NCCentral UNIVERSITY
Environmental Health and Safety

Controlled Substances Program for Research

Version 1.0

Contents

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Approved by: Kristin Long-Witter

I. Applicable Regulations

The Controlled Substances Act (CSA) (21 CFR) and the North Carolina Controlled Substances Act together place all substances which were in some manner regulated under existing federal law into one of five schedules based upon the substance's medical use, potential for abuse, and safety or dependence liability.

Individuals who manufacture, distribute, dispense, or conduct research with any controlled substance must comply with the latest US Department of Justice, Drug Enforcement Administration (DEA) and NC Department of Health and Human Services Drug Control Unit (NCDCU) mandates. For activities regulated by both state and federal agencies, the more stringent rule must be followed.

II. Purpose

The purpose of this program is to ensure that NC Central University (NCCU) faculty and staff are in full compliance with DEA and NCDCU requirements. This Plan applies to NCCU employees who utilize controlled substances for research purposes. Compliance with federal and state regulations will be accomplished by proper procurement, distribution, use, inventory, recordkeeping, storage, and disposal of controlled substances used in research labs.

III. Definitions

For a complete list of definitions please refer to Title 21 United State Code Controlled Substances Act, Section 802.

Controlled Substance - Drug or other substance that is tightly controlled by the government because it may be abused or cause addiction. The control applies to the way the substance is made, used, handled, stored, and distributed. Controlled substances include opioids, stimulants, depressants, hallucinogens, and anabolic steroids

Distribute - Delivering (other than by administering or dispensing) a controlled substance or a listed chemical. The term **"distributor"** means a person who so delivers a controlled substance or a listed chemical.

Non-retrievable - For the purpose of destruction, the condition or state to which a drug shall be rendered following a process that permanently alters that drug's physical or chemical condition or state through irreversible means and thereby renders the drug unavailable and unusable for all practical purposes.

Registrant - Person who is registered with federal and state agencies and licensed to procure, store and use controlled substances.

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IV. Responsibilities

Registrant/Department/Authorized Users

- Ensure that only DEA-registered individuals order controlled substances.
- Manage controlled substances in accordance with all regulatory requirements including security, inventory, use, disposal, and recordkeeping.
- If additional users will have access, request authorized users on registration, properly vet using the Authorized User Controlled Substance Questionnaire and keep current Authorized User Signature Log (Appendix A).
- Maintain complete and accurate inventory records (receipt, use, inventory, labeling, and disposal) of all controlled substances using the Controlled Substance General Inventory and Use Log (example in Appendix B). These records must be kept in or near the primary work area, separate from all other records and documents, and available for inspection during regular work hours.
- Screen persons using the prior to granting access to controlled substances for approved activities.
- Ensure all controlled substances, regardless of schedule, are kept under lock and key, in a substantially constructed cabinet or safe, and only accessible only to authorized personnel.
- Renew registrations with NCDCU and DEA annually
- Immediately report any theft, loss, or misuse of controlled substance

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- Develop and implement written Controlled Substances Program.
- Provide guidance to NCCU personnel on federal and state registration requirements including registration, acquisition, inventory, use, disposal and recordkeeping.
- During annual (research labs) and semi-annual (Animal Resource Center) inspections review controlled substances documentation including registration, list of authorized users, inventories, and ensure proper security.

V. Controlled Substance Schedules

Substances regulated under the U.S. Controlled Substances Act (CSA) are in one of five schedules. Schedule I substances have the most restrictions, and Schedule V substances the least. The North Carolina Controlled Substances Act has a sixth category. The CSA and NC Controlled Substances Act define the schedules as follows:

Schedule	Definition	Examples
I	High potential for abuse, with no currently accepted medical use in treatment in the US, or a lack of accepted safety for use in treatment under medical supervision	Heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote
II	High potential for abuse; currently accepted medical use in the United States, or currently accepted medical use with severe restrictions; and the abuse of the substance may lead to severe psychic or physical dependence	Cocaine, methamphetamine, methadone, hydromorphone (Dilaudid), meperidine (Demerol), oxycodone (OxyContin), fentanyl, amphetamine (Dexedrine, Adderall), and methylphenidate (Ritalin)
III	Potential for abuse less than the substances listed in Schedules I and II; currently accepted medical use in the United States; an abuse may lead to moderate or low physical dependence or high psychological dependence	Ketamine, anabolic steroids, testosterone
IV	Low potential for abuse and low risk of dependence; currently accepted medical use in the United States; and limited physical or psychological dependence relative to the substances listed in Schedule III	Xanax, Soma, Darvon, Darvocet, Valium, Ativan, Talwin, Ambien, Tramadol
V	Lower potential for abuse than Schedule IV and consist of preparations containing limited quantities of certain narcotics. Schedule V drugs are generally used for antidiarrheal, antitussive, and analgesic purposes	Lomotil, Motofen, Lyrica, Parepectolin
VI*	No currently accepted medical use in the United States; a relatively low potential for abuse in terms of risk to public health and potential to produce psychic or physiological dependence liability based upon present medical knowledge; and a need for further and continuing study to develop scientific evidence of its pharmacological effects	Marijuana and Tetrahydrocannabinols

*Class VI applies to NC; these are Schedule I substances under federal law

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Complete federal and state list of the schedules can be found at DEA and NC Controlled Substances Act § 90-89 through § 90-94, respectively.

Exempt Amounts

The DEA allows certain analytical standard, preparations and products to be purchased and used without the need for the user to have a DEA registration. Please refer to https://www.deadiversion.usdoj.gov/schedules/#exempt for information on the Exempted Lists.

List I and II Chemicals (Precursors)

In addition to the scheduled controlled substances, there are also chemicals that are regulated under the Chemical Diversion and Trafficking Act (CDTA) because they are precursors to, or reagents used in, the manufacture of illicit drugs. Many of these chemicals are common laboratory reagents; many have a threshold below reporting requirements and ordering does not require DEA registration. The DEA Chemical Handler's Manual can be consulted for additional information.

A table of these chemicals can be found at https://www.deadiversion.usdoj.gov/chem_prog/34chems.htm

VI. Registration

Possession, storage or use of any controlled substance requires registration with both state and federal administrations. **No persons or departments at NCCU may order, possess, store or use a controlled substance without proper state and federal licenses and certificates.**

For use of Schedule I and VI of controlled substances, individual registration is required without exception. If requested and granted during registration for research, Registrant may share schedules II-V substances with authorized individuals within their department for research purposes only. The registrant assumes sole responsibility for departmental compliance with all federal and state mandates related to use, storage, disposal, and documentation. NCDCU might require separate registrations for separate locations/buildings.

A. New Registration

1) Notify EHS by completing and submitting a NCCU Notification of Controlled Substance Registration. You may not proceed to Step 2 until you have received EHS approval.

2) Complete DHHS 225-C application form for researchers and email an electronic version and the signed signature page to: NCCSAREG@DHHS.NC.GOV.
3) Pay registration fee online with credit card or by mail.
4) NCDCU will perform an **inspection** (to ensure proper storage security) and a **background check** before granting registration approval.
5) Contingent upon successful inspection and background check you will receive a certificate from NCDCU.

Once you have received approval and your certificate from NCDCU you MUST register with the DEA before you are eligible to acquire the controlled substance.

1) Complete and submit the online DEA Form 225: New Application for Manufacturers, Import/Export, Distributors, Reverse Distributors, Researchers, Canine Handlers, Analytical Labs.
2) Because NCCU is a state institution, NCCU personnel are exempt from the Federal registration fee.
3) DEA may choose to schedule a second site inspection prior to issuing a license.

Provide EHS with a copy of both your NC and DEA licensure certificates upon receipt.

B. Renewal

1. NCDCU (annual)

1) Notify EHS of renewal by completing and submitting a NCCU Notification of Controlled Substance Registration.
2) Complete DHHS 227-C application form for researchers and email an electronic version with electronic signature to: NCCSAREG@DHHS.NC.GOV.
3) Pay registration fee online with credit card or by mail.

2. DEA (annual)

DEA research registrations must be renewed annually based on the initial approval date. Renew your registration online DEA website .

Other specific online forms can be find at DEA website for name, address, schedule and drug code changes.

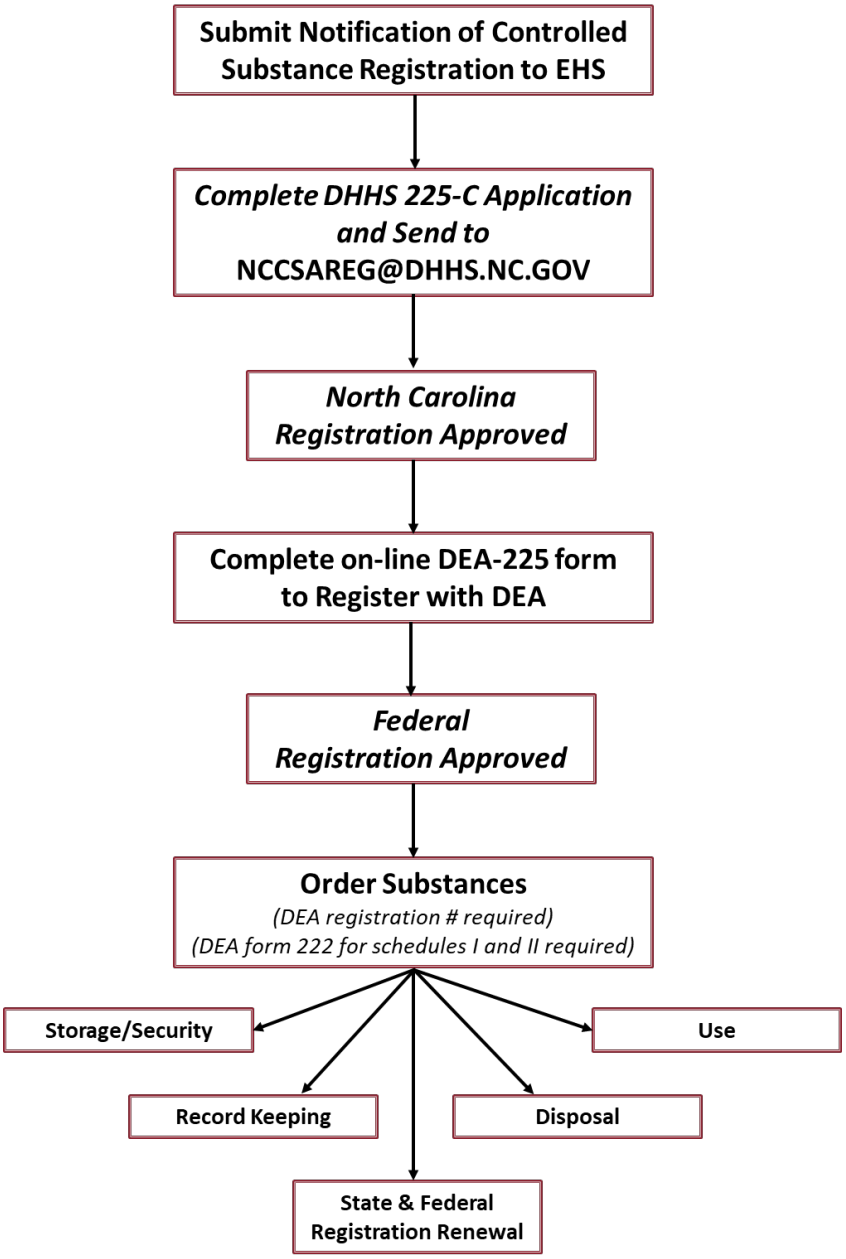

Figure 1. Flowchart for registration and ordering of controlled substances.

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VII. Authorized Users

Individuals who conduct research and teaching activities with controlled substances under licenses held by a Registrant must comply with applicable federal and state regulations relating to controlled substances. These requirements are intended to ensure that those who have access to controlled substances: a) do not have felony drug convictions; b) have not had a Drug Enforcement Administration (DEA) license revoked or surrendered for cause; and c) have not had an application for registration with the DEA denied. The requirements apply to University employees and any other individuals including students, volunteers, and visitors who have access to controlled substances for University research purposes.

NCCU has implemented a process to ensure compliance with this DEA requirement. Under the process, before a person is allowed access to controlled substances in the lab, they must first complete the Authorized User Controlled Substance Questionnaire. The process is as follows:

1) Registrant identifies individuals who need to be Authorized Users at their location and provides them with the Authorized User Controlled Substance Questionnaire.
2) The potential Authorized User completes the form and returns it to the Registrant for evaluation
    a. If the responses to the questionnaire indicate that the potential Authorized User is eligible to access controlled substances, the Registrant or lab manager will have the individual sign the Authorized Users Signature Log.
        i. The signature log is a typed listing of authorized users along with their corresponding handwritten signature and initials to ensure signature/initial identity throughout controlled substance documents.
    b. If the responses on the questionnaire indicate that the individual is not eligible to access controlled substances based on the above criteria, the lab manager will inform this individual and their supervisor. The individual will not be allowed to sign the Authorized Users Signature Log nor will they be allowed access to controlled substances used in that lab. The supervisor will determine the impact on this individual's job duties and assignment and, if necessary, will bring any concerns to the appropriate HR group.
3) Registrant retains all completed questionnaires in a secure, confidential file.

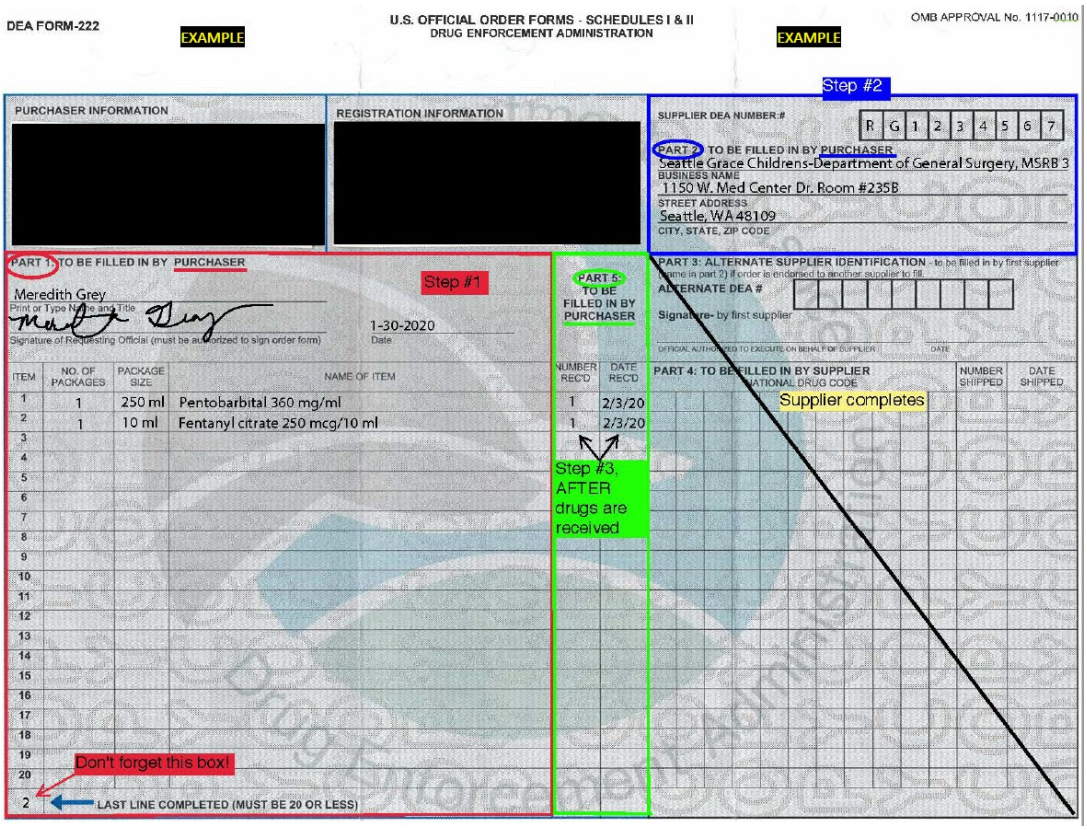
VIII. Ordering and Acquisition

Note that only DEA-registered individuals may order controlled substances and a valid DEA number is required for all controlled substance orders. Schedules III, IV, and V substances can be ordered directly

from manufacturer. The official order form for Schedule I and II controlled substances is DEA Form 222, which is available to registrants on the DEA website. If requested, these forms may be provided automatically with a new DEA registration. The registrant must verify that the information on their Form 222 is complete and accurate. DEA Order Forms should be kept in a secure location to prevent theft.

Completing Form 222

1) Complete Part 1 and Part 2
2) Make copy of form prior to placing order for your records.
3) Order controlled substances by providing the original signed form 222 to the supplier.
4) Upon receipt of the substances, complete Part 5 with the date and amount received.
5) All DEA Form 222s must be securely stored and be readily available if requested.



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Registrants must immediately report any missing or stolen Form 222s to the Raleigh District Office at 919-790-3004. All unused, unnecessary or inaccurate Form 222s must be returned to the DEA.

Importing and Exporting Controlled Substances

See the Import/Export pages of the DEA Office of Diversion Control Division website for additional information. Any import/export activity involving controlled substances **requires EHS pre-approval.** Please contact EHS at ehs@nccu.edu.

IX. Storage and Security

The registrant is responsible for managing the controlled substances in accordance with all regulatory requirements including security, inventory, and recordkeeping.

A. Storage Security Requirements

Registrants shall provide effective security controls and operating procedures to guard against theft and diversion of controlled substances. At NCCU, controlled substances used for research are all considered "small quantities" for the purposes of storage and security. While there must be only one inventory per registration, controlled substances under one registration may be stored in several approved physical locations within one building. Registrants should always limit the amount of stored controlled substances to the minimum that is necessary to accomplish immediate research goals.

The following factors, among others, are considered when evaluating the overall security system for a researcher: (21 CFR 1301.71(b)):

- Type, form and quantity of controlled substance
- Location of the premises and the relationship such location bears on security needs
- Extent of unsupervised public access to the area
- Number of employees and adequacy of supervisors over employees who have access to the storage areas

Regardless of schedule, all controlled substances must be stored behind at least two different locks (i.e. door and lockbox or safe) at all times. Keep controlled substances stored at all times when not in use by authorized persons. For keyed locks, never store the keys near the lockbox and do not store the keys to the two locks together. For combination locks, only the registrant and as few responsible individuals as possible should know the combination and whenever anyone who knows the combination is terminated from employment,

the combination(s) must be changed.

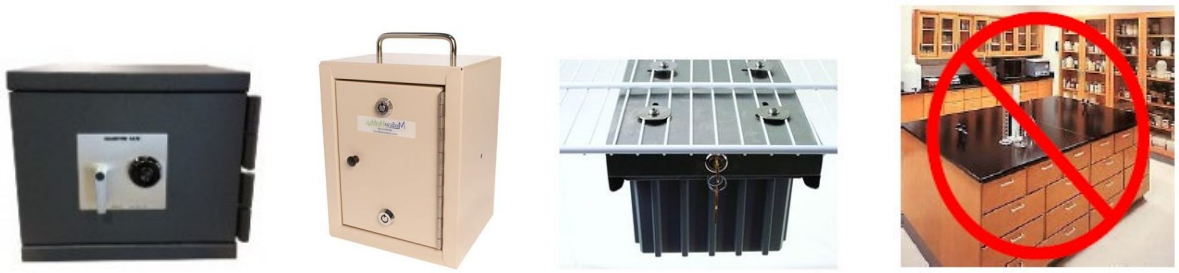

Figure 2. From left to right: 1) DEA approved safe for controlled substances storage bolted to the floor or wall; 2) A wall mountable controlled substance lockbox with two doors and two locks (each lock is keyed differently); 3) Lockbox for cold storage kept in a locked refrigerator or freezer or in a locked room; and 4) Wood laminated casework island with doors that could be pried open, and laminate wall cabinets with glass doors are not appropriate areas for secure storage of controlled substances.

Controlled substances are never stored with other laboratory chemicals.

Schedule I and II Substances

These substances have the highest security requirements, and those used for research must be stored in a safe or steel cabinet of substantial construction.

- If the safe or cabinet is less than 750 lbs., it must be mounted or secured to something of substantial construction (e.g., bolted to a wall or the floor, or the base imbedded in concrete).
- The safe/cabinet should have an inner and outer door with the locks for each door keyed differently.
- For storage at 4 °C or colder, a single-lock lockbox in a refrigerator or freezer that can also be locked is permitted. The room must also be lockable, and locked after hours.

Schedule III-V Substances

Schedule III, IV and V substances can be stored with Schedule I and II substances or stored separately using one of the following methods:

- Preferred method: a wall mountable controlled substance lockbox with two doors and two locks (each lock is keyed differently).

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- A single-lock lockbox that is stored in a drawer or cabinet that is secured at all times with a hasp and padlock. The drawer and cabinet should be substantially constructed such as in a drawer that is part of either a bench or cabinet that is mounted to the wall or floor.
- If a lab is not accessible to the public, then an option is to use a single-lock lockbox, stored in a drawer or cabinet in a room that is kept locked at all times.
- For storage at 4 °C or colder, a single-lock lockbox in a refrigerator or freezer that can also be locked is permitted. The room must also be lockable, and locked after hours.

B. Personnel Security

All Registrants are required to pass a background check as part of the application process. Additional authorized users may be requested in the registration application for substances in Schedules II-V. These personnel are screened as described in the Authorized Users section of this Program.

Schedule I substances may not be issued to anyone other than the registrant, or used by anyone other than the registrant. If additional personnel need to use Schedule I substances, they must individually register with NCDCU and DEA.

C. Loss, Theft, or Misuse

In the event that controlled substances are lost, stolen or used in an unauthorized manner, the registrant must immediately contact the NCCU Police at 911 or 919-530-6106, EHS at 919-530-7125. These groups will assist the registrant in making notification to the DEA Office of Diversion Control in Raleigh (919-790-3004) and assist with completion of DEA Form 106 – Report of Theft or Loss of Controlled Substances- if directed to do so.

X. Transfer of Controlled Substances

Registrants may only transfer schedule II-V controlled substances from a registered to a non-registered person within their department if specifically authorized in their registration. Note that in the event of this type of transfer, the registrant retains all liability for loss, theft, or misuse of the substance. Schedule I and VI substances require individual registration and shall not be shared, even within a department.

Transferring these substances to other DEA-registered individuals is prohibited at NCCU without pre-approval by EHS and completion of the DEA process.

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XI. Disposal

Substances that are expired, unused or contaminated substances must be stored under lock and key until ready for disposal or re-distribution to the original supplying/manufacturing company where the chemical was obtained Regardless of the method, the registrant must contact a NCDCU agent at 984-236-5100 or NCCSAREG@dhhs.nc.gov to obtain specific instructions.

Disposal of controlled substances must be witnessed by a NCDU special agent and requires proper documentation. Only the registrant may dispose of a controlled substance.

Under some circumstances, registrants may dispose of Schedule II-V controlled substances without NCDU notification as long as it is witnessed by two witnesses and properly documented on DEA form 41:

- Unused part of an injection
- Small residues in original container
- Contaminated dose such as unused in syringe or when controlled substances are reconstituted for use, but short shelf life prevents use of the residue

Form 41 does not require submittal to DEA unless specifically requested to do so. Registrant must retain this form as a record of destruction and made available to inspectors for at least two years.

Once a controlled substance is rendered "non-retrievable," it is no longer subject to DEA regulations.

The controlled substances inventory should immediately be updated as part of the disposal process.

Breakage of controlled substances does not constitute a "loss" of controlled substances and is not reported on a DEA Form 41. When there is breakage, damage, spillage or some other form of destruction, any recoverable controlled substances should be collected. If the breakage or spillage is not recoverable, the registrant must document the circumstances of the breakage in their inventory records. Registrants should immediately contact EHS while securing the spilled or broken materials to witness the incident and sign the inventory as a witness. EHS is unable to sign as the required witness if material cannot be accounted for.

XII. Inspections

NCDCU and DEA may make unannounced inspections at any time to any registrant regardless of the scheduled product they use. The DEA may also do an inspection of any potential registrant prior to granting actually registration.

Registrants are required to notify EHS immediately for any scheduled and/or unannounced inspection by any outside agency.

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EHS may also conduct periodic audits.

XIII. Inventory and Tracking

Registrants must track and maintain an accurate accounting of all controlled substances from the time they are ordered until they are completely used or otherwise disposed in accordance with regulations. See section on Recordkeeping for information on document storage and retention.

The DEA requires an initial and biennial (every two years) physical inventory of all controlled substances which is recorded on the Controlled Substances Inventory Record. Damaged, defective, expired, or impure substances awaiting disposal must be included in the inventory until they are disposed or re-distributed.

A. Acquisition Records

Registrant must sign, date and retain all records of receipt including supplier invoices or packing slips. These records must detail the date received, name and address of supplier, the type, strength, and concentration of substance, and the amount received.

B. General Inventory and Use Logs

A continuous General Inventory and Use Log must be created for each unique vial or container stock of drug and its associated strength or container size. This inventory tracks acquisition, current on-hand stocks, and disposal. Both stock solutions and any diluted product must be accounted for on separate use logs.

XIV. Recordkeeping

Controlled substance records must be maintained in conformity with federal regulations (21 CFR-Part 1304). The following records must be maintained and be "readily retrievable and available":

- State and DEA Certificate of Registration
- Authorized users background checks evaluation and list of authorized users (if applicable)
- Acquisition and ordering invoices
- Signed and dated supplier invoices or packing slips
- DEA Form 222s including used, voided and unused forms
- Inventory records

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- Usage and administration records
- Disposal records
- DEA Form 106-Report of Loss or Theft

Record requirements include:

- "Readily retrievable and available" means they can be separated from all other records and retrieved in a reasonable time frame.
- All records must be stored at the address listed on registrant's DEA registration.
- Records and inventories must be maintained for at least two years.
- All records must be stored in a secure location, preferably locked in the cabinet or safe containing the controlled substances.
- All records of schedule I and II controlled substances must be kept separately from those of schedule III-V substances.

XV. Appendix A Authorized Users Signature Log

Registrant Name: Click or tap here to enter text. **DEA License Number:** Click or tap here to enter text.
Location: Click or tap here to enter text.

I certify that I have designated the persons listed below as Authorized Users for this location. Person is no longer an Authorized User when a "Date Removed" is entered.

Registrant Signature: _____

Date	Name (Printed legibly)	Title	Signature	Initials	Date Removed

By signing above, you certify that:

- You have not been convicted of a felony within the last 5 years, a misdemeanor within the last 2 years or are presently formally charged with committing a criminal offense.
- You have not knowingly used any narcotics, amphetamines or barbiturates in the last 3 years unless prescribed to you by a physician.

XVI. Appendix B Example Controlled Substance General Inventory and Use Log

A separate form must be used for each controlled substance container unit and size

Controlled Substance:		
Container Unit:	Container size:	Concentration:
DEA Schedule:		
DEA Registrant Name:		
DEA Registrant Department/Building:		

Date	Amount received	Expiration Date	Amount dispensed	Balance	Authorized User	Comments (transferred to Multiple Dose Form or Diluted Dose Form; disposed of; administered directly to animal)
3/1/2022	*1.0 mg*	*4/2/2025*	*100 ug*	*900 ug*	*Scientist B*	*Used to make diluted stock; stored at 4 ºC lockbox room 2341*
						Note: An additional inventory sheet is started to track diluted stock

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