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DEA COMPLIANCE FOR UNIVERSITY AND HEALTH SYSTEM RESEARCH FACILITIES: IT'S NOT JUST FOR PHARMACIES ANYMORE



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Academic and institutional research facilities often use controlled substances while conducting research, including use in the development and analysis of drug compounds as well as use of such substances while conducting animal research. In particular, controlled substances may be used to anesthetize animals during research, as a substrate or other reagent in research, and generally in clinical, analytical and animal investigations. Research institutions and investigators are subject to federal and state law requirements that mandate proper maintenance, storage, use and disposal of controlled substances.

However, university and health system research facilities aren't always aware of the legal requirements concerning controlled substances. Although unclear, this lack of awareness may result from institutional habits that have fostered a culture that is focused on research and scientific doctrine without considering legal constraints that may require changed or increased compliance with controlled substances laws. Additionally, some settings may not be wholly involved with research on a regular basis, leading to a lack of recognition

of legal requirements when undertaking research protocols.

This article is intended to alert those using controlled substances of their compliance obligations under federal and state law, identify areas of vulnerability for research institutions, and describe a sampling of compliance objectives that research institutions and investigators must adhere to when maintaining, storing, using and disposing of controlled substances for research purposes.

Federal and State Registration Requirements

The Drug Enforcement Administration ("DEA") regulates compliance with and diversion of controlled substances pursuant to the Controlled Substances Act. Controlled substances include drugs that are subject to abuse or diversion and include narcotics, stimulants, depressants, hallucinogens, and cannabis. Controlled substances are "scheduled," with those requiring strictest control classified as 'Schedule I' and those requiring the least control classified as 'Schedule V.'¹ As a result, research facilities should be aware that persons engaged in synthesis (even temporarily), prescribing, dispensing, distribution, administration, conducting research or disposing of controlled substances must register with the DEA.

In a research setting, this typically means that the principal investigator using controlled substances in a research protocol will be required to submit a registration with the DEA in order to be legally permitted to possess, store and use a particular controlled substance.² Additionally, any research involving 'Schedule I' substances require additional special controls that include submission of the research protocol to

the DEA along with the required registration application.

Typically, the DEA requires separate registration at each laboratory where the researcher is engaged in the dispensing and administration of controlled substances for research purposes. Registered researchers may conduct only those activities with controlled substances for only those scheduled controlled substances authorized by their DEA registration, as set forth on the respective DEA Form 225.³ DEA Form 225 can be obtained through the Internet.⁴

In addition to federal DEA registration requirements, it is also likely that individual state registration is required for possession, distribution and use of controlled substances in a research facility. This may require registration with a local state board of pharmacy or a separate state administrative agency, depending on what state law requires. Typically, states require a separate application for controlled substances, may require an initial on-site inspection, and may have additional specific requirements.

Authorization To Use Controlled Substances and Background Checks

Although a research facility is subject to DEA and state law enforcement, the DEA will often require a principal investigator or supervisor of research in which controlled substances are used to bear full responsibility on behalf of the research facility for compliance with federal and state laws and regulations.⁵ Additionally, research settings often have controlled substances policies and procedures with which the principal investigator will be required to

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comply in addition to any federal or state law requirements. To that end, research settings will require that a principal investigator understand all applicable federal and state laws and regulations and to keep all required registrations, certificates, licenses and records in force. Additionally, the DEA will require DEA registrants (and individuals who will handle controlled substances in the course of their laboratory research) to undergo an initial background check.⁶

Laboratory Security

All controlled substances are required to be kept in a locked cabinet in a research facility. Because of the greater potential for abuse and diversion, Schedule I⁷ and Schedule II⁸ controlled substances have higher security requirements than drugs in Schedule III-V and are required to be kept under a double lock system in a safe.⁹ Access to keys or security devices for locked controlled substances should be limited to authorized personnel only, and not left unattended or otherwise readily available in the laboratory. While there may be designated persons who will be in charge of keys for the locked controlled substances, the DEA registrant is ultimately responsible for any drug loss or diversion.¹⁰

Recordkeeping and Inventory Compliance

The DEA requires a chain of custody from the time a controlled substance is received to when it is used or disposed of.¹¹ Periodic verification of records and re-counting of inventory should be done on a regular basis to document inventory. Inventory log books should assess the description and quantity of controlled substances on hand at all times.¹²

The DEA requires complete and accurate records to be kept by registrants who are storing or using controlled substances in the research laboratory.¹³ This includes all procurement, dispensing and inventories for a period of at least two years. In some cases, where state laws have been implemented to provide additional controlled substances requirements that are not inconsistent with federal requirements, state laws may require an even longer time period. Additionally, all Schedule II records must be maintained separate from Schedule III-V records.¹⁴ In the case where a principal investigator terminates a research study or departs from the research setting, all documentation should be maintained by such individual unless notification is made to DEA of the name, address, and registration number of the establishment maintaining such records.¹⁵

Purchasing Controlled Substances

Procurement of controlled substances is normally restricted to a designated department or individual in a research setting, in order to identify an accountable entity for purposes of DEA registration. This is accomplished by demonstrating accurate and comprehensive account information along with an authorized signature, a copy of a current DEA license and the completion of a triplicate order form (DEA Form 222) if purchasing any Schedule II controlled substances.¹⁶

DEA Form 222 must be carefully completed with respect to quantities and dates. No material alteration is permitted when completing DEA Form 222 and in the case of an error, special filing steps are required to be followed for the voided form. All triplicate copies must be signed by a DEA registrant and copies should be retained for the designated time period, as required by law.¹⁷

Disposal & Destruction

The DEA requires institutions and researchers to account for controlled substances and keep records to demonstrate how the controlled substances were used.¹⁸ Additionally, disposal of controlled substances must follow standardized procedures and may rely on authorized "reverse distributors,"¹⁹ filing appropriate DEA forms and promptly reporting thefts and diversions. In the case of large quantities, the DEA may require on-site field investigation and completion of required DEA forms prior to destruction of any quantities of controlled substances. Furthermore, state laws may require additional procedures to be in place prior to any such disposal or destruction.²⁰

Compliance and Enforcement

All research facilities are subject to unannounced DEA or state audits or inspection of their controlled substances, as well as of their records and procedures.²¹ The DEA has the authority to impose criminal sanctions and penalties for violation of the Controlled Substances Act. These may range from monetary penalties up to and including imprisonment, depending on the nature of the offense.

Compliance With Other Laws

In addition to DEA compliance, other federal laws may impact how a controlled substance may be stored and used in a research setting.²² If applicable, investigators should also be sure that their research protocols are compliant with other laws, such as the Animal Welfare Act,²³ as well as Food and Drug Administration ("FDA")²⁴ and National Institutes of Health regulations in instances where animal research is being conducted and for research involving human subjects, respectively.²⁵

Special Areas of Vulnerability for Research Institutions

There are several areas of particular non-compliance concern at research institutions, including the following:

- Orphaned products – products left behind by departing researchers and no longer under an appropriate registration or traceable to a proper registrant.
- Visiting researchers – who bring their own supply without appropriate location registration.
- Synthesis of drugs – laboratory manufacture of drugs during and for research purposes without recognizing that the drugs are controlled substances and subject to federal and state laws (including growth of botanicals in botanical collections).
- Expired drugs – frequently left in a lock up (either in original packaging or diluted for use) and ignored for long periods of time without proper recordkeeping.
- Non-compliant facilities – physical facilities that lack proper storage, proper recordkeeping and access controls.
- Theft – loss of controlled substances intended for research use, but diverted due to improper storage and poor access controls.
- Lack of written procedures – facilities that lack proper written protocols on how a laboratory should properly manage controlled substances including inventory, storage, security, use and disposal, among other things.
- Researcher screening – ensuring that individuals who are accessing and using controlled substances in research have no history of drug violations with legal authorities.

Absence of appropriate and stringent controls is an invitation to criminal activity. On several occasions, university research settings have been implicated

directly or indirectly due to non-compliance with federal and state drug enforcement laws. Such examples include, but are not limited to:

- In 2005, a California university laboratory was described as an illicit drug manufacturing site after a California graduate student was caught synthesizing methamphetamine, “ecstasy” and anesthetic that was thought to be eighty times more potent than morphine. The graduate student was already on probation with the legal authorities for prior drug violations.
- In 2004, a prominent Midwest university was the subject of a multi-agency federal criminal investigation after authorities uncovered the purchase of \$13,000 by the university of pre-cursor raw material that can be used to synthesize “ecstasy.”
- In 2001, a well-known Southwestern university suspended one of its professors after he was arrested as a suspect in an “ecstasy” ring. The professor allegedly ordered the chemicals and equipment that was to be used at the university for the purpose of manufacturing “ecstasy.”

Conclusion

This article has addressed how research institutions and investigators are subject to federal and state law requirements that mandate proper maintenance, storage, use and disposal of controlled substances. Compliance issues that arise are unique, and have the propensity to represent significant risk to reputation as well as monetary and criminal penalties.

Parties intending to possess and use controlled substances in their research setting should (1) have well defined written policies covering all activities from procurement through use and disposal; (2) conduct training of researchers; and (3) periodically audit their internal compliance. Experienced legal counsel should be sought promptly if and when compliance issues arise.

However, an ounce of prevention is worth the proverbial pound of cure and maintaining compliance to prevent problems from developing in the first instance argues strongly for universities or health systems to engage in early consultation with legal experts.

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McDermott's Health Law Department. Ned has been involved with multiple legal issues relating to pharmacy matters. Additionally, he has licensed pharmacies in over 40 states in various board of pharmacy licensure proceedings, including obtaining state-authorized controlled substance licensure. He is also versed in DEA pharmacy licensure requirements and DEA compliance activities, including destruction of controlled substances through reverse distributors and government agencies.

Mr. Milenkovich has also been involved with several 340B drug discount pricing analyses and also has extensive HIPAA privacy, security, transaction code sets and national provider number compliance experience and has counseled countless clients respecting HIPAA matters and has both spoken and written on the subject numerous times. Furthermore, he has experience relating to state-mandated prescription drug monitoring programs and preventing diversion as well as the federal NASPER program. He has also been involved with numerous health and welfare benefits issues, including the most recently enacted Medicare Part D prescription drug benefit on various issue specific

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Endnotes

- ¹ See Controlled Substances Act, 21 U.S.C. § 801 *et seq.* See also 21 C.F.R. § 1308. Some states, such as Massachusetts, for example, have introduced additional 'Schedule' levels in their regulations. Massachusetts contains an additional 'Schedule VI' which includes all prescription drugs not in Schedule II-V. See 105 C.M.R. 700.002(A-F).
- ² Researchers, similar to pharmacies, that store and dispense any controlled substance must be registered with the DEA.
- ³ 21 C.F.R. § 1301.18 (2007).
- ⁴ http://www.deadiversion.usdoj.gov/drugreg/reg_apps/225/225_form.htm.
- ⁵ 21 C.F.R. § 1301.18 (2007).
- ⁶ 21 C.F.R. §§ 1301.90, 1301.93 (2007).
- ⁷ 21 C.F.R. § 1308.11 (2007). Schedule I controlled substances are drugs or other substances that (A) have a high potential for abuse, (B) have no currently accepted medical use in treatment in the United States, and (C) for which there is a lack of accepted safety for use under medical supervision.
- ⁸ 21 C.F.R. § 1308.12 (2007). Schedule II controlled substances are drugs or other substances that (1) have a high potential for abuse, (2) have a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions, and (3) may lead to severe psychological or physical dependence.
- ⁹ 21 C.F.R. § 1301.72 (2007).
- ¹⁰ 21 C.F.R. § 1301.71 (2007).
- ¹¹ 21 C.F.R. §§ 1301.71, 1301.74 (2007).
- ¹² 21 C.F.R. § 1304.11 (2007).
- ¹³ 21 C.F.R. § 1304.22 (2007).
- ¹⁴ 21 C.F.R. § 1304.04 (2007).
- ¹⁵ 21 C.F.R. § 1304.03 (2007).
- ¹⁶ 21 C.F.R. § 1305.04 (2007). See, e.g., http://www.deadiversion.usdoj.gov/online_forms.htm.
- ¹⁷ 21 C.F.R. §§ 1305.11-1305.13 (2007).
- ¹⁸ 21 C.F.R. §§ 1304.21, 1304.22 (2007).
- ¹⁹ A reverse distributor is an entity that is registered with the DEA and approved to destroy controlled substances.
- ²⁰ For example, in addition to any federal DEA requirements, a state may require an on-site visit by one of its controlled substances inspectors to meet any state inspection requirements.
- ²¹ Although this varies from state to state, typically a state board of pharmacy governs controlled substances audits or inspections, to the extent there are any. Some states, however, have created separate drug control divisions for this purpose. Massachusetts, for example, regulates controlled substances registrations under the Massachusetts Department of Public Health.
- ²² 21 C.F.R. § 1307.02 (2007).
- ²³ 7 U.S.C. §§ 2131-2156. See also, FDA's current good laboratory practices (cGMP) requirements, 21 C.F.R. Part 58.
- ²⁴ 21 C.F.R. Parts 312, 812.
- ²⁵ 45 C.F.R. Part 46.

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