

Harvard University Researchers' Guide for Use of Controlled Substances

Introduction

Due to their potential for abuse, items identified by the United States Department of Justice, [Drug Enforcement Administration](#) (DEA), and the [Massachusetts Department of Public Health](#) (DPH) as Controlled Substances are subject to extensive licensing, registration, storage, security, use, disposal, and inventorying requirements. The regulations governing Controlled Substances include the following: United States Department of Justice, Drug Enforcement Administration, Controlled Substances Act, 21 [C.F.R. Sections 1300 et. seq.](#); and Massachusetts Department of Public Health, [105 C.M.R. 700.000 et. seq.](#)

In general, the regulations are designed to ensure a system of security and accountability in the acquisition, use and disposal of Controlled Substances. Thus, they require license holders to document the receipt of Controlled Substances once they are ordered and to continue to document use until the time they are properly disposed of. They also call upon license holders to keep track of the individuals who are authorized to have access to the substances and the places in which the Controlled Substances are stored.

The government has indicated that substantial compliance with the security regulations depends on the following factors:

1. The type of activity conducted (e.g., processing of bulk chemicals, preparing dosage forms, packaging, labeling, buying, possessing, and conducting research, etc.);
2. The type and form of controlled substances handled (e.g., bulk liquids or dosage units, usable powders, nonusable powders);
3. The quantity of controlled substances handled;
4. The location of the premises and the relationship such location bears on security needs;
5. The type of building construction comprising the facility and the general characteristics of the building or buildings;
6. The type of vault, safe, and secure enclosures or other storage system (e.g., automatic storage and retrieval system) used;
7. The type of closures on vaults, safes, and secure enclosures;
8. The adequacy of key control systems and/or combination lock control systems;
9. The adequacy of electric detection and alarm systems, if any, including use of supervised transmittal lines and standby power sources;
10. The extent of unsupervised public access to the facility, including the presence and characteristics of perimeter fencing, if any;

11. The adequacy of supervision over employees having access to manufacturing and storage areas;
12. The procedures for handling business guests, visitors, maintenance personnel, and non-employee service personnel;
13. The availability of local police protection or of the registrant's or applicant's security personnel; and
14. The adequacy of the registrant's or applicant's system for monitoring the receipt, manufacture, distribution, and disposition of controlled substances in its operations.

Violations of the Controlled Substances laws, even when unintended, can lead to substantial civil and criminal liability.

1. Responsibilities

In order to ensure compliance with Harvard's obligations under the Controlled Substance regulations and licenses, it is important that authorized faculty and research staff, laboratory administrators, and affected departments understand their responsibilities in connection with obtaining, preparing, handling, and using Controlled Substances.

Principal investigators (PIs) shall have responsibility for managing the use of Controlled Substances in their labs. PIs shall have responsibility for ensuring that Controlled Substances are licensed and registered for use in their labs and stored and accounted for in the manner that is required for the particular drug classes authorized by the license holder's registration, as indicated on the license; for restricting access only to users they authorize (Authorized Individuals or AI); for providing to the departmental administrators updated information of additions and deletions of Authorized Individuals; and for ensuring that usage logs, purchase orders, inventories, disposal records and other necessary documentation are properly kept and submitted to departmental administrators in accordance with this guide. In the event that the PIs are on leave or are otherwise absent, they may designate another appropriate Authorized Individual to carry out the duties under the Controlled Substance program on their behalf.

Departmental administrators shall have primary responsibility for assisting faculty, researchers, and their staff in complying with the requirements set forth in this guide; for ensuring that security and access procedures are in place in each of the labs; for ensuring that all licenses are regularly updated; for purchasing and distributing Controlled Substances and, in appropriate circumstances, securing Controlled Substances that are not used regularly in the labs; for maintaining records and reports relating to the Controlled Substances program; for providing training to faculty and research staff concerning obligations for handling Controlled Substances under the licenses, regulations, and any applicable Harvard policies; and for working with PIs to implement any corrective actions that may be needed.

Environmental Health & Safety Department (EH&S) shall have responsibility for conducting annual surveys of any laboratories that have licenses to use Controlled Substances. EH&S will also

provide informational materials to departmental administrators for distribution to PIs and Authorized Individuals. EH&S shall also have responsibility for assisting departmental administrators in the disposal of Controlled Substances and providing options for proper disposal. Periodically, EH&S will provide an inspection summary report, including corrective action recommendations, to the departmental administrator, PI, and Environmental and Safety Compliance Officer for the School or department.

The Center for Animal Resources and Comparative Medicine (ARCM) and the Office of Animal Resources (OAR) shall have responsibility for assisting departmental administrators in the disposal of animals injected with Controlled Substances. ARCM and OAR (along with EH&S) may also be called upon to assist departmental administrators in determining how best to store and maintain certain Controlled Substances that are not used on a regular basis in the labs.

2. Definitions

“Controlled Substance” is defined as a drug or other substance, or immediate precursor, included in schedule I, II, III, IV, or V of the Controlled Substances Act. In addition, under Massachusetts law, Controlled Substance is also defined as a **prescription** drug that is not otherwise included in schedules I-V. The DEA does *not* regulate Schedule VI prescription drugs.

In general, the schedules identify materials containing any quantity of a substance with a stimulant, depressant, or hallucinogenic effect on the higher functions of the central nervous system, and having the tendency to promote abuse or physiological or psychological dependence, as designated in state and federal Controlled Substance schedules. Schedules I and II are the most stringently regulated, and include many widely known street drugs, including heroin, LSD, GHB, and cocaine as well as such drugs as pentobarbital. Schedule III compounds include many stimulants and depressants, pain killers, and anesthetics, including ketamine and buprenorphine. Schedule IV substances cover the balance of lower-abuse potential stimulants and depressants, while Schedule V includes therapeutic drug mixtures containing very limited quantities of Controlled Substances. Each Controlled Substance has a specific drug code assigned to that particular drug. A general list of schedule I-V Controlled Substances can be found at <http://www.usdoj.gov/dea/pubs/scheduling.html>.

Schedule VI Controlled Substances under Massachusetts law include all prescription drugs. Non-prescription grade pharmaceuticals are *not* included in Schedule VI nor are Over-the Counter (OTC) drugs.

“Authorized Individuals” (AIs) are those lab personnel who handle or manage Controlled Substances in approved research. Authorized Individuals must be trained in Controlled Substance shipping, receiving, security, inventorying, and recordkeeping procedures as outlined in this Guide.

3. Licensing and Registration

Generally a license from DEA and the DPH is required to acquire, make, possess or use a Controlled Substance. Generally licenses are (i) issued to an individual, who may authorize other individuals to operate under his/her license, (ii) specific to drug schedules identified on the license, and further limited to specific drug codes applied for, and (iii) identifies a specific location where the Controlled Substances are to be stored and must be amended when the location of storage changes.

It is the responsibility of the departmental administrators to assist laboratories in obtaining appropriate licenses and registration. Departmental administrators or individual PIs must obtain licensure from both the Massachusetts Department of Public Health and from the federal Drug Enforcement Administration. The DEA will not grant an applicant a license until he/she has already obtained a license from DPH although both applications may be submitted at the same time.

Because the University cannot, by law, maintain a blanket registration for Controlled Substances, individuals must obtain appropriate licenses and registration. In some cases, it may be appropriate or required to have PIs apply for licenses. Once PIs obtain licenses for their labs, they can authorize others in their labs to access the materials. In other cases, it might be more appropriate for a departmental administrator to hold the license. Again, the departmental administrators, with the input from the PIs in their labs or departments, can authorize others to access the materials. Regardless of how the licensing is structured, copies of licenses shall be provided to an appropriate departmental administrator. This will help to ensure that a departmental administrator is aware of the individuals who are licensed to use Controlled Substances as well as the location of all Controlled Substances on campus. It is ultimately the individuals identified on the licenses that have responsibility for ensuring proper acquisition, use, maintenance, and accountability of Controlled Substances.

PIs who wish to work with Controlled Substances should complete and submit the Harvard [University-Controlled Substances Application \(Attachment A\)](#) or equivalent to the departmental administrators. This form serves several purposes. First, it identifies all Controlled Substances the Authorized Individuals wish to handle. Second, it identifies all researchers, staff, and administrators authorized to handle such substances. Third, it identifies the location where the Controlled Substances will be stored. Fourth, it provides a current list of Authorized Individuals that the departmental administrators can use to coordinate with other interested departments and committees, such as the IACUC. This form will also serve as the first step in license application. If a PI intends to apply for a license to use Schedule I-V substances, he or she should, as a matter of good practice, be sure to include in his/her application to the state agency a request for Schedule VI prescription drugs, as well.

Synthesis of chemicals or drugs that have been deemed illegal or illicit by the DEA or state authority are prohibited unless pre-approved by an appropriate University official and are consistent with a research protocol that is submitted to the DEA or state authority with appropriate application. Registration for Schedule I substances requires submission of a research protocol to DEA.

PIs who wish to obtain a license or have obtained a license may authorize members of their research staff or other administrators to access Controlled Substances by identifying those individuals on the Harvard University-Controlled Substances Application (Attachment A) or equivalent. DPH generally requires a license holder upon application or renewal to provide the agency with personal

information pertaining to *all* Authorized Individuals. DEA does not generally require this information on its application.

If, during the course of the year, there are additions or deletions or changes to the information provided on Attachment A, license holders should take steps to ensure that they have a record of any such changes. License holders are not obligated, however, to notify DPH of additional Authorized Individuals during the term of their license. Except for Schedule I substances, license holders are also not obligated to notify DPH if they wish to purchase additional Controlled Substances, provided their license includes the schedule within which the new Controlled Substance falls. DEA does, however, want to be notified (a letter is acceptable) whenever a new drug code within an authorized schedule is added to the license. Drug codes may be found in Title 21 Part 1308 of the Code of Federal Regulations. The local office of the DEA will also provide drug codes upon request. In any event, license holders must provide complete, updated information about AIs, drug codes, schedules, and licenses when they renew their licenses with both DPH and DEA.

The number of Authorized Individuals should be kept to the minimum essential for efficient operation. By limiting the number of Authorized Individuals, labs can better ensure accountability. Persons previously convicted of a felony offense relating to Controlled Substances or who had an application for registration with a state or federal agency denied or who surrendered a registration for cause may not be authorized to work with these materials.

Importantly, the Schedule I-V Controlled Substances must be stored in the place indicated on Attachment A for license holders and in other facilities used by Authorized Individuals; provided, however, that the other facilities occupied by the Authorized Individuals are connected to the license holder's place of storage by a courtyard, walkway, hallway, or tunnel. If an Authorized Individual is not connected to the license holder's place of storage by such means, then the Authorized Individual must arrange to obtain his/her own license. If the license holder changes location and wishes to change the storage location indicated on his/her license, he/she should notify the DPH and DEA in writing and make certain that the new storage cabinet meets the Controlled Substances requirements. In some cases, the regulators may approve the move without further action. In other cases, the regulators may request that the license holder apply for a new license.

Researchers that occupy Harvard space but are employed at other institutions or affiliated hospitals should contact their primary institutions or hospitals for assistance in obtaining appropriate licenses from the state and federal authorities.

4. Scope of Use

Controlled Substances may only be used for duly authorized, legitimate medical or scientific research purposes to the extent permitted by the registrant's license and registration and in conformity with state and federal statutes and regulations.

5. Initial Purchase

Once the individuals authorized to access Controlled Substances have been identified and licenses have been granted from the state and federal agencies, individuals that are licensed to work with Controlled Substances who wish to purchase Schedule I-V substances should complete the Harvard University-[Controlled Substances Purchase Request Form \(Attachment B\)](#) or equivalent and submit it to the departmental administrator. License holders or individuals designated by them by a Power of Attorney should take responsibility for all ordering of Schedule I-V Controlled Substances. The form of purchase should include the following information:

- (a) Basic purchase information;
- (b) Proof of legitimate research use;
- (c) Storage location;
- (d) DEA and MPH registration number.

The stocks of Controlled Substances should be kept to the smallest quantity needed for efficient operation to conduct the indicated research. It is strongly suggested that diluted mixtures be made in a timely manner, so that little, if any, non-diluted Schedule I-V Controlled Substances are maintained in the laboratory environment.

For Schedule II Controlled Substances an official [DEA Order Form \(Form 222\)](#) will have to be prepared. Form 222 is available on DEA's website or by calling the DEA's Boston at (617) 557-2468. The top portion and middle portion of the form will be forwarded to the supplier and the remaining portion will be kept with other Controlled Substance records. Once the shipment is received the Order Form will be annotated to show the actual amount received and the date of receipt in the appropriate column of the Order Form.

The departmental administrators will coordinate with the Authorized PIs for the purchase and delivery of Schedule I-V Controlled Substances.

6. Maintaining Security in the Lab

Schedule I-V Controlled Substances shall be stored in securely locked, substantially constructed drug cabinets or safes in locations where access is limited. Contact the departmental administrator to ensure that appropriate cabinets or safes conform to the federal and state requirements. The vendor of the safes should be able to confirm the appropriateness storage of Controlled Substances. Generally, standard file cabinets are not sufficient for the storage of Controlled Substances. Under Massachusetts regulation, Schedule VI prescription drugs need not be stored in safe or locked drug cabinet. Schedule VI substances can be stored together on a nearby shelf to the drug cabinet or in an unlocked cabinet but should not be stored with Schedule I-V substances.

Schedule I-V Controlled Substances must be maintained separately from Schedule VI Controlled Substances unless the license holder obtains specific permission from the DEA to store Schedule VI

prescription drugs with the substances that the DEA regulates. In addition, particular laboratories may find that they only use in experiments diluted forms of Schedule III, IV, and V Controlled Substances. Thus, they may wish to segregate further in separate safes or vaults non-diluted substances from diluted substances. Laboratories may wish to call upon ARCM, OAR, EH&S or their departmental administrator to assist them in determining how best to store and maintain certain Controlled Substances that are not needed on a regular basis in the labs.

All Schedule I-V Controlled Substances must be kept locked in their storage location except for the actual time required for Authorized Individuals to remove, legitimately work with and replace the Controlled Substances. They must not be left unattended, and when they are not being used for research, they must be securely stored in a safe or vault. In connection with some experiments, it may be necessary to prepare and use many doses of highly diluted Schedule I-V Controlled Substances over a relatively short period of time. In those instances, Authorized Individuals should log out the smallest quantity needed for efficient operation, generally no more than a single vial at one time, and must return any unused portions to the safe or vault during those times when they cannot attend to them or no longer need them.

Controlled access to the drug cabinet is critical to establishing security for Controlled Substances. For this reason, keys and combinations to the cabinets or safes should be secure and under the control of a limited number of Authorized Individuals.

7. Reporting of Loss, Destruction, Theft, or Unauthorized Use

Thefts, suspect thefts, unauthorized uses, or other losses of any Controlled Substance must be reported immediately to the departmental administrator and to the Harvard University Police Department upon discovery. The laboratory may have an obligation to report promptly the loss to the state or federal authorities. For example, the Massachusetts Department of Public Safety and the Federal Drug Enforcement Agency requires laboratories to report losses within one business day of discovery. [DEA Form 106](#), available on DEA's website, is required to be used by both DEA and the DPH when a formal report is made, after an initial investigation.

In addition, any unauthorized persons who gain access to Controlled Substances for the purpose of diversion or theft may be reported to the Harvard University Police Department and may be subject to the disciplinary policies of the University.

8. Recordkeeping and Inventorizing

Laboratories are required to keep track of Schedule I-V Controlled Substances using the [Harvard University-Controlled Substance Usage Log \(Attachment C\) or equivalent](#). Usage Log sheets shall be numbered and bound, and, if the size of the safe or cabinet permits, maintained at all times in the locked safe or cabinet along with the Controlled Substances. Usage Log sheets must be maintained for a minimum of three years after the complete use and disposal of Schedule I-V Controlled Substances and

be readily available for inspection by the DEA, Massachusetts Public Safety, or Harvard University. Laboratories are not required to maintain usage logs for Schedule VI Controlled Substances.

All laboratories that work with Schedule I-V Controlled Substances are to conduct self-inspections on a quarterly basis to ensure that the laboratory's Controlled Substance Usage Logs match the physical inventory. The results of those self-inspections shall be recorded on the [Harvard University-Controlled Substances Inventory Form \(Attachment D\)](#) or equivalent and shall be maintained by the license holder for a minimum of three years.

In addition, on a biennial institutional cycle, all laboratories licensed to work with Controlled Substances will be directed by the departmental administrators in January to report their current inventory of Controlled Substances in order to comply with the federal requirement to conduct biennial inventories. For such biennial requirements, laboratories should use the Harvard University-Controlled Substances Inventory Form (Attachment D). License holders shall sign this form in addition to the Authorized Individuals who conducted the inventory.

All records generated in connection with the Controlled Substances program should be maintained by the license holder for at least three years following termination of any licenses.

9. Controlled Substances of Unknown Origin

Occasionally, laboratories or animal facilities may come across Controlled Substances of an uncertain origin, sometimes referred to as "orphaned drugs." For example, a licensed PI may leave the University and a researcher may come upon the Controlled Substances that he/she left behind. Similarly, a researcher may come upon a Controlled Substance that was inadvertently left in an animal facility that Harvard shares with the affiliated hospitals. In those circumstances, the laboratory or other facility should take the following steps: (1) make sure that the Substance is secured in a license holder's locked safe or cabinet; (2) contact the EH&S office for disposal assistance and coordination; and (3) provide the DEA in writing with a brief description of how the laboratory came into possession of the Controlled Substances, of the type of substance and quantity, and a proposed method of disposal for approval by the DEA. Once the DEA approves of the method of disposal, such orphaned drugs can be destroyed in accordance with that method.

10. Disposal

Controlled Substances consumed in a reaction or converted into a hazardous waste mixture from which a Controlled Substance is not recoverable may be disposed of through routine waste disposal procedures from Environmental Health & Safety. Animal carcasses that were injected with Controlled Substances must be disposed of through the Center for Animal Resources and Comparative Medicine or the Office for Animal Resources.

When Controlled Substances expire, Authorized Individuals should request waste pick-up from Environmental Health & Safety to ensure they are properly disposed of. Sometimes, at the conclusion of an experiment, a small amount of a Controlled Substance will remain in the vial or syringe. In those circumstances, in addition to requesting waste pick-up for those small remaining amounts, researchers may dispose of the substances by transferring the substance to absorbent lab wipes and then arrange for disposal through EH&S. In any event, no materials should be disposed of through laboratory drains without the prior approval of the regulatory authorities. If you have any questions about waste disposal, EH&S will provide guidance, but will not take possession of Controlled Substances. See the following EH&S web link for further details: [DEA Controlled Substances: Disposal Requirements](#).

11. Shipping Procedures

Federal law prohibits the export of Controlled Substances unless certain requirements are met, including, in most cases, export and import permits or declarations. Violators of the law risk arrest or fines both in the United States and the foreign country. Licensed brokers are available for transport of controlled substances. Contact EH&S for assistance in arranging for any necessary transport of Controlled Substances.

12. Resources and References

The departments identified below may be a resource for questions about the Researchers' Guide for Use of Controlled Substances:

Environmental Health and Safety: (617) 495-2060 (Cambridge)
Environmental Health and Safety: (617) 432-1720 (Longwood/Southborough)
Center for Animal Resources and Comparative Medicine: (617) 432-1289
Office for Animal Resources: (617) 432-1289
Director of Operations, Harvard Medical School: (617) 432-4321
Director of Office for Research Compliance: (617) 432-3884
Dean of Operations, Harvard School of Public Health: (617) 432-3508
Associate Dean for Research Administration, Faculty of Arts and Sciences: (617) 495-4083
Office of the General Counsel: (617) 495-1280

For additional information about the regulatory requirements, you may consult the following websites:

Massachusetts Department of Public Health, Drug Control Program:
<http://www.mass.gov/dph/dcp/>.

United States Department of Justice, Drug Enforcement Administration, Controlled Substances Act: <http://www.dea.gov/pubs/csa.html>.

Copies of this Researchers' Guide for Use of Controlled Substances are available on the [EH&S website](#).