

Using Controlled Substances in Research at the University of Virginia

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Questions should be addressed to the Office of Animal Welfare @ 924-5752.

Controlled Substance Website – <http://www.virginia.edu/vpr/ControlledSubstances/>

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Introduction

This manual provides detailed information to assist individuals that need to register with the Drug Enforcement Administration (DEA) and Virginia Board of Pharmacy (VBP) to use Controlled Substances for their research. The DEA and VBP regulate the use of Controlled Substances in basic and applied research settings whether the use is *in vitro*, or for anesthetics and analgesics given to animal models. The intent of the regulations is to maintain a closed system of distribution wherein a Controlled Substance is tracked from its acquisition through to its use and/or disposal through a chain of custody. Strict accountability of the use of Controlled Substances within a closed system deters diversion. Researchers whose laboratories use Controlled Substances Schedules I through V must submit a laboratory location specific application to both the DEA and VBP. VBP also defines Schedule VI and researchers who use drugs listed in this category need only submit a laboratory specific registration with VBP (discussed in detail in manual). The registration(s) must be approved by these agencies prior to ordering or possessing Controlled Substances.

All Registrants, and personnel using Controlled Substances under the location specific registration, must comply with state and federal regulations regarding the acquisition, record keeping, inventory, storage, use, and disposal of Controlled Substances. Individuals having reservations about assuming the responsibility of possessing Controlled Substances and/or maintaining the required records are discouraged from applying for registration. Only the DEA Registrant and members of their laboratory that are designated by the Registrant are allowed to have access to their inventory of Controlled Substances and to administer and possess Controlled Substances. The DEA and VBP hold the Registrant responsible for purchasing, securing, inventory, and administration of Controlled Substances. Individuals who are fined or individuals who have violated the law will not be reimbursed by UVA nor defended by UVA for criminal actions. The Vice President for Research (VPR) is the University's Institutional Official with responsibility for ensuring appropriate conduct of research at UVA. The VPR is vested with the authority to suspend, revoke, or deny any researcher's controlled substance registration application submission or reserves the right to contact the federal and state agencies regarding revoking a researcher's registration if warranted.

Questions about procurement, secure storage, use, disposal, required documentation, or regulatory questions regarding Controlled Substances and their use in research using laboratory animals should be submitted to the Director of the Center for Comparative Medicine (CCM) or the Director of the Office of Animal Welfare (OAW).

Definitions and Terminology

For purposes of this manual, the following terms are defined as:

Administration

The act of dosing, injecting, or applying a Controlled Substance to an animal or subject.

Authorized User

A University member authorized to temporarily possess and use Controlled Substances for research under oversight by the DEA Registrant who procures it. An Authorized User should be a direct report of the Registrant or be funded by the Registrant. An authorization form must be kept on file containing the signature of each Authorized User and the signature of the Registrant documenting when the Authorized User was given authorization by the Registrant. The form must be kept on file by the Registrant for a period of two years after the Authorized User leaves the institution.

Bulk Form

A Controlled Substance as received from the manufacturer or supplier to be used in, or capable of use in, the manufacture of the same or other non-controlled substances in Finished Form (diluted or working form). Depending on the concentration of the Bulk Form, this form may be a concentrated stock form which is compounded by dilution or combination with other drugs into a Finished Form for administration to an animal or for *in vitro* use.

Controlled Substance (CS)

Any substance listed in the Controlled Substances Act, Code of Federal Regulations (21 CFR, part 1300 to end) and Title 54.1, Section 3400 of the Code of Virginia. Controlled Substances are identified in the Schedules I through V contained within the “[List of Scheduling Actions, Controlled Substances, Regulated Chemicals](#) (10-Dec-18)” published by the DEA (orange book).

In addition, the Code of Virginia recognizes Schedule VI drugs and the Board of Pharmacy administers the State laws related to Schedule I-VI substances.

Controlled Substance Research Protocol

A document submitted to the DEA and VBP which describes the need for and use of Controlled Substances in the Registrant’s research. This form is used instead of the IACUC animal use protocol. For Schedule II through V substances, use the form provided - “University of Virginia Controlled Substances Research Protocol” on the website associated with this manual. To register to conduct research with Schedule I controlled substances the Registrant must complete and submit to the DEA

the form described in 21 CFR 1301.18. Once DEA registration is granted for use of Schedule I substances, the Registrant must submit a registration application to VBP.

Compounding

The mixing or diluting of pharmaceutical agents into a Finished Form for administration for which no similar Bulk Form is available. Compounding of pharmaceutical agents for use in experimentation is allowed. However, transfer (see definition) of compounded Controlled Substances by a pharmacy or wholesale distributor is restricted under State law unless necessary for treatment of an emergent condition.

Disposal/Destruction

Expired, unusable, or unwanted Controlled Substances (CS) must be disposed of using a DEA and VBP approved method. Registrants are responsible for destroying unwanted or expired CS by reverse distribution by transferring CS to an authorized Reverse Distributor for destruction.

Diversion

A transfer of a Controlled Substance from a lawful to an unlawful channel of distribution or use. This includes administration of a Controlled Substance by an individual that is not listed as an Authorized User associated with the Registrant.

Center for Comparative Medicine (CCM)

A division of the Office of the VPR that provides animal husbandry and veterinary care to the animal care and use program to facilitate research and teaching at UVA in compliance with state and federal regulations.

Drug Enforcement Administration (DEA)

The agency within the United States Department of Justice that enforces the federal Controlled Substances laws and regulations.

Expired and/or Unusable Substances

Controlled Substances or mixtures containing Controlled Substances for which the expiration date has passed for tablets, injections, liquid, powders, or preparations compounded. This also includes Controlled Substances that can no longer be used for research due to contamination, animal care and use requirements, expiration date, etc.

Finished Form

A Controlled Substance altered (e.g. diluted, compounded) from Bulk Form which will be administered for research. For example, Bulk Form diluted 1:10 becomes a Finished Form. Finished Form substances may be retained and secured by Authorized Users until depleted or unusable. All vials of finished form substances must be properly labeled and have a usage form.

Institutional Official

The Vice President for Research.

Location

For purposes of this policy, a location is a room or designated area where the inventory of Controlled Substances are securely stored. A location is managed by a single DEA Registrant and has a single building and room address with which it is associated. All Controlled Substances must be returned at the end of their use each day to the storage area on the registration.

Office of Animal Welfare (OAW)

A division of the Vice President for Research Office that provides training and compliance investigation for all research and teaching involving animal use at the University of Virginia.

Principal Investigator (PI)

The individual with final responsibility for the conduct of research or other activity described in a research proposal or an award.

Power of Attorney

The Registrant is the only individual who may order, dispense, or dispose of Controlled Substances listed in their registration. The Registrant must generate a Limited Power of Attorney document in order to allow an Authorized User to perform specific functions specifically involving Schedule I or Schedule II substances. The persons(s) having a Limited Power of Attorney (POA) may perform the following functions on behalf or in the absence of the Registrant: sign the DEA Form 222 to receive Schedule II drugs and transfer Schedule I or II substances for destruction, or perform biennial inventory. The Registrant must show the Limited Power of Attorney documents to the DEA upon request and a copy must be provided to CCM (if purchasing Schedule II substances from CCM). A sample POA is available on the Controlled Substances website. A Power of Attorney document is not needed for Schedules III – VI. https://www.deadiversion.usdoj.gov/21cfr/cfr/1305/1305_05.htm

Registration

Formal grant of specific authority for Controlled Substances activities by the DEA and/or VBP sometimes referred to as a Registration Certificate. The Registration is specific to a single physical location. If multiple Controlled Substance storage locations are needed, then multiple Registration Certificates are required. The Registrant is responsible for maintaining their Controlled Substance Registration current and active. Typically, the Registrant covers a single individual laboratory, and in rare instances may cover multiple labs (strongly discouraged).

Registrant

A University Member that holds an active DEA Registration and or VBP Registration Certificate and is ultimately responsible for ordering, storing, using, recordkeeping, and disposing of Controlled Substances kept in their specified physical location. The VBP often refers to this individual as the “Responsible Party.” Typically, the Registrant holds the single Registration for an individual laboratory **AND** is the Principal Investigator on an approved Animal Care and Use protocol. The Registrant must be responsible for the individuals (Authorized Users) using and having access to their Controlled Substances. (See section – Roles and Responsibilities)

Teaching Institution Registration

At UVA the Attending Veterinarian in CCM holds this registration for the administration of Controlled Substances to research animals while providing veterinary care. A DEA registration issued to a teaching institution (for Schedules II-V only) is overseen by an Institutional Veterinary Practitioner.

Transfer

To move a Controlled Substance from the inventory of one DEA Registrant to another DEA Registrant. The routine transfer of Bulk Form and Finished Form Controlled Substances between Registrants is **prohibited**. Limited transfers may be permitted pending strict criteria (See section – Transfer).

University Member

All UVA full- and part-time faculty, classified or University staff, administrative staff, paid student assistants, students (under certain conditions as described in this policy), volunteers, fellows and trainees, visiting faculty and researchers, and those employees and visitors covered by sponsored program agreements or other contractual arrangements are considered University Members for purposes of complying with Controlled Substances regulations.

Usage Records

Maintaining accurate, continuous, and current records reflecting the acquisition, administration, disposal, and biennial inventory of Controlled Substances is necessary to properly document the use of the Controlled Substances within a closed system of distribution. Controlled Substance usage records are retained by each Registrant and Authorized Users. Several recommended forms for recording various aspects of Controlled Substance acquisition, administration, use and disposal are provided on the website associated this manual. The Registrant may choose to use the forms provided or any form that captures the necessary information in an accurate, logical, structured and auditable manner. Records must be maintained for two years after depletion or destruction of the substance. Typically, a file folder or notebook is used to store transactions of Controlled Substances (See section – Notebook).

Virginia Board of Pharmacy (VBP)

The agency authorized by the Commonwealth of Virginia to administer the Drug Control Act and enforce State laws and regulations overseeing the conduct and professional competency of Virginia Board of Pharmacy registrants.

Controlled Substance Definitions (Schedules)

Controlled Substances (CS) are drugs or other chemicals that have the potential to be addictive or habit forming. Both the State and federal law divide controlled substances into five schedules based on their potential to be habit forming (I = greatest, V = least habit forming) and usefulness in medicine as a drug. DEA and VBP jointly regulate these substances. For a more comprehensive listing, see <http://www.deadiversion.usdoj.gov/schedules/>. State law further defines an additional Schedule VI identified in the Code of Virginia. Only the VBP has jurisdiction for Schedule VI drugs.

Schedule I

Drugs or other substances that have a high potential for abuse and no currently accepted medical use in the United States; this category of controlled substances lack accepted safe use under medical supervision.

Examples: Heroin, LSD, Tetrahydrocannabinols (Delta-9-THC), Marijuana, and Cathinone

Schedule II

Drugs or other substances that have a high potential for abuse; currently have an accepted medical use in treatment in the United States, or have a currently accepted medical use with severe restrictions; abuse may lead to severe psychological or physical dependence.

Examples: Fentanyl, Pentobarbital, Morphine, Cocaine, Amphetamine, Oxycodone, and Methadone

Schedule III

Drugs or other substances that have a potential for abuse less than Schedule I or II; currently have an accepted medical use in treatment in the United States; abuse may lead to moderate or low physical and high psychological dependence.

Examples: Ketamine, Buprenorphine, Euthasol® (Pentobarbital/phenytoin mix), Androgens (testosterone), Inactin, and anabolic steroids

Schedule IV

Drugs or other substances that have a low potential for abuse relative to those listed in Schedule III; currently have an accepted medical use in the United States; abuse may lead to limited physical or psychological dependence relative to those in Schedule III.

Examples: Midazolam, Chloral hydrate, Phenobarbital, Benzodiazepines, valium

Schedule V

Drugs or other substances that have a low potential for abuse relative to Schedule IV; currently have an accepted medical use in the United States; abuse may lead to limited physical or psychological dependence relative to those in Schedule IV.

Examples: Zolpidem, Zopiclone, Pregabalin, some Codeine cough preparations (Robitussin)

Schedule VI (VBP only)*

Drugs or other substances recognized by Code of Virginia containing any drug not in Schedules I–V, however, because of potential toxicity, must be prescribed by a prescriber (essentially any prescription medication not included in Schedules I–V).

The following classes of drugs and devices are controlled by Schedule VI:

1. Any compound, mixture, or preparation containing any stimulant or depressant drug exempted from Schedules III, IV or V and designated by the Board as subject to this section.
2. Every drug, not included in Schedules I, II, III, IV or V, or device, which because of its toxicity or other potential harmful effect, or the method of its use, or the collateral measures necessary to its use, is not generally recognized among experts qualified by scientific training and experience to evaluate its safety and efficacy as safe for use except by or under the supervision of a practitioner licensed to prescribe or administer such drug or device.

Examples:

- Inhalation anesthetics such as isoflurane, desflurane, sevoflurane, and enflurane
- Medications requiring prescriptions such as antibiotics, antihypertensive agents, and hormones such as insulin and estrogen
- Some analgesics such as Ketoprofen and Bupivacaine

***Note:** This Schedule is specific to the Commonwealth of Virginia. The federal DEA does not have jurisdiction over the Schedule VI designation.

Registration – Who Must Register

Any Principal Investigator (PI) that orders, stores, or administers **Schedule I - V** Controlled Substances for research use **must register with both the VBP and the DEA**.

PIs that use **only Schedule VI drugs need only register with the VBP**, and do not need to register with the DEA.

Registrants are typically PIs and are linked to an individual laboratory. Registration is linked to a specific physical address (a single physical location) where Controlled Substances are stored. The Registrant must have oversight of the Controlled Substance use to serve as the DEA and or VBP Registrant.

Current Registrants Holding Clinical Practitioner Registrations

A Practitioner Registration from the DEA does permit the following coincidental activities: human investigation, research and physician instructional activities with those substances for which registration was granted. Therefore, a Practitioner may conduct research under their Practitioner registration. However, since a *CS Registration is linked to both the Registrant and a specific physical storage location, a second registration with both VBP and DEA may be needed to store CS in a research laboratory*. If only the Clinical Practitioner's Registration is maintained, then CS used for research must be stored in the same location on the Practitioner Registration.

Registration – Application Process and Initial Inspection

Each Registrant is responsible for obtaining appropriate registrations and adhering to applicable state and federal regulatory requirements when working with Controlled Substances. Registrants must not allow their registration to lapse until all Controlled Substances are used or transferred for Reverse Distribution.

Schedule I – Application for DEA Registration must be sent to the DEA and an application for a Controlled Substances Registration Certificate (CSR) sent to the VBP, simultaneously. A scheduled inspection will be performed by VBP and the DEA. Pursuant to State law, DEA must issue the DEA Registration for Schedule I *prior* to VBP issuing a CSR. A copy of the DEA Registration Certificate must be sent to the VBP in order for the CSR to be issued.

Schedule II – V – Application for VBP for a Controlled Substances Registration Certificate (CSR) is sent prior to the application for DEA Registration. A scheduled inspection will be performed by VBP. After obtaining the VBP registration number, an application for registration must be sent to the DEA. The DEA will perform their own inspection of the registrant.

Schedule VI – Application for a Controlled Substances Registration (CSR) is only sent to VBP. VBP will perform the scheduled inspection and issue the CSR, assuming all is compliant.

Multiple Schedules – For researchers needing to possess drugs in multiple drug Schedules, submission of a single CSR application and a single DEA Registration application is sufficient. Simply note all requested drug Schedules on the applications. First, apply for the VBP CSR and once granted, apply for the DEA Registration. The VBP CSR number will be required in the DEA application.

Examples of completed registration application forms are included on the website associated with this manual. <http://www.virginia.edu/vpr/ControlledSubstances/>

Applying for Virginia Board of Pharmacy Controlled Substance Registration (CSR) Certificate

Obtain the VBP CSR prior to applying for a DEA Registration.

Schedule II – V or Schedule VI

1. Identify the *individual to be the Responsible Party* (Registrant). This individual is typically the PI for an individual laboratory. The Responsible Party will be responsible for the oversight of *all* Controlled Substances on the application. The Responsible Party must provide documentation showing professional competence (curriculum vitae, educational credentials, professional licensure, and training documentation) to use Controlled Substances within the scope of their research activity. Refer to the section Roles and Responsibilities section of this manual.
2. Identify the *secured location* of the Controlled Substances (*physical address*). The one physical location will be linked to the CSR and Registrant. For storage and security requirements, refer to the Storage and Security section of this manual.

It is absolutely required that Controlled Substances are returned to the approved secure location listed on the CSR at the end of each work day, as well as when not in use.

3. Each individual desiring a registration for the use of Controlled Substances in research must complete a *VBP Application for a Controlled Substance Registration Certificate*. Request *all* Schedules II – VI on the same application form. The CSR application must be downloaded (see below) and completed.
4. There is an application *fee* (\$90 in 2019), and federal grants (NIH funds) *cannot* be used. NIH Grants Policy prohibits the use of federal funds for this purpose. Departmental funds, non-federal funds, or personal funds can be used.
5. The *completed application packet* must be *mailed* to the Virginia Board of Pharmacy at the address listed on the top of the application. (All forms and logs below are available on the CS website).

A complete application packet contains all of the items listed in the table below.

VBP Application for a Controlled Substance Registration Certificate form - https://www.dhp.virginia.gov/Forms/pharmacy/0220ControlledSubstanceRegistrationApp.pdf
Check for fee
UVA Controlled Substance Research Protocol form. This form contains excerpts from the animal care and use protocol(s) to describe specifically how the Controlled Substances are to be used and detailing why it is necessary to use the Controlled Substances within the research.
Curriculum Vitae of the Responsible Party (Registrant)
Controlled Substance Inventory Log (blank)
Controlled Substance Usage and Disposal Log (blank)
Completed Controlled Substance Personnel Screening forms for all Authorized Users
Floor plan with security features (using Excel, something basic)
Picture of storage/safe
Power of Attorney letter (for Schedule II only)

6. Prior to issuance of a Controlled Substance Registration Certificate, a VBP inspector will schedule and conduct an *interview and inspection with the applicant* (e.g. Responsible Party, Registrant) to ensure that appropriate safeguards are in place to secure Controlled Substances. A VBP inspector will call the Responsible Party to confirm readiness for inspection and schedule an inspection date. If the inspector does not call to confirm the date, the responsible party should call the Enforcement Division at (804) 367-4691 to verify the inspection date with the inspector. A 14-day notice is required for scheduling an opening or change of location inspection.

The VBP CSR registration is *valid for up to one (1) year beginning February 28th*. Application fees after February 28th are not prorated.

Schedule I

The application process with the VBP for Schedule I use is very similar to the guidelines above; however, **DEA must issue the DEA registration prior to the VBP issuing the CSR**. Once DEA Schedule I Registration is obtained, a copy of the DEA Registration Certificate must be sent to the VBP with the VBP registration form to complete the process of Schedule I registration.

Applying for DEA Registration

Obtain the VBP CSR prior to applying for a DEA Registration.

Schedule II – V

1. The individual that was the Responsible Party on the VBP CSR will be the *Registrant* on the *DEA Registration*. Refer to the section Roles and Responsibilities section of this manual. The VBP registration number is required to complete the DEA application.
2. The *secured location* of the Controlled Substances (*physical address*) will be the same location as listed in the VBP CSR. The one physical location will be linked to the Registrant and Registration. For storage and security requirements, refer to the Storage and Security section of this manual.

It is absolutely required that Controlled Substances are returned to the approved secure location listed on the Registration at the end of each work day, as well as when not in use.

3. Each individual desiring a registration for the use of Controlled Substances in research must complete a *DEA Application for Registration* (Form 225) for Researcher. Request *all* Schedules II – V that were identified on the VBP Registration in the same DEA application form **online** at: <https://apps.dea diversion.usdoj.gov/webforms/jsp/regapps/common/newAppLogin.jsp>
4. There is an application *fee*; however, the fee is *waived* for research applications with tax exempt status. Failure to use the tax-exempt status will result in an annual fee.
5. Prepare a *completed application packet* similar to the one used for the VBP application; however, remove all references to Schedule VI drugs. The DEA does not recognize Schedule VI.
 - A completed application packet contains all of the items listed in the table below.
 - Create one pdf containing all of the items. The pdf will be attached to the online application and/or sent directly to the DEA Inspector.
 - The forms and logs and examples of completed applications are available on the CS website. <http://www.virginia.edu/vpr/ControlledSubstances/>

A complete application packet contains all of the items listed in the table below.

<p>Application for Registration, DEA Form-225 is completed online</p> <ul style="list-style-type: none"> • https://apps.deadiversion.usdoj.gov/webforms/jsp/regapps/common/newAppLogin.jsp • Section 1 – select Individual Registration • UVA Tax Identification Number: 54-6001796; Provide Registrant’s SSN • Section 2 – select Researcher • Section 3 – Ketamine is Schedule IIIN; Buprenorphine, Euthasol, and Inactin are Schedule III; pentobarbital is Schedule II • Section 4 – List the VBP CSR number and expiration date • Section 6 – Exemption from Application Fee Certifying Official: Jenn Glassman, Director Procurement & Supplier Diversity Services, JGLASSMAN@virginia.edu , 434-924-4019 • Drug Codes can be found online https://www.deadiversion.usdoj.gov/schedules/orangebook/c_cs_alpha.pdf
<p><i>UVA Controlled Substance Research Protocol form.</i> This form contains excerpts from the animal care and use protocol(s) to describe specifically how the Controlled Substances are to be used and detailing why it is necessary to use the Controlled Substances within the research. Remove all references to Schedule VI.</p>
<p><i>Curriculum Vitae</i> of the Registrant</p>
<p>Controlled Substance Inventory Log (blank)</p>
<p>Controlled Substance Usage and Disposal Log (blank)</p>
<p><i>Completed</i> Controlled Substance Personnel Screening forms for all Authorized Users.</p>
<p><i>Completed</i> Access Forms for all Authorized Users This is specifically for DEA applications (not needed for VBP) Only include the last 4 digits of the SSN on the form</p>
<p><i>Copy</i> of Virginia Board of Pharmacy License</p>
<p>Floor plan with security features</p>
<p>Picture of storage/safe</p>
<p>Power of Attorney letters (for Schedule II only)</p>

6. Prior to issuance of a Registration, a DEA inspector will schedule and conduct an *interview and inspection with the applicant* (Registrant) to ensure that appropriate safeguards are in place to secure Controlled Substances. A DEA inspector will contact the applicant to confirm readiness for inspection and schedule an inspection date.

The DEA Registration is *valid for up to one (1) year from the date of issuance.*

Schedule I

The application process with the DEA for Schedule I use is very similar to the guidelines above; however, **DEA must issue the DEA registration prior to the VBP issuing the CSR.** Schedule I applications for the DEA cannot be submitted online. Schedule I registration application DEA Form 225 form is found at URL: https://www.deadiversion.usdoj.gov/drugreg/reg_apps/225/225_form.pdf and must be mailed to the address provided in Section 7 of the application.

Troubleshooting the Application Forms

Use the checklists provided in the UVA Controlled Substance Research Protocol. Keep the following points in mind when completing the application forms:

- Addresses for state and federal registrations must be the same.
- Address must be a single physical geographic location (building name and room number) for secure storage of the Controlled Substances.
- Postal Address vs Physical Address: If the specific location does not have a US Postal delivery (the storage location is a lab bench in the back room), then list the nearest postal delivery address, and on the next line list the geographic location by building/room number. Addresses must have the geographic location of the Controlled Substance storage cabinet.
- Shipping Address: The “Ship To” address is the address on the federal DEA registration. It is a violation to ship to any address other than the federal DEA address listed on the Registration certificate. This address must be the storage location (not a PO Box).
- The Schedules of substances listed on one registration (federal DEA) must be the same as the Schedules listed in the other registration (VBP). The only exception is Schedule IV.
- Any Schedule of agents listed on either a state or federal registration must have that agent as part of their ACUC animal care and use protocol.

Filing VBP Registration Certificates and/or DEA Registrations with UVA

In order to obtain Controlled Substances by distribution from the Center for Comparative Medicine (CCM) wholesale pharmacy, the Registrant *must* provide a copy of their *current* VBP Registration Certificate and DEA Registration to CCM (Box 800737, shf2B@virginia.edu).

Maintaining the Registration

Registration Amendments

Registrants that require the **addition of Controlled Substances in Schedules not currently listed** on their Registration Certificates must amend their Registrations by submitting the CSR application to VBP and DEA indicating “change in drug schedule”. Amendments are not needed when obtaining Controlled Substances that are within the Schedule(s) on the approved Registrations. Amendments to registrations Controlled Substance Schedules must be approved by the DEA and VBP prior to ordering, inventorying, or using such substances.

A *new Registration* is required for each *new location* for secure storage. Amendments *do not* change storage or use locations.

Schedule I Amendments – A letter with the revised UVA Controlled Substance Research Protocol, specifically highlighting the changed information must be sent to: US Department of Justice, Drug Enforcement Administration, ATTEN: Registration Section ODR, PO Box 2639, Springfield, VA 22152-2639.

Schedule II – V Amendments – A letter with the revised UVA Controlled Substance Research Protocol, specifically highlighting the changed information must be sent to the Richmond DEA Office for updating their database. The Richmond DEA Office will not issue specific approvals for additional Schedule II-V substances. A copy of the Controlled Substance protocol approval forwarded to the Richmond DEA Office will be sent to the Registrant.

Required Notifications

Registrants must notify the DEA and VBP after changes in name, address, telephone, Schedules, or any information required on the application or Registration. Changes must be submitted within six (6) days of the change.

Registration Renewals

Renewals for both VBP and DEA Registrations are completed *online annually*.

- **VBP** typically sends a reminder notice to the Registrant approximately two months prior to the annual expiration (February 28th) and provides the website link and passcode to enter in the renewal site. There is a fee associated with renewals. <https://www.dhp.virginia.gov/mylicense/renewalintro.asp>
- **DEA** typically sends a reminder notice approximately three (3) months prior to the annual expiration. The annual fee can be waived for research applications with tax exempt status. DEA online renewals are completed at:
<https://apps.dea.diversion.usdoj.gov/webforms/jsp/regapps/common/renewalAppLogin.jsp>

Ending or Closing Out a Registration

Under no circumstances are Controlled Substances to be abandoned by a DEA/VBP Registrant. Registrants are expected to properly dispose of Controlled Substance inventory when Controlled Substances are no longer required or prior to their departure from their University position. See “Controlled Substance Disposal” section in this manual. Any person who is registered with the DEA who violates record-keeping requirements or abandons Controlled Substances is subject to the civil penalties outlined in the United States Code (USC): 21 USC Sec. 842. Note that abandoning substances is equivalent to diversion of a Controlled Substance to an unauthorized person.

VBP and DEA Inspections

The VBP and DEA typically call the Registrant listed on the application to schedule a time for their initial inspection. The Registrant must be present for the initial inspection. After the initial inspection, both the DEA and the VBP may conduct unannounced routine inspections. VBP generally performs unannounced routine inspections every 2-3 years. In preparing for an inspection, the DEA will refer to their database for the list of substances approved for the Registrant, so ensuring that DEA is notified via the amendment process is extremely important. *Substances in a Registrant’s inventory that do not match the DEA’s database is cause for a finding of violation of the law.*

Institutional Monitoring

The Vice President for Research provides guidance to faculty members for registering with state and federal agencies through the use of this manual and the associated online website. *There is no statutory requirement for institutional management of Controlled Substance registrations.*

Registrations for the use of Controlled Substances are a Principal Investigator individual obligation.

The OAW, as part of the animal care and use post-approval monitoring program and members of the Animal Care and Use Committee (ACUC), as part of the semi-annual inspection of animal use areas will review Controlled Substances, storage, and usage records for compliance with USDA regulations and NIH Guidelines. These institutional inspections do not constitute a review of a Registrant's compliance with DEA and/or VBP Regulations. The OAW and ACUC inspections are mandated under the University's PHS Assurance to NIH and required by the USDA for research using regulated species. The Registrant is solely responsible for the compliance of their Authorized Users associated with their Registration in accordance with DEA and or VBP Regulations.

Institutional Registration

CCM is registered with VBP and DEA as a Wholesale Distributor within the University of Virginia. CCM maintains a database of current Researcher Controlled Substance Registrations (both DEA and VBP) for the purpose of internal sales of veterinary Controlled Substances. CCM stocks veterinary Controlled Substances and will only distribute them to a laboratory that has current VBP and DEA Controlled Substance Registrations; in the case of Schedule VI drugs, the lab must possess a current VBP Controlled Substance Registration.

Operational Roles and Responsibilities

Registrant Responsibilities Include:

- Submission of application, amendments, and renewals involved with their Registration(s).
- Must be present for initial inspection by VBP and DEA.
- Must submit copies of in-date VBP CSR and DEA Registration to CCM Office if acquiring Controlled Substances from CCM (see Ordering section of this manual).
- Manage the Controlled Substances in their possession in accordance with the requirements of federal and state regulations. Oversee the use of Controlled Substances by all Authorized Users. Create laboratory-specific training as needed to train Authorized Users.
- Select, screen, and train Authorized Users (see screening process below).
- Ensure that only the Registrant submits orders (acquisition) for Controlled Substances and appropriate forms must be used. Registrants must exercise signature authority for purchases of Schedule I and II drugs (see Ordering section of this manual).
- Ensure that Controlled Substances are secured and stored in accordance with federal and state regulations, and maintain strict control over inventory (see Storage and Security section of this manual).
- Supervise inventory, dispensing, and disposal of Controlled Substances when used in vivo or in vitro by Authorized Users (see associated sections of this manual).
- Maintain all required usage logs and documentation (see Documentation section of this manual and refer to forms and logs on CS website).
- Conduct and document initial and biennial (every two years) inventory as per DEA Regulations and for Schedule VI per VBP Regulations (see Documentation section of this manual).
- Report theft or loss of any Controlled Substances to the DEA and VBP (see theft and diversion sections of this manual).
- Report DEA and VBP inspection audit findings of non-compliance to the VPR within five (5) business days of notice received by Registrant.

Registrant Screening and Selection Process for Authorized Users

Having Authorized Users associated with the VBP and/or DEA Registration is not required; however, it is necessary if anyone other than the Registrant will have access to the Controlled Substances storage or administration under the Registration. Every University Member identified by the Registrant as being an Authorized User must complete the screening process and complete several forms. Forms are available on the CS website - <http://www.virginia.edu/vpr/ControlledSubstances/>

- **Personnel Screening Form** - (21 CFR 1301.90). This form must be completed *prior* to the Registrant authorizing the individual to work with Controlled Substances. The three questions on the form (below) are listed within the regulations. If the answer to any question is “yes”, then the person should not be allowed to possess or administer Controlled Substances.
 1. Within the past five years, have you been convicted of a felony, or, within the past two years, any misdemeanor, or, are you presently charged with committing a criminal offense?
 2. In the past 3 years, have you knowingly used narcotics, amphetamines, or barbiturates other than those prescribed to you by a physician?
 3. Have you ever been denied a DEA registration, had a DEA registration revoked or surrendered a DEA registration for cause?

A copy of this form must be sent to the VBP and DEA during the initial application process. Both new hires and students must complete the form prior to becoming an Authorized User. Keep the questionnaires in a separate secured file at the registered location for *two years* after the departure of the Authorized User. These documents are considered sensitive and should be locked securely as with other sensitive employment information held by the Registrant.

- **Personnel with Access to Controlled Substances** – This form is specific to the DEA and completed copies must be sent to the DEA during the initial application process. This form must be completed by all Authorized Users. The Registrant will determine on this form what type of access each Authorized User has – indirect or direct. *Indirect access* Authorized Users only have access to small diluted amounts of Controlled Substances and do not have storage access privileges. Authorized Users with *direct access* have storage access privileges and access to bulk quantities. Only provide the last four digits of the social security number. Keep the questionnaires in a separate secured file at the registered location for *two years* after the departure of the Authorized User. These documents are considered sensitive and should be locked securely as with other sensitive employment information held by the Registrant.
- **Authorized Users Signature Log for Schedule II – VI Controlled Substances** – This form must be initially completed by each Authorized User after the Registrant screens and then certifies the person is an Authorized User associated with their Registration. The “date departed” is completed by the Registrant once the Authorized User is no longer authorized to come in contact with the Registrant’s Controlled Substances. A similar form is used for Schedule I Controlled Substances. This form is maintained within the Controlled Substances documentation notebook.

Authorized User Responsibilities Include:

Authorized Users must be identified, screened, and certified by each Registrant who allows the individual to engage in approved activities under the Registrant's Registration. Examples of Authorized Users could include: post-doctoral fellows, University Staff, Classified Staff, or graduate students. Typically, the Authorized User reports directly to the Registrant or is funded by the Registrant.

- Complete Personnel Screening form and Personnel with Access to CS form prior to commencing use of Controlled Substances for the Registrant.
- Complete laboratory –specific training on procedures for using Controlled Substances prior to working with them.
- Once certified by the Registrant, sign the Authorized Users Signature Log specific to the Schedule of authorized use.
- Complete all required usage logs and documentation (see Documentation section of this manual). Return usage logs to the Registrant (or designee) once a Controlled Substance has been used, expired, or no longer needed.
- Store Controlled Substances appropriately in the location listed on the Registration and based on the Registrant's requirements for securing them by the end of each workday or when not in use.
It is absolutely required that Controlled Substances, when not used, are returned to the secure location at the address on the Registration by the end of each day.
- Immediately report any discrepancy or suspected theft to the Registrant (see theft and diversion sections of this manual).
- Immediately report to the Registrant any felony violations or convictions.

Theft or Significant Loss

If theft is suspected, the Registrant will **immediately notify the UVA Police, VBP and the DEA.**

The *DEA* requires that theft or loss of Controlled Substances be reported within 24 hours on DEA Form-106, Report of Theft or Loss of Controlled Substances -

<https://apps.deadiversion.usdoj.gov/webforms/dtlLogin.jsp>. A copy of Form-106 will be kept with the inventory records (21 CFR 1301.91). Phone: 202-305-8888.

Virginia State law requires a theft or unusual loss to be immediately reported to the *VBP* using the DEA Form-106 (see above link) with a written itemization of the drugs lost or stolen within 30 days (54.1-3404 of the Drug Control Act). Retain a copy of Form-106 with the inventory records. Phone: 804-367-4456.

If an *open container* of a Controlled Substance is *broken*, it must be documented in the usage record and a witness must sign and date the form. If an *unopen container* of a Controlled Substance is *broken*, then it must be given its own usage record and then documented in that record.

Employee Responsibility to Report Drug Diversion (21 CFR 1301.91)

Diversion is the transfer of a Controlled Substance from a lawful to an unlawful channel of distribution or use (using it illegally). According to Code of Federal Regulations,

"Reports of drug diversion by fellow employees are not only a necessary part of an overall employee security program but also serve the public interest at large. It is, therefore, the position of DEA that an employee who has knowledge of drug diversion from his employer by a fellow employee has an obligation to report such information to a responsible security official of the employer. The employer shall treat such information as confidential and shall take all reasonable steps to protect the confidentiality of the information and the identity of the employee furnishing the information."

An employee who has knowledge of drug diversion associated with the actions of a fellow employee, student, or supervisor has a legal obligation to report such information to their supervisor.

Storing and Securing Controlled Substances

Registrants must keep Controlled Substances in a substantially constructed, not easily moved, and securely locked cabinet (or safe) that meets DEA/VBP requirements. Controlled Substances must **not be visible** through a glass panel. The Registrant is responsible for securing access to the storage location and physical storage containment. Records and documentation on Controlled Substances must also be secured.

Keys to Controlled Substance storage must be secured such as establishing a key control system (e.g., a log to track who has a key). Cipher lock (combination locks) combinations should be extremely limited or changed periodically as Authorized Users terminate use of Controlled Substances.

Schedule I

Must be stored in a substantially constructed, securely locked cabinet (safe), **separate** from other Scheduled Controlled Substances. The cabinet must be secured to a wall or otherwise not removable, as per Federal Regulations. *DEA Form 222 must be secured/locked.*

Schedule II

Must be stored in a substantially constructed, securely locked cabinet (safe), **separate** from other Scheduled Controlled Substances. The separation of Schedule II substances from other Controlled Substances can be on a separate shelf, in a separate box, or in a separate compartment from other Controlled Substance Schedules. The cabinet must be secured to a wall or otherwise not removable, as per Federal Regulations. *DEA Form 222 must be secured/locked.*

Schedule III – V

Must be locked cabinet or safe. The cabinet must be secured to a wall or otherwise not removable, as per Federal Regulations.

Schedule VI

Substances **not in use** must be in a locked cabinet or safe.

All Controlled Substances must be kept locked in their storage location except for the actual time required to remove and legitimately work with them and then be replaced back into the approved secure storage location listed in the Registration. Standard narcotic cabinets can be purchased through various vendors. Remember that DEA Regulations require that the cabinet be secured so that it cannot be easily removed.

The Registrant must **restrict access** to locked rooms and locked storage cabinets containing Controlled Substances, and the Registrant must determine how their Authorized Users will access substances. At the room location on the Registration, Controlled Substances, either Bulk or Finished Form, can be stored in one or more locations as long as they are locked in a container that is not easily moved (e.g., file cabinet, desk, safe, etc.). Usage logs must be completed for each secured location and returned to

the DEA Registrant upon completion. At the end of the workday, all Controlled Substances must be returned and physically secured at the location written on the Registration.

Requirements for Working with Controlled Substances

Working with Controlled Substances requires specific procedures to ensure that practices are in accordance with federal and state regulations. The associated documentation must demonstrate a ***closed system of distribution*** wherein each controlled substance is accounted for from acquisition through to use and disposal. *The chain of custody and usage must be documented.*

Typical categories include: acquisition (ordering), receiving, administration (use), inventory, and disposal. Each of these categories must be documented. Sample forms are available on the Controlled Substances website associated with this manual (<http://www.virginia.edu/vpr/ControlledSubstances/forms.html>). The use of these specific forms is not required; however, these templates incorporate all the required elements from the applicable regulations. Any format used must meet the requirements of all pertinent regulations. Individuals should determine a consistent documentation process to ensure best compliance practices.

Maintaining usage records or log book to record all Controlled Substances in Schedules I – V is required. An accurate, continuous, and current record is required and necessary to validate proper use of Controlled Substances. Organization and retention of documentation are discussed in the Recordkeeping section of this manual.

For **VBP Schedule VI substances**, evidence of acquisition (copy of packing slip) is the only required recordkeeping document that must be maintained. Bi-annual inventory, usage, and disposal recordkeeping documents are not required for Schedule VI substances (54.1-3404, Chapter 34 of Title 54.1 of the Code of Virginia the Drug Control Act

<https://www.dhp.virginia.gov/pharmacy/leg/Chapter%2034%20Drug%20Control%20Act.doc>).

Acquisition: Purchasing CS

Registrants may *only* acquire substances identified on their approved DEA Protocols (Schedule I) and VBP and DEA Registrations (Schedule II-VI).

Controlled Substances may be ordered/purchased through standard procurement processes such as through Wholesale Distributors and Pharmacies. CCM is a Wholesale Distributor and stocks some commonly used veterinary Controlled Substances in Schedules II-VI. CCM will only sell Controlled Substances to Registrants that have provided CCM with scanned copies their valid DEA Registration and VBP Registration Certificate. Purchases are made through NetBadge Authentication within the CCM purchasing system. Users must request a username and password from CCM in order to access the purchasing system. Additionally, the purchasing database only allows purchasers to select substances within the schedules listed on their Registration.

CCM only distributes Bulk Form substances and will not compound them into Finished Form compounds since this is prohibited by law. A compounding formulary is provided on the CCM website (<https://www.virginia.edu/vpr/ccm/docs/Rodent%20anesthetic-analgesic%20drug%20mixtures.pdf>) so that researchers can dilute and compound substances for animal use (for example - anesthetic mixtures of ketamine and xylazine). Controlled Substances often have expiration dates in the near future, and so should be ordered and maintained in the smallest quantity necessary to achieve research goals. As a Wholesale Distributor, CCM will provide a packing slip for all purchases. All packing slips must be retained in the record log book (see Recordkeeping section of this manual).

Schedule II – Requires DEA Form 222 and maybe a Power of Attorney

DEA and VBP Registrants can only obtain Schedule II substances using a completed and signed DEA Form 222, regardless of the source (Wholesale Distributor or Pharmacy). The Registrant must submit the completed Form 222 (produces two carbon copies) to the Distributor for their signature. The Distributor will complete the form of transfer, retain a copy, submit the other copy to the Regional DEA Office in Richmond, VA, and return one copy with the Controlled Substance to the Registrant.

DEA Form 222 is unique to each Registrant. DO NOT share DEA Form 222 with other Registrants. The Registrant must place requests to the DEA for ordering DEA Form 222. Instructions for ordering DEA Form 222 can be found at: <http://www.dea diversion.usdoj.gov/faq/dea222.htm>.

DEA Form 222 must be maintained separately from all other records. If Form 222 is lost or stolen it must be reported to the Special Agent in charge of the DEA Divisional Office.

A limited ***Power of Attorney*** document must be used if the Registrant plans to give another individual signatory authority to sign Form 222 and obtain Schedule II Controlled Substances on their behalf. If the Registrant personally orders and obtains the Schedule II substance, then a Power of Attorney (POA) document is not needed. A copy of the POA must be on file with CCM prior to placing the Schedule II order. A sample POA is located on the Controlled Substance website associated with this manual.

Obtaining Schedule II substances from CCM:

- Limited Power of Attorney document is on file with CCM (as applicable).
- The Registrant must submit their own multipart DEA Form 222 with the order to CCM.
- After signing and submitting Form 222, CCM will mail a copy of the form to the Richmond DEA Office and retain a copy for their own records
- CCM will return a copy to the Registrant to retain for their records as well as provide a packing slip reflecting the Controlled Substances purchased and the registration DEA information of CCM and the purchaser.

Schedule III – V – These controlled substances must be ordered/purchased by a DEA and VBP Registrant through standard procurement processes and procurement records (packing slip) must be maintained. Purchases through the CCM Wholesale Distributor are made through the online purchasing system, and packing slip must be retained.

Schedule VI – Controlled Substances must be ordered/purchased by a Registrant with a VBP Registration Certificate. The DEA does not recognize Schedule VI; therefore, registration with the DEA is not required for this particular schedule of compounds. All packing slips must be retained.

Schedule I – Requests to obtain Schedule I substances not commercially available must be made to the National Institute on Drug Abuse (<http://www.nida.nih.gov/>). Registrants can only obtain Schedule II substances using a completed and signed DEA Form 222 (see details above regarding Form 222 for Schedule II). Schedule I substances are NOT available through CCM.

The *NIDA Drug Supply Program (NDSA)* provides various Controlled Substances, other chemical substances, and marijuana and nicotine research cigarettes for research purposes to research investigators working in the area of drug abuse, drug addiction, and related disciplines at academic institutions. In order to obtain these substances from NIDA, research investigators and other users are required to submit their requests along with necessary documents to the NIDA Drug Supply Program for consideration. <http://www.drugabuse.gov/sites/default/files/files/OrderingGuidelinesUS.pdf>.

Transferring Controlled Substances Between Registrants

Registrants with valid VBP and DEA Registrations are *prohibited from routinely transferring CS* to another VBP/DEA Registrant or Registration. Transfers of CS between two Registrations are limited to two types of transfers and *can only occur once* or at most very infrequently:

- Between the Clinical and Researcher DEA Registrations for the same Registrant. Both Registrations must have approval for the same schedule of the compound being transferred.
- Between two Researcher DEA Registrations (two different people) and both Registrations must have approval for the same schedule of the compound being transferred.

The *following conditions MUST apply* (to the two scenarios described above):

- Transfer is permitted only once or at most very infrequently
- Transferred substance cannot be more than 5% of the inventory of the transferor
- Transferred substance must be a completely unopened stock vial (no partial vials)
- Transferor *must* generate an appropriate *typed packing slip* that includes the following:
 - Name and Address of each Registrant with designation of “Transferor” and “Recipient”
 - DEA Registration numbers for both parties
 - Drug name, National Drug Code (NDC) #, Lot #, and manufacturer
 - Volume and Concentration of the drug(s) transferred
 - Number of units transferred (number of bottles)
 - Signature of the Receiver and date of transfer
 - Both parties keep a copy of the signed and dated form

Receiving CS

Controlled Substances must be shipped directly to the DEA Registrant at the address indicated on the DEA Registration. Once received, the Controlled Substances must be opened and the contents verified by the Registrant. Any discrepancies must be rectified with the supplier and/or vendor. If discrepancies cannot be rectified, the DEA Registrant must contact the DEA and VBP to report the discrepancy within five (5) business days.

CS in Schedules II – V obtained from the CCM Wholesale Distributor can only be picked up during specific Controlled Substances Office Hours and with the Authorized Users University-issued identification badge. Substances are picked up in the CCM Office, MR-5, room G010. Contact the CCM Office for current CS Office Hour times.

The DEA Registrant must sign and date the purchase receipt (packing slip) and file it with their Controlled Substances records. Schedule I and II packing slips must be maintained *physically separated* from Schedules III-VI. Once received, the Controlled Substances must be immediately secured in the location indicated on the Registration and in accordance with federal and state regulations (see the Storage and Security section of this manual).

Administering (Dispensing) CS

The DEA/VBP Registrant and their Authorized Users are the only individuals permitted access to the Controlled Substances in the inventory. The Registrant will determine what type of access each Authorized User has – indirect or direct. *Indirect access* Authorized Users only have access to small diluted amounts of Controlled Substances and do not have storage access privileges. Authorized Users with *direct access* have storage access privileges and access to bulk quantities.

Administering or dispensing Controlled Substances occurs when an Authorized User (AU) obtains the required quantity of CS from the CS storage for administration during an experiment. The AU must complete documentation of CS removal from storage and CS administration by making a written record of the substance administered, quantity used, and any wastage. Every ml, mg, or tablet of a Controlled Substance must be accounted for in the usage records (see recordkeeping section of this manual).

At the end of each research use, Authorized Users must return all Controlled Substances in Schedules I - V to the secure approved storage area at the physical location on the Registration Certificate. There can be individual secure storage areas, or a collective secure storage area, at the same physical address on the Registration. Containers of Schedule VI (isoflurane) currently in use may be kept in the use area (beside the precision vaporizer).

Transporting CS Between University Buildings

Small quantities of Finished Form substances for administration may be transported between different building addresses on Grounds and the use (not location of use) must be noted on the usage log sheets. In all cases, CS must be stored in accordance with DEA and VBP regulations. Bulk form substances **cannot** be transported between University buildings unless being distributed (i.e. via a Form 222 or packing slip) from a Wholesale Distributor or Pharmacy to a Registrant.

Disposal and Destruction of CS

Appropriately dispose of Controlled Substances that are no longer supported by an active approved protocol, or are expired, damaged, contaminated, residual (waste) or otherwise unusable or unneeded. CS must be disposed of by a mechanism rendering them unusable, irretrievable and unrecoverable by an approved DEA and VBP method.

Bulk (Stock) Vials

Registrants are responsible for destroying sealed or partially used Bulk (stock) CS by Reverse Distribution. Destruction is accomplished by transferring the sealed or partially used Bulk (stock) form CS (in original container) directly to a Reverse Distributor for destruction. The Registrant must complete **DEA Form 41** - https://www.deadiversion.usdoj.gov/21cfr_reports/surrend/41_form.pdf and supply the NDC or NADA number on the form. The number is typically found on the original container. *Schedules III, IV, and V substances are submitted on a single completed DEA Form 41.* The usage records must document Reverse Distribution and retain Reverse Distribution documentation (including copy of DEA Form 41).

Schedule II CS are shipped separated from the other Schedules in tamper-resistant packaging supplied by the reverse distributor *and* Schedule II substances requires that the Reverse Distributor first send the Registrant their DEA Form 222 for signatures prior to shipping Schedule II substances. A separate DEA Form 41 must be used for all Schedule II substances.

Registrants can use any DEA approved Reverse Distributor. Reliable Pharmaceutical Returns (RPreturns.com) provides an online system to generate the DEA Form 41 (see guidance document on the CS website associated with this manual).

Bulk/Stock vials containing less than 10% of the original volume may be rendered unusable and discarded in the CCM Cactus Sink located in MR5, G010. Documentation of this waste must be documented and witnessed by another Authorized User.

Finish (Compounded) Form Vials

Finished Form or compounded drugs (anesthetic mixtures or CS dilutions) that are expired or no longer usable must be discarded in the Cactus Sink (or comparable method rendering the substance unusable, unrecoverable, and irretrievable) located in the CCM Office (MR5, G010). This wastage must be documented on the usage logs as well as on the documentation located at the CCM Cactus Sink. Very small quantities (less than 0.2ml) of CS wastage can be discarded in the Cactus Sink and recorded on the usage log sheet and witnessed by another Authorized User.

Labeling Expired Drugs Awaiting Reverse Distribution

Expired or unusable substances must be labeled, separated, and stored securely according to DEA requirements for the highest level Schedule associated with the Controlled Substances that require disposal. Each vial must be labeled as “expired” or “waste” and placed into a separate box or bag labeled as “DO NOT USE-EXPIRED” clearly on the outside of the box. The closed, labeled box must

be kept within the same cabinet where inventory is stored. Expired compounds must remain on the inventory until reverse distributed.

Empty vials or bottles should be discarded as glass waste.

CS Inventory Requirements

Once a DEA Registration is issued, the Registrant must take an **initial inventory**, which is an actual physical count of all Controlled Substances in their possession. The Registrant should make a record showing what is on hand, typically zero, during the registration inspection.

The Registrant must perform a **complete Controlled Substance inventory every two (2) years (biennial)** to meet DEA requirements (21 CFR 1304.11) for all Schedule I – V substances. *The inventory may be taken on any date which is within two years of the previous biennial inventory date and must indicate whether it was performed at the opening or closing of the day.* The inventory must be updated on the effective date of a rule (from the DEA) when a substance is added to the Schedule (list of Controlled Substances). Sample inventory log sheets are available on the CS website associated with this manual. The inventory must be maintained in the documentation notebook.

Inventory requirements for each substance that is expired, damaged, defective, impure or expired and awaiting disposal are: name of substance; total quantity of the substance to the nearest metric unit weight or the total number of units of finished form (i.e. fifty 10 mg tablets or 10 ml of 50 mg/ml); and reason the substance is being maintained by the Registrant and whether such substance is capable of use in the manufacture of any Controlled Substance in Finished form. This information is typically on the “Controlled Substance Usage and Disposal Log” form.

The Registrant is responsible for maintaining a Controlled Substances inventory for Schedule I – V substances. The inventory must be maintained at the registered location (unless a notification has been sent to DEA notifying that records will be maintained at a specified central location) and made available for two (2) years after the substance has been used or disposed. This type of inventory is typically within the usage log sheet. See Recordkeeping section of this manual.

Recordkeeping Requirements and CS Notebook Organization

There are a number of records that must be maintained by the Registrant at the location identified on the Registration – **Authorized User records** and **usage and disposal records**. Requirements for use are located in sections of this manual. Sample templates of the forms listed below are available on the CS website associated with this manual (<http://www.virginia.edu/vpr/ControlledSubstances/forms.html>); however, any form that captures the same required information in an accurate, logical, structured and auditable manner can be used by the Registrant.

A **CS notebook** must be maintained (file, folder, binder) containing the documentation of CS transactions demonstrating a closed system of distribution. An accurate, continuous, and current record reflecting the acquisition, administration (use), disposal, and biennial inventory of CS in Schedules I – V is necessary to validate proper documentation of use of CS.

Schedule II Controlled Substance records must be physically separated from the documentation and records of Schedules III – VI, similar to the physical separation of these substances in locked storage.

- Schedules I – Maintain separate storage area, usage/disposal logs, and inventory in a *physically separate notebook* from other Schedules
- Schedule II – Maintain separate storage area, usage/disposal logs, and inventory in a *physically separate notebook* from other Schedules
- Schedules III – V – Maintain in the same notebook
- Schedule VI – Maintain a separate notebook from other Schedules

Authorized User forms

As described in the Authorized User section of this manual, the Registrant must maintain clearance records for every Authorized User associated with the Registration. These forms contain sensitive information and should not be stored in the CS notebook and instead be locked securely as with other sensitive employment information maintained by the Registrant. The Authorized User Signature form must be maintained with the CS notebook associated with the appropriate Schedule. Personnel forms included below must be **retained for two (2) years** after the Authorized User is no longer associated with the Registration.

- *Maintained in a secure personnel file:*
 - **Personnel Screening form** – required for all Authorized Users for all Schedules
 - **Personnel with Access to CS** – required for Authorized Users for Schedules regulated by the DEA (Schedules I – V)
- **Authorized User Signature form** – maintained **inside** the CS Notebook based on Schedule. Schedules I and II are maintained separately from Schedules I – VI.

Suggested CS Notebook Sections Based on Required Documentation

Records must be **maintained for at least two (2) years** after the depletion or destruction of the Controlled Substance.

Documentation requirements depends on the Schedule of CS approved on the Registration. The Registrant is ultimately responsible for compliance with VBP and DEA regulations regarding documentation and recordkeeping and for ensuring that all Authorized Users complete records accurately and completely.

Schedule I – V: maintain bi-annual inventory, acquisition, usage, and disposal documentation in order to demonstrate a closed system of distribution for all CS transactions – starting with the time a Controlled Substance is received on Grounds through to usage and disposal. Every ml, mg, or tablet of CS must be accounted for in the documentation demonstrating a record of the chain of custody and usage. Each point at which the CS changes Registrations or is used must be documented.

Schedule VI (VBP): Evidence of acquisition (copy of packing slip) is the only required recordkeeping document that must be maintained. Bi-annual inventory, usage, and disposal documents are not required for these substances (see 54.1-3404, Chapter 34 of Title 54.1 of the Code of Virginia the Drug Control Act <https://www.dhp.virginia.gov/pharmacy/leg/Chapter%2034%20Drug%20Control%20Act.doc>).

Below are recommended sections within a CS Notebook. Page dividers and plastic sheet protector pockets are very useful when organizing the different sections and individual vials. The notes of “optional” and “required” are based on information above.

1. **Background Information** (optional)
 - Copy of current in-date DEA Registration and VBP Registration Certificate
 - Controlled Substance Research Protocol including *theft procedures* (as submitted with original Registration application)
 - Copy of amendments to Registration(s)
2. **Authorized Users** (*required*)
 - Authorized User Signature form specific to Schedules in Registration(s)
 - Copy of Power of Attorney (for Schedule II only)
3. **Inventory** (*required*)
 - Initial inventory
 - Biennial inventory
4. **Acquisition/Purchasing** (*required*)
 - Purchasing log/Tracking –form used to track Controlled Substance acquisition, numbering/tracking system, and disposal. Suggested columns include:
 - Date of acquisition/purchase
 - Name, concentration, assignment of unique tracking number of stock vial
 - Expiration date (is desired)
 - Individual Authorized User assigned to bottle/vial (if needed)

- Date notation of when vial/bottle was disposed/emptied
 - Packing slips (signed and dated) – photocopy packing slip when multiple substances are purchased at once. Each CS vial will need to be easily associated with its packing slip and making copies simplifies this process.
 - Copy of completed DEA Form 222 – Required for Schedule II purchases. Keep blank original locked and separated from Schedules III – VI.
5. **CS Usage and Disposal Log form** (*required*)
- *Stock (Bulk form) vial log* - Every vial must have a unique tracking number and associated Usage/Disposal log (see the labeling requirement section in this manual).
 - *Compounded/Dilution (Finished form) vial log* – each compounded vial created must have a usage log. The compounded vial must have a unique tracking number that references/links it to the original Stock/Bulk vial number.
 - Usage logs must be completed immediately after every use. The last entry in the usage portion of the form should refer to the record of disposal method at the bottom of the same form (expired, empty, Reverse Distributed, waste).
 - Registrants are responsible for training and auditing Authorized Users.
6. **Reverse Distribution** (*required*)
- DEA Form 41 must be used for Reverse Distribution of CS.
 - Maintain copies of Reverse Distribution confirmation.
7. **Completed Transactions** (optional)
- After the stock (bulk) vial and *all* associated compounded/diluted solution vials have been used/emptied/destroyed, it may be useful to collect all associated documents related to the transaction and place them together within the stock vial’s plastic sheet protector pocket (or other method). Documents would include: packing slip, usage records (stock and all dilutions), DEA Form 41. Records must be maintained for two years after the depletion or destruction of the Controlled Substance.

Labeling Requirements

All containers of Controlled Substances (CS) must be properly labeled. If the CS is used in vertebrate animals must also be labeled in accordance with ACUC policy. If the laboratory re-packages, compounds, or dilutes Controlled Substances, then appropriately label the repackaged, compounded or diluted substance and store it in the approved secure location listed on the Registration. ***Compounded Controlled Substances (mixed cocktails or diluted Controlled Substances) cannot be transferred between DEA Registrants.***

All vials require a specific unique tracking number to be present **on the vial and associated usage log**. Lot numbers can be used on Bulk (stock) form vials as the unique tracking number; however, additional designations (i.e. letters) are required when multiple vials contain the same lot number. Finished form (diluted solutions) must be labeled with a unique tracking number that links the diluted vial back to the Bulk (stock) vial used to create the Finished (diluted) form. For example, if the stock vial is numbered “100”, then the first diluted vial from the bottle would be numbered “100-A” and the second dilution from the stock vial would be “100-B.” Each Finished form vial must have a corresponding usage and disposal log documentation.

Diluted or compounded Controlled Substances that will be stored at least overnight in the safe/secured location must be properly labeled with the following information:

- Name of Controlled Substance
- Unique tracking number
- Final concentration
- Volume per container
- Expiration date

Refer to the *ACUC Policy on the Use of Laboratory Mixtures or Dilutions of Anesthetics or Analgesics* for additional information related to CS administration to vertebrate animals.

https://researchcompliance.web.virginia.edu/acuc/pi/policy/policy_MixDilutAnesthAnalgesics.pdf

Labeling Expired Drugs Awaiting Reverse Distribution

Expired or unusable substances must be labeled, separated, and stored securely according to DEA requirements for the highest-level Schedule associated with the Controlled Substances that require disposal. Each vial must be labeled as “expired” or “waste” and placed into a separate box or bag labeled as “DO NOT USE-EXPIRED” clearly on the outside of the box. The closed, labeled box must be kept within the same cabinet where inventory is stored. Expired compounds must remain on the inventory until reverse distributed.