the required report to DEA.

When determining whether a loss is significant, a registrant should consider, among others, the following factors:

1. The actual quantity of controlled substances lost in relation to the type of business.

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2. The specific controlled substances lost.
3. Whether the loss of the controlled substances can be associated with access to those controlled substances by specific individuals, or whether the loss can be attributed to unique activities that may take place involving the controlled substances.
4. A pattern of losses over a specific time period, whether the losses appear to be random, and the results of efforts taken to resolve the losses.
5. Whether the specific controlled substances are likely candidates for diversion.
6. Local trends and other indicators of the diversion potential of the missing controlled substances.

If the registrant determines that the loss is not significant, DEA recommends that the registrant should place a record of the occurrence in a theft-and-loss file for future reference.

### In-Transit Loss

When all or part of an in-transit shipment of controlled substances fails to reach its intended destination, the supplier is responsible for reporting the in-transit loss of controlled substances to DEA. [21 CFR 1301.74\(c\)](#). The purchaser is responsible for reporting any loss of controlled substances after they have signed for or taken custody of a shipment. The purchaser must then submit a DEA Form 106. [21 CFR 1301.76\(b\)](#). If the purchaser does not take custody of the shipment, it is the supplier's responsibility for reporting any loss of controlled substances in the original shipment.

### Breakage and Spillage

While neither the CSA nor DEA's regulations specifically address the breakage and/or spillage of a controlled substance, DEA offers the following guidance, which was also published in the 2003 Notice of Proposed Rulemaking and guidance document, Reports by Registrants of Theft or Significant Loss of Controlled Substances. [68 FR 40576, 40578](#) (Jul. 8, 2003). The witnessed breakage or spillage of a controlled substance does not constitute a loss of controlled substances because the registrant can account for the controlled substances. These types of incidents do not require notification to DEA. If there is breakage, spillage, or other damage to controlled substances, but the controlled substances are still recoverable, there are options for disposing of them:

1. Promptly destroy that controlled substance in accordance with [21 CFR 1317.90](#) using an on-site method of destruction. [21 CFR 1317.05\(a\)\(1\)](#).
2. Send those controlled substances to an entity registered with DEA to handle returns/disposals (known as a reverse distributor). [21 CFR 1317.05\(a\)\(2\)](#).

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3. Contact the local DEA Diversion Field Office to request assistance to dispose of the controlled substances pursuant to [21 CFR 1317.05\(a\)\(4\)](#).

A record of the destruction should be kept pursuant to [21 CFR 1304.21\(e\)](#).

If the breakage or spillage is clearly observed, but the controlled substances are not recoverable, the registrant should document the circumstances of the event in their records. It is DEA's position that, in order to maintain complete and accurate records in accordance with [21 CFR 1304.21\(a\)](#), non-recoverable breakage or spillage must be recorded on a DEA Form 41 and, as with any other form of disposal under [21 CFR part 1317](#), must be signed by two individuals who can testify that a breakage or spillage occurred. These records must be maintained in the registrant's files and contain such information as required by [21 CFR 1304.22\(c\)](#).

## SECTION VIII - DISPOSAL OF CONTROLLED SUBSTANCES

### Disposal of Controlled Substances

All controlled substances to be destroyed by a registrant, or caused to be destroyed by a registrant pursuant to [21 CFR 1317.95\(c\)](#), must be destroyed in compliance with applicable federal, state, tribal, and local laws and regulations and must be rendered non-retrievable. [21 CFR 1317.90\(a\)](#). A researcher may dispose of its controlled substances inventory in the following manner pursuant to [21 CFR 1317.05](#):

1. Promptly destroy that controlled substance in accordance with [21 CFR 1317.90](#) using an on-site method of destruction. [21 CFR 1317.05\(a\)\(1\)](#).
2. Send those controlled substances to an entity registered with DEA to handle returns/disposals (known as a reverse distributor). [21 CFR 1317.05\(a\)\(2\)](#).
3. Contact the local DEA Diversion Field Office to request assistance to dispose of the controlled substances pursuant to [21 CFR 1317.05\(a\)\(4\)](#).
4. For the purpose of return or recall, promptly deliver that controlled substance by common or contract carrier pick-up or pick-up by other registrants at the registrant's registered location to: The registered person from whom it was obtained, the registered manufacturer of the substance, or another registrant authorized by the manufacturer to accept returns or recalls on the manufacturer's behalf. [21 CFR 1317.05\(3\)](#).

A record of the destruction should be kept pursuant to [21 CFR 1304.21\(e\)](#).

In no case should drugs be forwarded to DEA unless the registrant has received prior approval from DEA. DEA procedures established for the disposal of controlled substances must not be construed as authorizing or permitting any person to do any act which such person is not authorized or permitted to do under other federal laws or obligations under international treaties, conventions, or protocols, or

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under the law of the state in which they desire to do such act, nor shall compliance with such parts be construed as compliance with other federal or state laws unless expressly provided in such other laws. [21 CFR 1307.02](#).

**Reverse Distributors Authorized to Dispose of Controlled Substances**

A researcher may transfer controlled substances to a DEA registered reverse distributor who handles the disposal of controlled substances. [21 CFR 1317.05\(a\)\(2\)](#). When a researcher transfers schedule I or II controlled substances to a reverse distributor for destruction, the reverse distributor must issue an official order form (DEA Form 222) or the electronic equivalent to the researcher. [21 CFR 1305.03](#), [1317.10\(b\)](#). When schedules III-V controlled substances are transferred to a reverse distributor for destruction, the researcher must maintain a record of distribution that lists the drug name, dosage form, drug strength, quantity, and date transferred. [21 CFR 1317.10\(a\)](#), [1304.22\(a\)\(2\)\(iv\)](#). A DEA-registered reverse distributor who destroys the controlled substances is responsible for submitting a [DEA Form 41](#) (Registrants Inventory of Drugs Surrendered) to DEA when the controlled substances have been destroyed. [21 CFR 1304.21\(e\)](#). A DEA Form 41 should not be used to record the transfer of controlled substances between the researcher and the reverse distributor disposing of the drugs.

A paper version of the DEA Form 41 can be requested by writing to:

Drug Enforcement Administration  
Diversion Control Division  
Attn: Registration & Program Support Section/DRR  
P.O. Box 2639  
Springfield, VA 22152-2639

# Appendices

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**APPENDIX A - List of Abbreviations**

CFR	Code of Federal Regulations
CSA	Controlled Substances Act
CSOS	Controlled Substances Ordering System
DEA	Drug Enforcement Administration
DRR	DEA Headquarters Registration Section
FDA	Food and Drug Administration
IND	Investigational New Drug
NIDA	National Institute on Drug Abuse
NIH	National Institutes of Health
U.S.	United States
U.S.C.	United States Code

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**APPENDIX B - Guidelines for Completing the DEA-Form 106**

Instructions for completing the DEA Form 106 are provided when filling out either the hard copy or the electronic version of the form. Listed below are additional guidelines:

- Do not use a DEA Form 106 to report an accidental spillage. Save the broken bottles, salvage the product if possible, and contact your local [DEA Diversion Field Office](#) for additional instructions.
- Do not use a DEA Form 106 to report miscounts or adjustments to inventory involving clerical errors. A separate log documenting the discrepancies may be kept at the researcher's discretion.

**The following guidelines apply only if you are using the hard copy version of the DEA Form 106:**

- If thefts have occurred due to employee pilferage over a period of time, document on the DEA Form 106 the date of the theft or loss (or first discovery of theft or loss). Provide estimated beginning and ending dates of the thefts in the comment section with an explanation.
- On the next line, enter the number of thefts or losses experienced in the last 24 months, but do not include the current theft or loss being reported. If the current theft or loss was the only theft or loss in the last 24 months, enter "0" (zero).
- In section five, enter the amount paid for the controlled substances.
- In section three, if you accepted receipt of the controlled substance(s) before discovering a loss in transit, identify the supplier and its DEA registration number.
- When explaining how many losses occurred from the same carrier, do not include the current loss.
- The date next to the signature and title on page 4 should be the date the form was completed and transmitted to DEA.
- If amending a paper version of a prior DEA Form 106, print **Amended** in the upper front page margin, with the date of the theft.

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**APPENDIX C - Internet Resources**

DEA's Diversion Control Division Website - [www.DEADiversion.usdoj.gov](http://www.DEADiversion.usdoj.gov)

DEA Homepage - [www.dea.gov](http://www.dea.gov)

DEA E-Commerce Program (CSOS) website - [www.deaecom.gov](http://www.deaecom.gov)

U.S. Government Printing Office/Code of Federal Regulations - [www.fdsys.gov](http://www.fdsys.gov)

Provides access to the CFR, Parts 1300 to End, primary source for the Researcher's Manual, and the Federal Register which contains proposed and finalized amendments to the CFR.

Office of National Drug Control Policy (ONDCP) - [www.whitehousedrugpolicy.gov](http://www.whitehousedrugpolicy.gov)

Food and Drug Administration - [www.FDA.gov](http://www.FDA.gov)

National Association of State Controlled Substances Authorities - [www.nascsa.org](http://www.nascsa.org)



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**APPENDIX D - Small Business and Agriculture Regulatory Enforcement Ombudsman**

The Small Business and Agriculture Regulatory Enforcement Ombudsman and 10 Regional Fairness Boards were established to receive comments from small businesses about federal agency enforcement actions. The Ombudsman annually evaluates the enforcement activities and rates each agency's responsiveness to small business. If you wish to comment on DEA enforcement actions, you can contact the Ombudsman at 1-888-REG-FAIR (1-888-734-3247).

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**APPENDIX E - Additional Assistance and Plain Language**

**Additional Assistance**

This publication is intended to provide guidance and information on the requirements of the CSA and its implementing regulations. If you require additional clarification or assistance, or wish to comment on any matter regarding DEA's requirements or regulatory activities, please contact your local [DEA Diversion Field Office](#). Every effort will be made to respond promptly to your inquiry.

**Plain Language**

DEA has made every effort to write this Researcher's Manual in clear, plain language. If you have suggestions as to how to improve the clarity of this Researcher's Manual, please contact us at:

Drug Enforcement Administration  
Attn: Policy Section/DPY  
8701 Morrissette Drive  
Springfield, VA 22152  
Telephone: (571) 362-3260

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**APPENDIX F - DEA Office Locator**

**Drug Enforcement Administration  
Diversion Field Office Locations**

Visit [www.DEAdiversion.usdoj.gov](http://www.DEAdiversion.usdoj.gov) for current addresses and telephone numbers.

**Diversion Field Registration Specialists**

To locate your local DEA Diversion Field Registration Specialist, open the hyperlink below by right-clicking on the hyperlink, and then select "Open Hyperlink." Then, in the appropriate search box, enter the zip code, or in the alternative, the city or county and the state, then press "Enter" on your keyboard.

<https://www.deadiversion.usdoj.gov/contactDea/spring/fullSearch>