PROCEDURES

OFFICE OF THE CENTER DIRECTOR
Forecasting Schedule I And II Substance And Drug Needs

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PURPOSE

This MAPP establishes specific responsibilities in the Center for Drug Evaluation and Research (CDER) for offices reporting usage data applied in forecasting medical need for Schedule I and Schedule II substances, additional controlled drugs, and list I chemicals to the Drug Enforcement Administration (DEA).

BACKGROUND

The Department of Health and Human Services (HHS) is responsible for providing the DEA with annual estimates of the amounts of specific Schedule I and Schedule II substances, additional controlled drugs[1], and list I chemicals that will be needed for medical and scientific use. The DEA relies on these estimates to establish annual manufacturing quotas for the substances and drugs [Controlled Substances Act (CSA) and the Public Health Services Act (PHSA)]. The specific Schedule I and Schedule II substances, additional controlled drugs, and list I chemicals for which DEA requests usage data are hereafter referred to as "quota-relevant drug substances". The Controlled Substances Initiatives (CSI) group within the Controlled Substances Program in CDER is the group that acts on behalf of HHS to provide DEA with these annual estimates, along with additional drug development and policy information relevant to the medical and scientific use of these quota-relevant drug substances. CSI gathers quantitative information from offices in

[1] The DEA has certain reporting mandates under international treaties. In accordance with Article 19 of the Single Convention on Narcotic Drugs, 1961, and Article 16 of the Convention on Psychotropic Substances, 1971, the DEA must report the quantities of internationally controlled substances manufactured in the United States, the total quantities exported and imported, and the United States' assessment of the maximum quantity of controlled substances imported into the United States. Therefore, the DEA requests that HHS provide estimates of the quantities which will be required to meet the legitimate medical and scientific domestic needs for the substances termed "additional controlled drugs" in this MAPP. The specific "additional controlled drugs" are defined annually in the request letter from DEA to HHS.

CDER and from the Drug Shortage Staff for all quota-relevant drug substances under current Investigational New Drugs (INDs), New Drug Applications (NDAs), Abbreviated New Drug Applications (ANDAs), supplemental NDAs (sNDAs), New Animal Drug Applications (NADAs), and Abbreviated New Animal Drug Applications (ANADAs), or that are discontinued or in short supply. CSI provides this information to the DEA in an official letter.

RESPONSIBILITIES

1. The Controlled Substances Initiatives (CSI) group will:

    - Send out consult requests to the appropriate CDER offices (Office of New Drugs Review Divisions, Office of Surveillance and Epidemiology, Office of Generic Drugs, Drug Shortage Staff, and other offices as needed), Food and Drug Administration's (FDA's) Center for Veterinary Medicine (CVM), and other government agencies, requesting information regarding INDs, NDAs, ANDAs, sNDAs, NADAs, ANADAs, discontinued products, and product shortages needed to forecast quota-relevant drug substance needs. CSI will also send a consult request to the Office of Translational Sciences/Office of Biostatistics (OTS/OB) to provide forecasts of drug needs for the current year and upcoming year.
    - Request data on cannabis production from the National Institute on Drug Abuse (NIDA).
    - Request data on the use of quota-relevant drug substances in Substance Use Disorder Treatment Programs as well as information on emerging policy issues that could influence usage of these substances from the Substance Abuse and Mental Health Services Administration (SAMHSA).
    - Collate data received and prepare usage estimates for quota-relevant drug substances for the coming year in collaboration and discussion with consulted subject matter experts.
    - Analyze drug usage, incidences of drug shortage, significant regulatory actions, forecasts of future needs, and other data received from FDA offices and other government sources. Identify current developments in the areas of drug shortages, approvals, manufacturing, and regulatory actions that may affect availability, thus requiring quota adjustments.
    - Prepare an annual report letter summarizing usage and shortage data, prescribing trends, and forecasts of future needs for quota-relevant drug substances and forward the letter to the DEA.

2. The Office of New Drugs (OND) Review Divisions will:

    - Respond to CSI requests for information on INDs, NDAs, sNDAs, discontinued products, and product shortages for quota-relevant drug substances received for the reporting year. Ensure the responses are delivered in a timely manner.

3. The Office of Generic Drugs (OGD) will:

    - Respond to CSI requests for information on ANDAs, discontinued products, and product shortages for quota-relevant drug substances received for the reporting year. Ensure the responses are delivered in a timely manner.

4. The Office of the Center Director, Drug Shortage Staff (DSS) will:

    - Respond to CSI requests for information on product shortages for quota-relevant drug substances received for the reporting year. Ensure the responses are delivered in a timely manner.

5. The Office of Surveillance and Epidemiology (OSE) will:

    - Provide CSI and the OTS/OB with an analysis of drug sales distribution data (in kilograms) of selected drug substances sold from wholesale distributors and manufacturers to retail, mail, and non-retail pharmacy channels, including information on data interpretation. These data are obtained from proprietary databases available to the Agency under contract. Ensure the data are delivered in a timely manner.

    - Include in the analysis a comparison to previous years' data to identify potential data errors or anomalies that may impact trend analyses.

    - Include a list of drugs in their review for which data are not available and cannot be provided for the analysis performed by the Office of Biostatistics.

    - Collaborate with OTS/OB, DSS, CSI, and other stakeholders, to inform on usage estimates for quota-relevant drug substances for the coming year based on drug sales distribution data and other resources.

    - Provide information on drug sales calculations in the context of incidences of drug shortages, significant regulatory actions, forecasts of future needs, and other data received from FDA offices and other government sources.

6. The Office of Translational Sciences/Office of Biostatistics (OTS/OB) will:

    - Evaluate and utilize statistical models to provide annual forecasts and develop/refine modeling approaches as needed.
    - Make recommendations on statistical methodology for incorporating factors that may impact the selection of forecasting models.
    - Analyze data provided by OSE, OND, and other sources for quota-relevant drug substances for which data are available to establish trends and forecast future needs.
    - Provide forecasted drug needs for quota-relevant drug substances for the current reporting year and upcoming year in tabular form to CSI, including percentage change in usage year over year for past years. Ensure forecasts are delivered to CSI in a timely manner.
    - Work with CSI in generating the final report.

PROCEDURES

1. CSI Procedures

    a. The official request for the annual quota report will generally arrive from DEA in late January, requesting a response from FDA by April 1. To give the consulted groups the most time to prepare their responses, it is recommended that CSI contact DEA in December or early January prior to receiving the official letter to request the list of substances for which DEA will be requesting reporting, in order to begin consultation preparation.

    b. Prepare consultations for all required groups, requesting information regarding INDs, NDAs, ANDAs, sNDAs, NADAs, ANADAs, discontinued products, and product shortages needed to forecast quota-relevant drug substance needs.

    c. Send the consultations as soon as possible, and request a due date, typically within 30 to 60 days. Note that OSE cannot begin the analysis of drug sales data until data for a full calendar year (previous year) are available in the proprietary data source (early February) due to data-lag. OTS/OB will typically request a due date that is two to four weeks later than when OSE's drug utilization data become available to them in order to complete their analyses.

    d. Send the consultations via email to the designee for the consulted group [usually the Chief Project Manager or designated project manager for consultations for the FDA/CDER Division or Office, or a pre-determined contact for outside Centers or Agencies]. For consultation requests to CVM, submit the request through the FDA ICCR system.

    e. Compile the consultation responses for all groups and add relevant information into the draft letter to DEA using narratives or data tables, as appropriate.

    f. Route the letter for clearance to OSE, OTS/OB, other groups as needed, and the CDER Deputy Center Director for Substance Use and Behavioral Health.

    g. The final cleared letter is signed by the CDER Deputy Center Director for Substance Use and Behavioral Health.

2. OND Divisions, DSS, and OGD Procedures

    a. Upon receipt of the consultation from CSI, notify CSI of the designated individual assigned to respond to the CSI request for information.

    b. Notify CSI of any expected or unexpected delays that will impact providing a response by the requested due date.

    c. Respond to the request for information in the consult by the requested due date.

3. OSE and OTS/OB Procedures

    a. Upon receipt of the consultation from CSI, notify CSI of the designated individual assigned to respond to the CSI request for information.

b. Upon completion of its review, OSE will send the analysis of sales distribution data to OTS/OB and copy CSI.

c. OTS/OB will analyze the data provided by OSE and other sources and provide the annual forecasts to CSI.

d. In collaboration with CSI, OSE and OTS/OB will contribute to the interpretation of the forecasting estimates.

e. OSE will obtain data vendor clearance from the proprietary data vendors.

f. Upon receipt from CSI, OSE and OTS/OB will review the data and interpretations in the letter, obtain clearance, and respond in a timely manner.

g. Notify CSI of any expected or unexpected delays that will impact providing a response by the requested due date.

h. Respond to the request for information in the consult by the requested due date.

REFERENCES

1. Comprehensive Drug Abuse Prevention and Control Act of 1970. Public Law 91-513, as amended (primarily 21 U.S.C. 812 and 826).

2. US Code of Federal Regulations, Title 2, Part 1300, Definitions relating to controlled substances.

3. Public Health Service Act. Public Law 118 – 15, as amended. Title 42 U.S.C. 242 (a).

4. Single Convention on Narcotic Drugs, as amended. Article 19.

5. Convention on Psychotropic Substances, as amended. Article 16.

DEFINITIONS

- **Schedule I Substances and Drugs:** Drugs with high abuse potential and no currently accepted medical use in the United States. Examples of Schedule I drugs are heroin, lysergic acid diethylamide (LSD), peyote, and methaqualone. A complete list of current Schedule I substances and drugs maintained by the DEA can be found on the Internet at https://www.ecfr.gov/current/title-21/chapter-II/part-1308. For more information see additional links at this site: https://www.deadiversion.usdoj.gov/schedules/schedules.html

- **Schedule II Drugs:** Drugs with high abuse potential and an accepted medical use in the United States. Examples of Schedule II drugs include morphine, methadone, oxycodone, hydrocodone, amphetamine, methylphenidate and pentobarbital. A complete list of current Schedule II drugs maintained by the DEA can be found on the Internet at https://www.ecfr.gov/current/title-21/chapter-II/part-1308. For more information see additional links at this site: https://www.deadiversion.usdoj.gov/schedules/schedules.html

- **List I Chemicals:** Chemicals that are used in the manufacture of controlled substances and are important to the manufacture of the substances, as defined in 21 CFR 1300.2. Some examples are ephedrine and phenylpropanolamine, which can be used to manufacture methamphetamine. For more information see additional links at this site: https://www.deadiversion.usdoj.gov/schedules/schedules.html

- **Quotas:** The quantities of Schedule I and Schedule II substances and drugs that DEA allows pharmaceutical companies to manufacture or procure each year, as permitted by the CSA.

- **Quota-relevant Drug Substances**: For the purposes of this MAPP, the term "quota-relevant drug substances" is defined as the specific Schedule I and Schedule II substances, additional controlled drugs, and list I chemicals for which DEA annually requests that HHS provide usage data.

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
05/08/03	N/A	Initial
12/21/20	1	1. MAPP 4200.2 was converted into the current template. 2. Office of New Drugs and Office of Generic Drugs responsibilities were separated. 3. The Drug Shortages Staff responsibilities were added. 4. Language under responsibilities for all groups was revised to reflect current practices. 5. Added a Procedures section.
5/8/24	2	1. Reflects the new responsibilities of the CSI group. 2. Responsibilities and procedures updated to reflect current practices. 3. Minor additional edits.