PROCEDURES

OFFICE OF THE CENTER DIRECTOR

Procedures For Review Of Protocols Referred By DEA That Use Schedule I Controlled Substances and Drugs

Table of Contents

PURPOSE

This MAPP establishes responsibilities and procedures for the Controlled Substance Staff (CSS) within the Office of the Center Director in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA) for review of research protocols (i.e., schedule I registration requests) sent to CSS from the Drug Enforcement Administration (DEA).

BACKGROUND

- Title 21 Code of Federal Regulations (CFR) Part 1300, Sections 1301.18 and 1301.32, requires the Department of Health and Human Services (HHS) to review and comment on the scientific merit of the studies and qualifications of investigators conducting research with schedule I controlled substances and to respond on these matters to the DEA.

- Guidance for the delegation of authority from HHS to the FDA Commissioner, and from the FDA Commissioner to the Controlled Substance Staff within CDER is found at: Delegations of Authority, Volume II (1400): https://www.fda.gov/about-fda/staff-manual-guides/delegations-authority-volume-ii-1400. The delegation of authority specifically covers the function of determining the qualifications and competency of investigators wishing to conduct research with controlled substances and drugs listed in schedule I, and the merits of the research protocol.

RESPONSIBILITIES

CSS will:

- Serve as the HHS and FDA liaison to the DEA on schedule I research protocols (21 CFR 1301.18).

- Review schedule I nonclinical protocols (which may or may not be part of an IND) using schedule I substances and drugs to advise the DEA on acceptability for schedule I registration.

- Review schedule I clinical protocols and confirm that they have been reviewed by the Office of New Drugs (OND) review division under an active IND. CSS will contact the appropriate division regarding clinical protocols pending review or previously reviewed, if necessary, to confirm that the protocol is authorized to proceed under the IND.

- Communicate with DEA on the scientific merit of the protocols, research, and the qualifications of investigators, as required by the CSA. DEA makes the final determination on approving registration applications for research using schedule I substances and drugs (21 CFR 1301.32).

PROCEDURES

Protocol Review for Schedule I Registration Requests

The process described below for protocol review requests received from DEA is separate from the FDA review for new INDs and amendments to pre-existing INDs by the respective reviewing division within OND (21 CFR 312). For clinical protocol schedule I registration requests, new protocols or protocol amendments must be submitted to an IND before investigators submit their schedule I DEA registration applications. DEA will refer schedule I protocol applications to FDA, with CSS delegated to act on behalf of FDA for this regulatory role.

CSS will:

- Review schedule I application protocols received from DEA and advise DEA on the "qualifications and competency of the applicant, as well as the merits of the protocol" (21 U.S.C. 823(f)(5) and 21 CFR 1301.32(c). DEA will review the recommendations from FDA before issuing their final decision on the registration application.

    - Review process for nonclinical protocols:

        - CSS is allotted 21 days to review a nonclinical protocol before providing a recommendation to the DEA.
        - CSS reviews the application for a schedule I license, including but not limited to a review of the source and quantity of the requested schedule I substance, the affiliation and qualifications of the applicant, the purpose of the proposed study, and the merit of the study protocol.

- CSS will contact the applicant with requests for additional required information, if necessary.
- CSS will correspond with DEA regarding the acceptability of the schedule I protocol(s) via a letter signed by the CSS Director or designee.

- Review process for clinical protocols:

  - CSS is allotted 30 days to review a clinical protocol before providing a recommendation to the DEA.
  - CSS must assure that any proposed clinical studies are to be performed under an active IND. This includes confirming that the protocol has been received by FDA, reviewed, and deemed safe to proceed by the OND Review Division. If review of the protocol by OND has not been documented as complete in the FDA archives of record, CSS will contact the OND Review Division and request review within the 30-day time limit.
  - CSS reviews the application to DEA for a schedule I license, including but not limited to a review of the source and quantity of the requested schedule I substance, the affiliation and qualifications of the applicant, the purpose of the proposed study, and the merit of the study protocol.
  - CSS will review the protocol submitted under the IND to ensure that the IND applicant has listed all clinical investigators who will be implementing the protocol, e.g., for a multi-site study, and that the applicant for DEA schedule I license registration is among the listed investigators.
  - CSS will contact the DEA schedule I license applicant with requests for additional required information if necessary, including instances in which the new protocol or protocol amendment has not been submitted to the applicant's IND or documented as received by FDA.
  - CSS will correspond with DEA regarding the acceptability of the schedule I protocol(s) via a letter signed by the CSS Director or designee.

- Convey information, policy issues, and concerns from DEA to OND and CDER management.

- Maintain records of correspondence with DEA regarding FDA review of protocols involving a schedule I drug.

REFERENCES

1. Controlled Substances Act (CSA) of 1970, as amended (primarily 21 U.S.C. 823(f))
2. 21 Code of Federal Regulations (CFR) Part 1300

DEFINITIONS

- **Schedule I Substances and Drugs:** Drugs with high abuse potential and no accepted medical use in the United States. Examples of schedule I drugs are heroin, marijuana, lysergic acid diethylamide (LSD), synthetic cannabinoids, synthetic fentanyl analogues, and methaqualone. A complete list of current schedule I substances and drugs is maintained by the DEA and can be found in the Code of Federal Regulations at: https://www.ecfr.gov/cgi-bin/text-idx?SID=0abfcca8788eb9046dd99c9364049d69&mc=true&node=se21.9.1308_111&rgn=div8

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
05/08/03	N/A	Initial
11/13/20	1	1. MAPP 4200.1 was converted into the current template. 2. Links and citations were updated. 3. Language throughout MAPP 4200.1 was revised to reflect current practices.
8/27/25	N/A	Recertified with no changes.