
POLICY AND PROCEDURES

OFFICE OF THE CENTER DIRECTOR

Drug Shortage Management

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PURPOSE

This MAPP establishes CDER’s policy and procedures for notification, evaluation, and management of drug shortage situations for all CDER-regulated products including those marketed under new drug applications (NDAs), biologics license applications (BLAs), abbreviated new drug applications (ANDAs), and unapproved drugs marketed without an approved application.

This MAPP also establishes the responsibilities and procedures in CDER Offices and Divisions, including the Drug Shortage Staff (DSS) which serves as CDER’s focal point for the evaluation and management of drug shortages.

This MAPP does not establish procedures for interactions between CDER and other FDA centers or offices outside of CDER, with the exception of FDA’s Office of Regulatory Affairs (ORA).

BACKGROUND

- In 1999, the need to expand and enhance the management of shortage situations across the Center resulted in the formal establishment of the DSS. The DSS serves as

CDER's focal point for the evaluation and management of drug shortages. Through communication, facilitation, and negotiation, the DSS works with internal and external stakeholders to prevent, alleviate, and resolve shortages, in support of FDA's mission.

- On October 31, 2011, the President of the United States signed Executive Order (EO) 13588, Reducing Prescription Drug Shortages. This EO highlighted the serious public health threat of drug shortages and directed the FDA to take steps "that will help to prevent and reduce current and future disruptions in the supply of life saving medicines."
- On July 9, 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) was signed into law. Title X of FDASIA included new drug shortages provisions requiring FDA to submit to Congress an annual report on drug shortages and FDA's efforts to address them. In accordance with section 506C of the Federal Food, Drug, and Cosmetic Act (FD&C Act), manufacturers of most prescription drugs that are life-supporting, life-sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition (whether approved or unapproved) must report permanent discontinuance or temporary interruption in manufacturing that is likely to lead to a meaningful disruption in the supply of that drug in the United States.
- On October 31, 2013, FDA issued its Strategic Plan for Preventing and Mitigating Drug Shortages. The plan explains the root causes of drug shortages, FDA's procedures for helping to prevent or mitigate shortages, and FDA's goals and strategy for strengthening those procedures. The plan outlined recommended stakeholder actions to help prevent or mitigate shortages.
- On October 31, 2013, FDA issued a proposed rule, *Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products*, which proposed to implement certain sections of the FD&C Act as amended by FDASIA. This final rule was published on July 8, 2015. It became effective on September 8, 2015. The rule modifies FDA's regulations to implement sections 506C and 506E of the FD&C Act as amended by FDASIA.
- On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) was signed into law, to aid response efforts and ease the economic impact of COVID-19. Among other things, the CARES Act amended the FD&C Act to help FDA address drug shortages, including by adding requirements related to notifying FDA about finished product and active pharmaceutical ingredient (API) manufacturing discontinuances and interruptions.
- On April 6, 2023, FDA issued a draft guidance, *Notifying FDA of a Discontinuance or Interruption in Manufacturing of Finished Products or Active Pharmaceutical Ingredients Under Section 506C of the FD&C Act*. The draft guidance is intended to assist applicants and manufacturers in providing FDA timely, informative notifications about changes in the production of certain finished drugs and biological products as well as certain API that may, in turn, help the Agency in its efforts to

prevent or mitigate shortages. The draft guidance also explains how FDA communicates information about products in shortage to the public.

POLICY

- The DSS serves as CDER's focal point for the evaluation and management of drug shortages.
- The DSS resides in the CDER Office of the Center Director, Immediate Office and is overseen by the Associate Director for DSS, who reports to the CDER Deputy Director for Regulatory Programs.
- The DSS establishes and maintains a network of designated contacts within CDER to address drug availability issues comprehensively and proactively and serves as subject matter expert for any drug shortage-related issues within CDER.
- The DSS monitors drug supply and demand to ensure availability for emergency situations.
- The DSS serves as a liaison to private industry, other FDA centers, and other government organizations, including but not limited to the Centers for Disease Control and Prevention (CDC) and the Department of Defense (DoD).
- The DSS receives and evaluates information regarding potential or actual drug shortages from additional sources, such as the American Society of Health-System Pharmacists (ASHP) and other external entities, including health care professionals and patients.
- When the DSS confirms a drug shortage exists, the DSS posts this information on the CDER Drug Shortage Website.

RESPONSIBILITIES

The DSS will:

- Receive reports from all sources, including industry, other FDA offices, the ASHP and other external entities, health care professionals, and patients related to potential drug shortages permanent discontinuances, and interruptions in manufacturing.
- Verify a shortage or discontinuation (see definitions section) exists through communications with manufacturers, other FDA offices, and external entities such as the ASHP, and through the use of market research data.
- Search the internal drug shortage database and other available databases for drug supply history, information on other drugs in the same class, related CDER Office of Compliance (OC) and Office of Pharmaceutical Quality (OPQ) activity, and any existing medical necessity determination.

- Request a new or updated Medical Necessity Determination Form from the Office of New Drugs' (OND) clinical division with expertise on that drug, if the existing Medical Necessity Determination Form is more than one year old.
- Work with CDER offices and staff with defined drug shortage management or supply chain insight responsibilities, other FDA offices, industry, and outside entities to share information on a drug shortage, including the medical necessity of the drug, to develop a recommendation accounting for risks and benefits for impacted products and plan to address the shortage. Identify and review related information and monitor the supply of products from non-U.S. sources related to drug shortages, when necessary.
- Evaluate the need for distribution of drug products that would otherwise violate the FD&C Act and consider exercising enforcement discretion, when appropriate.
- After verifying the shortage, post shortage and discontinuation information provided by firms on CDER's Drug Shortage Website.
- Monitor each drug shortage situation from first report to resolution.
- Communicate information in a timely manner to the appropriate stakeholders both within and outside of the Agency.
- Include CDER stakeholders and stakeholders from other centers in discussions with industry related to drug shortage situations, as appropriate.¹
- Ensure the CDER Drug Shortage Website contains an up-to-date list of drugs that are determined to be in shortage. Information on this Website includes current drug shortages, resolved shortages, and discontinuations.
- Manage and update information on current shortages, pending issues, resolved shortages, averted shortages, and notifications from manufacturers and the public, in the internal drug shortage database.
- Maintain the drugshortages@fda.hhs.gov email account. Respond to drug shortage inquiries received through the DSS email account or by phone to 240-402-7770.
- Submit the Annual Report on Drug Shortages to Congress. This report includes FDA's efforts to address shortages.
- Notify CDER's Counter-Terrorism and Emergency Coordination Staff (CTECS) of issues relating to possible shortages or supply problems of any medical countermeasure (MCM) drugs.
- Provide CDER's Office of Communications (OCOMM) with materials, as appropriate.

¹ CDER's OC or Office of Pharmaceutical Quality (OPQ) or both should be included in discussions with industry that have Current Good Manufacturing Practices (CGMP) issues, drug quality issues, or other manufacturing issues related to drug shortages.

The Deputy Director for Regulatory Programs will:

- Oversee the DSS activities. The Associate Director will supervise the DSS.
- Provide guidance on policy issues related to shortages.
- Provide guidance on shortage management.

CDER Office of New Drugs (OND) will:

- Provide staff to work with the DSS when drug shortages are for innovator products without a generic product, or there is not enough generic product available to meet demand. The appropriate OND Office Directors, Division Directors, Team Leaders, Medical Officers, and Office of Regulatory Operations (ORO) staff will assist in the assessment of the shortage, in particular, the clinical implications of the shortage.
- Complete the Medical Necessity Determination Form when requested by the DSS, obtain the necessary clearance, and return the form to the DSS.
- Provide feedback on changes in clinical practice and new indications to the DSS.

CDER Office of Pharmaceutical Quality (OPQ) will:

- Facilitate prevention, mitigation, and resolution of drug shortage situations that involve drug quality (i.e., chemistry, manufacturing, and controls (CMC)) related issues. Quality concerns may relate to drug substance, drug product, microbiology, biopharmaceutics, and facilities assessments, or other areas.
- Provide supply chain data in response to natural disasters, geopolitical events, or other emergency situations and share with the DSS for further analysis to identify potential shortage concerns.
- Consult with the DSS before any facility inspection occurs to determine if there are shortage concerns with products manufactured at the facility and if so, include these concerns in the dossier for the facility.
- Participate in regulatory and compliance discussions with industry that involve an actual or likely drug shortage related to drug quality, including facility issues.
- Appoint an OPQ Drug Shortage Coordinator (OPQ DSC) and any additional points of contact within OPQ sub-offices to act as liaisons between OPQ staff and the OPQ DSC.
- Immediately forward all notifications of a drug shortage or potential drug shortage received by OPQ staff to the OPQ DSC.

OPQ Drug Shortage Coordinator (DSC) will:

- Act as liaison and provide guidance and expertise to OPQ management and staff, the DSS, and other CDER offices for drug shortage matters related to drug quality, including facility issues.
- Coordinate with OPQ sub-offices regarding quality, including facility issues, if the shortage involves more than one OPQ office.
- Immediately forward all notifications of a drug shortage or potential drug shortage to the DSS and, as appropriate, to the Office of Generic Drugs (OGD) Drug Shortage Coordinator (OGD DSC).
- Obtain confirmation from the DSS that the drug is in shortage, or there is likely to be a shortage, before expediting the review of an NDA or BLA supplement in response to an applicant's request claiming drug shortage-related reasons pursuant to CDER MAPP 5310.3: *Requests for Expedited Review of New Drug Application and Biological License Application Prior Approval Supplements Submitted for Chemistry, Manufacturing, and Controls Changes*.
- Coordinate with the DSS regarding an NDA, BLA, or supplement to an NDA or BLA to prevent, mitigate, or resolve a drug shortage.
 - When there is a need to expedite the quality review of an application or supplement to prevent, mitigate, or resolve a drug shortage.
 - Before taking a complete response action on a manufacturing supplement to evaluate any potential drug shortage implications.
 - If an API supplier has a discontinuance or interruption in manufacturing, to determine whether any drug products that use the API supplier are in shortage or at risk of shortage.
- Coordinate with the DSS, OGD DSC, OC, and ORA, as appropriate, when there is a need to expedite the review of a manufacturing supplement, for which an inspection is needed, to help prevent, mitigate, or resolve a drug shortage.
- Coordinate with the DSS, OGD DSC, OC, and ORA, as appropriate, on a manufacturing site with compliance-related issues to determine if any of the drugs manufactured at the site are in shortage or are at risk of shortage.
- Provide data elements to the DSS for inclusion in the Annual Report on Drug Shortages that is submitted to Congress.

CDER Office of Compliance (OC) will:

- Assign a point of contact from the Incidents, Recalls and Shortages Branch (IRSB) in OC, Office of Drug Security, Integrity, and Response (ODSIR) to coordinate OC program actions for managing a shortage.
- Participate in any compliance and regulatory discussions when compliance actions, risk mitigation measures, recalls, or drug withdrawals are under discussion and involve an actual or potential drug shortage.
- Provide shipping histories, as needed, and facilitate shortage drug shipments, when appropriate through the Imports Compliance Branch in ODSIR.
- Consult with the DSS, through the IRSB, before any enforcement action or issuance of a warning letter to evaluate any potential drug shortage implications. If it is determined an action or warning letter could lead to or exacerbate a shortage, OC will work with the DSS and other appropriate offices to evaluate the risks to patients. Such consults are requested through the IRSB.
- Forward notifications of a drug shortage or potential drug shortage received by OC staff to the IRSB to communicate with the DSS.
- Review proposals and determine risk control measures to be implemented by the manufacturer or distributor to help prevent, mitigate, or resolve a drug shortage.
- Provide registration and listing guidance to firms providing non-U.S. sources of drugs to alleviate a shortage.
- Inform the DSS through the IRSB when CDER OC/Office of Compounding Quality and Compliance (OCQC) becomes aware of specific risks or actions that may lead to disruptions in supply from an outsourcing facility that compounds or repackages drugs.
- Inform ORA, as needed, regarding drugs in shortage when compliance actions, recalls, or drug withdrawals are under discussion. Facilitate the U.S. entry process for drugs in shortage, as needed.
- Collaborate with ORA and OPQ to develop options required to facilitate expedited inspections.

CDER Office of Generic Drugs (OGD) will:

- Facilitate prevention, mitigation, and resolution of regulatory and scientific issues for drug shortages related to a generic drug, and for drug shortages related to situations where availability of a generic drug could address shortage related issues.
- Appoint an OGD DSC.
- Immediately forward all notifications of a drug shortage or potential drug shortage to the OGD DSC.
- Participate in any regulatory and compliance discussions with industry that involve an actual or likely drug shortage related to a generic drug.

OGD Drug shortage Coordinator (DSC) will:

- Act as liaison and provide guidance and expertise to OGD management and staff, the DSS, and other CDER offices on drug shortages related to generic drugs; provide advice on how generic drugs currently available can address the shortage; and provide advice on and expedite ANDAs that are currently under review and may help prevent or resolve a drug shortage.
- Coordinate with the DSS and the OPQ DSC, as appropriate, when there is a need to expedite an ANDA or a supplement to an ANDA to help prevent, mitigate, or resolve a drug shortage.
- Immediately forward all notifications of a drug shortage or potential drug shortage to the DSS, and as appropriate, the OPQ DSC.
- In collaboration with the DSS, and, as needed, the OPQ DSC, participate in any regulatory and compliance discussions that involve an actual or potential shortage that is related to a generic drug.
- Apprise the DSS of all ANDA approvals and discontinuations of drugs in shortage.
- Provide data elements to the DSS for inclusion in the Annual Report on Drug Shortages that is submitted to Congress.
- With respect to pending ANDAs related to a drug in shortage, ensure that review of all pending applications and supplemental applications has been appropriately prioritized in accordance with OGD MAPP 5240.3, *Prioritization of the Review of Original ANDAs, Amendments, and Supplements*.

CDER Office of Surveillance and Epidemiology will:

- Support the DSS's efforts in data analyses, including analysis of sales distribution data, on how drugs may be used, market share, or potential changes in demand based on historical sales data trends.
- Provide global drug sales market data by manufacturer for insights into drug products actively marketed to inform potential foreign importation mitigation efforts.
- Conduct a medication error focused risk assessment of labels and labeling, as needed, for products intended to help alleviate a drug shortage such as unapproved marketed drugs available in the U.S. or through importation.
- Review Dear Healthcare Provider letters for potential safety concerns, including medication error risks.
- Provide information regarding medication errors, adverse events, or other data and information for which OSE input is needed due to a product shortage.

CDER Office of Communications (OCOMM) will:

- Appoint coordinators within OCOMM's Division of Digital and Online Communications (DDOC) and Division of Drug Information (DDI) to work with the DSS.
- Forward new drug shortage inquiries and notifications received by DDI to the DSS.
- Assist the DSS by coordinating responses to inquiries regarding drug shortage issues.
- Assist with development and dissemination of information regarding shortages.

OCOMM Division of Drug Information (DDI) Coordinator will:

- Collaborate with the DSS to handle shortage reports received by DDI.

OCOMM Division of Digital and Online Communications (DDOC) Coordinator will:

- Collaborate with the DSS to post drug shortage information on the FDA Website.

CDER Counter-Terrorism and Emergency Coordination Staff (CTECS) will:

- Work with the DSS on issues related to the Strategic National Stockpile (SNS) and emergency preparedness and response activities.
- Serve as CDER's principal liaison with the SNS and other strategic emergency stockpiles.
- Notify the DSS of issues relating to possible shortages or supply problems of any MCM drugs.
- Collaborate with the DSS when shortages of CDER-regulated products may be anticipated during incidents coordinated by CTECS.

CDER Office of Executive Programs (OEP) will:

- Report important drug shortage and discontinuation information to the CDER Center Director and the Office of the Commissioner.
- Consult with the DSS and obtain clearance on press releases and internal background documents and talking points relating to shortages.
- Obtain clearance on correspondence relating to shortages that require Center-level clearance.

CDER Strategic Initiatives, International Program will:

- Provide shortage management expertise to non-U.S. regulatory authorities.
- Assist with identifying potential non-U.S. sources of drug products in shortage when no or insufficient FDA-approved products are available in the U.S.
- Notify the DSS of potential or actual shortages in non-U.S. countries, which may impact the drug product supply in the U.S.

FDA Office of Regulatory Affairs (ORA) will:

- Provide shortage management expertise to FDA Districts.
- Notify IRSB of potential shortage situations discovered during inspections.
- Notify the DSS of completion of Establishment Inspection Reports for firms inspected as they are completed.
- Notify CDER Imports Compliance Branch (ICB) of potential shortage situations due to product being held at a port. ICB will work with IRSB to determine CDER recommendations for such shipments.
- Facilitate the entry process for drugs from non-U.S. approved sources in conjunction with ICB to alleviate drug shortages.

PROCEDURES

The following steps are to be taken by DSS when a potential or actual drug shortage is reported from a manufacturer, FDA office, or an external entity:

The DSS will determine whether an actual drug shortage exists by:

1. Determining if the current product demand is stable or increasing based on historical data using a market research database.
2. Contacting product manufacturer(s) to provide accurate inventory information, manufacturing schedules, and any changes in ordering patterns.
3. Evaluating product distribution at the wholesale level, if needed.
4. Assessing information obtained from market research, manufacturer(s), and wholesaler(s) to determine if an actual drug shortage exists.
5. Requesting a new or updated Medical Necessity Determination Form from the OND division(s) with the requisite expertise on that drug product, if the existing Medical Necessity Determination Form is more than one year old or if needed.
6. Collecting the same information as in steps 1 – 4, above, for acceptable therapeutic alternative drug product(s) if acceptable therapeutic alternative drug product(s) exist.

7. Establishing a risk versus benefit profile related to an OC or OPQ action and the potential for a resulting drug shortage, when applicable. This profile will be established with input from the DSS and any other organizational entity mentioned in the Responsibilities section of this MAPP.
8. Monitoring the shortage situation until resolution.

The DSS will consider that a product is in shortage if all of the following exist:

1. The national supply available for product within the U.S. is not adequate.
2. The manufacturer of the product and those making therapeutic equivalent products and therapeutic alternative products, if relevant, are not able to meet demand or to increase production to cover the shortfall.
3. There is notice from the public or practitioners about the lack of product available in the market.

Requests for Expedited Review or Expedited Inspection:

If the DSS is requesting an expedited review or expedited inspection, the DSS will notify OND, OGD, OPQ, OSE, or OC, as appropriate, that such expedited action is requested. The request will be accompanied by information to justify the expedited review or inspection or both, such as the extent and severity of the shortage.

Exploration of Non-U.S. Approved Sources:

When a potential or actual shortage might be resolved by obtaining a drug from a non-U.S. approved source, the DSS will:

- Contact CDER Strategic Initiatives, International Programs (IP) to identify a potential drug supplier. If a drug supplier is identified, request relevant information from the drug supplier(s).
- Coordinate an internal review of relevant information with other Agency offices. Meet with the potential supplier to discuss compliance requirements.
- Notify the Centers for Medicare and Medicaid Services (CMS) of the product(s) to be obtained from the non-U.S. approved source.
- Coordinate issuance and clearance of a Dear Healthcare Provider Letter to outline to physicians and practitioners any differences between the non-U.S. approved source product and the U.S. marketed product in shortage.
- Discuss shipping logistics with the non-U.S. approved source, including entry information.
- Notify IRSB of the product port location and entry information for communication to the district and port.
- Monitor the shortage situation. Determine when product from the non-U.S. approved source is no longer needed.

- Communicate with appropriate Agency offices to ensure the proper controls are in place when product from the non-U.S. approved source is no longer needed.

When the DSS identifies a firm willing and able to divert existing product into the U.S. market to address a shortage, the DSS will ask for the following information from the firm to start the review of the non-U.S. approved source product:

- Amount of product available for supply. Product should be currently manufactured because there is not enough time to dedicate a new manufacturing line to address the shortage need.
- Product strength(s), dosage form(s), presentation(s), and expiration date(s) for the batch(es) and lot(s).
- Addresses for all drug substance and finished dosage form manufacturing and testing sites, and inspectional histories, including the relevant regulatory authority.
- Batch records, Certificates of Analysis, tests, and release specifications for the batch(es) and lot(s).
- Copies of the current labels and label inserts and English translations, if necessary.
- Draft of the Dear Healthcare Provider letter (to outline to physicians and practitioners any differences between the non-U.S. approved source product and the U.S. marketed product in shortage and detail any actions that should be taken while using the product).
- Distribution plan for the product. All costs associated with procurement of the product, shipment, and distribution are covered by the sponsor. The DSS may request sensitivity to the price, in light of the drug shortage; however, the DSS will not advise the firm or manufacturer on distribution or price.

Shortages of Controlled Substances and Requests for Adjustment in Drug Enforcement Agency (DEA) Quotas:

When the DSS receives notification related to a potential or actual shortage of a Schedule II controlled substance subject to a product quota, the DSS will:

1. Determine if the shortage notification is related to Drug Enforcement Agency (DEA) quota allocation (notification either from an API manufacturer or a finished dosage form manufacturer).
2. If the shortage notification is related to a DEA quota allocation, assess whether an increase in quota allocation is necessary to help prevent or mitigate a shortage. In making this assessment, request from the manufacturer the expected timeframe when manufacturing will cease and when a shortage may begin, if additional quota is not granted. As appropriate, the DSS assessment will also take account whether other manufacturers have sufficient quota and could cover the market in the absence of an increase in quota allocation.

3. If a shortage is confirmed for the Schedule II product, the product and related shortage information will be posted on the CDER Drug Shortage website under current shortages.
4. If the DSS determines that an increase in quota is necessary to help prevent or mitigate a shortage, contact the DEA, under the Memorandum of Understanding 225-15-11, to facilitate the manufacturer's request to the DEA for an increase in quota. In particular, DSS will provide the DEA information related to the expected market impact if the manufacturer's quota request are denied in part or in full.
5. If the DEA denies the manufacturer's request for an increase in quota related to a Schedule II drug on the shortage list, and provides the denial letter to the DSS, post the denial letter on the CDER Drug Shortage Website.
6. If the DSS's work to facilitate the manufacturer's request for additional quota does not yield a sufficient increase in quota allocation to address the shortage, FDA will submit a formal written request to the DEA to increase the quota allocation, taking into consideration the levels determined necessary by the manufacturer.
7. If the formal FDA request to the DEA to increase the quota allocation is denied, post the denial letter on the CDER Drug Shortage Website.

MCM Drug Shortages:

When the DSS receives notification of a permanent discontinuance or interruption in manufacturing of an MCM, the DSS will:

- Notify CTECS of all potential or actual shortages and discontinuances related to drugs with known MCM uses or that involve the SNS or the US military.
Note: Information on this group of drugs (MCMs) may not be posted on the CDER Drug Shortage Website because of national security considerations.
- Enter MCM drug shortage information in the internal drug shortage database.

Outsourcing Facilities:

The DSS will review the drugs made at the outsourcing facility and the risks related to the facility to enhance overall understanding of the marketplace involving the identified products. The DSS will:

1. Notify CDER OC if the drugs made at the outsourcing facility are currently in shortage or known to be vulnerable to shortage.
2. Respond to CDER OC if there could be worsening of shortages, at the local or national level, for the drugs that are already in shortage taking into consideration that actions may need to be taken due to the risks observed at the facility.
3. Continue to use all the tools available under FDA's current authority to address the identified potential shortages.

DSS Website Updates:

When the DSS has confirmed an actual drug shortage exists, the DSS will post specific information related to the drug shortage on the CDER Drug Shortage Website.

Information that is posted for “current” shortages includes:

- The drug name and presentation, the therapeutic categories, the drug manufacturer, and contact information for the manufacturer of the drug.
- The date of the initial posting on the CDER Drug Shortage Website.
- Any relevant information related to the shortage.
- Shortage reason per FDASIA.

Note: The CDER Drug Shortage Website is updated daily. The DSS does not post products until they are determined to be in shortage. This is to avoid hoarding of product and exacerbating a supply concerns. All information is verified with manufacturers.

Changing the status of a shortage on the CDER Drug Shortage Website from “current” to “resolved” occurs when the DSS determines a shortage has been resolved based on drug supply information from applicant(s) or manufacturer(s) and pre-shortage market data.

Information that is posted for “resolved” shortages includes:

- The drug name and presentation, the therapeutic categories, the drug manufacturer, and contact information for the manufacturer of the drug.
- The date of the initial posting on the CDER Drug Shortage Website and the date of the resolution.
- Any relevant information related to the shortage resolution.

Updates to the “Discontinuations” section of the CDER Drug Shortage Website with information provided by manufacturers regarding products that will no longer be manufactured include:

- The drug name and presentation, therapeutic categories, the drug manufacturer, and contact information for the manufacturer of the drug.
- The date of the notification and posting.
- Any relevant information related to the discontinuation.

REFERENCES

1. The White House, 2011. Executive Order 13588, Reducing Prescription Drug Shortages.
2. Public Law 112-144. Food and Drug Administration Safety and Innovation Act, 2012, Title X.

3. Public Law 116-136. Coronavirus Aid, Relief, and Economic Security Act, 2020. Section 3112.
4. FDA, 2022, Center for Drug Evaluation and Research, MAPP 5240.3: Prioritization of the Review of Original ANDAs, Amendments and Supplements.
5. FDA, 2021, Center for Drug Evaluation and Research, MAPP 5310.3: Requests for Expedited Review of New Drug Application and Biological License Application Prior Approval Supplements Submitted for Chemistry, Manufacturing, and Controls Changes.
6. FDA, 2013, Strategic Plan for Preventing and Mitigating Drug Shortages.
7. FDA, 2012, Office of Regulatory Affairs, FMD 15, Product Shortage Communication.
8. FDA, 2023, Draft Guidance for Industry: Notifying FDA of a Permanent Discontinuance or Interruption in Manufacturing of Finished Products or Active Pharmaceutical Ingredients Under Section 506C of the FD&C Act.
9. Memorandum of Understanding 225-15-11 Between Center for Drug Evaluation and Research and US Department of Justice Drug Enforcement Administration. February 27, 2015.

DEFINITIONS

Drug shortage: A period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug. In general, the DSS focuses on shortages of medically necessary products that have a significant effect on public health.

Drug Shortage Staff (DSS): The program office designated by the CDER Director to oversee and facilitate the resolution of all drug shortage situations. The DSS also monitors the production and availability of emergency and MCM drug products.

Medical Countermeasure (MCM): Medical countermeasures, or MCMs, are FDA-regulated products (biologics, drugs, devices) that may be used in the event of a potential public health emergency stemming from a terrorist attack with a biological, chemical, or radiological/nuclear material, or a naturally occurring emerging infectious disease. MCMs can be used to diagnose, prevent, protect from, or treat conditions associated with chemical, biological, radiological, or nuclear (CBRN) threats, or emerging infectious diseases.

Medically necessary drug: Any drug product used to diagnose, treat, or prevent a serious disease or medical condition for which there is no other drug that is judged by the CDER clinical review division to be an appropriate substitute or there is an inadequate supply of a therapeutic alternative as determined by the DSS. Off-label uses of approved drugs, marketed unapproved drugs, and Investigational New Drug (IND) drugs may be

considered medically necessary. Patient convenience alone is an insufficient reason to classify a drug product as medically necessary.

Medical necessity determination: A formal, written assessment made by a CDER medical officer or officers with requisite expertise on the drug, stating whether the drug meets the definition of medically necessary. Multiple CDER divisions may be asked to make this determination when there are approved indications or off-label uses requiring the expertise of more than one division. This determination is provided to the DSS on the Medical Necessity Determination Form (see Attachment 2).

Prevented Shortage: A prevented shortage is one where DSS received a notification of a discontinuance or interruption in manufacturing, assessed the potential for shortage, and determined that a shortage was likely given various factors. DSS then took specific actions to prevent the shortage from occurring.

Resolved Shortage: A “Current” shortage is moved to a “Resolved” status when all the manufacturers combined are able to meet total national pre-shortage supplies as seen with market data, or what meets current market needs, as supply amounts level out. In addition, DSS verifies each firm has enough safety stock prior to resolving each shortage.

Strategic National Stockpile (SNS): A federal (non-FDA) asset of medical supplies, including drugs, to be used in response to national emergencies (both natural and man-made). The SNS is maintained by the Administration for Strategic Preparedness and Response (ASPR).

EFFECTIVE DATE

This MAPP is effective upon publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
11/12/95	Initial	Posted as CDER MAPP 4730.1.
9/28/06	1	Office of ownership changed from OC to OCD. MAPP number changed from 4730.1 to 6003.1, Rev. 1.
2/3/12	n/a	Document recertified, S. Loewke. No changes made.
9/03/14	2	MAPP number changed from 6003.1 to 4190.1, Rev.2 Attachments 3 – 5 added. Changed the name of the Drug Shortage Program to the Drug Shortage Staff. Added Executive Order 13588, FDASIA, Strategic Plan for Mitigating and Preventing Drug Shortages, and the proposed rule, <i>Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products</i> , to the

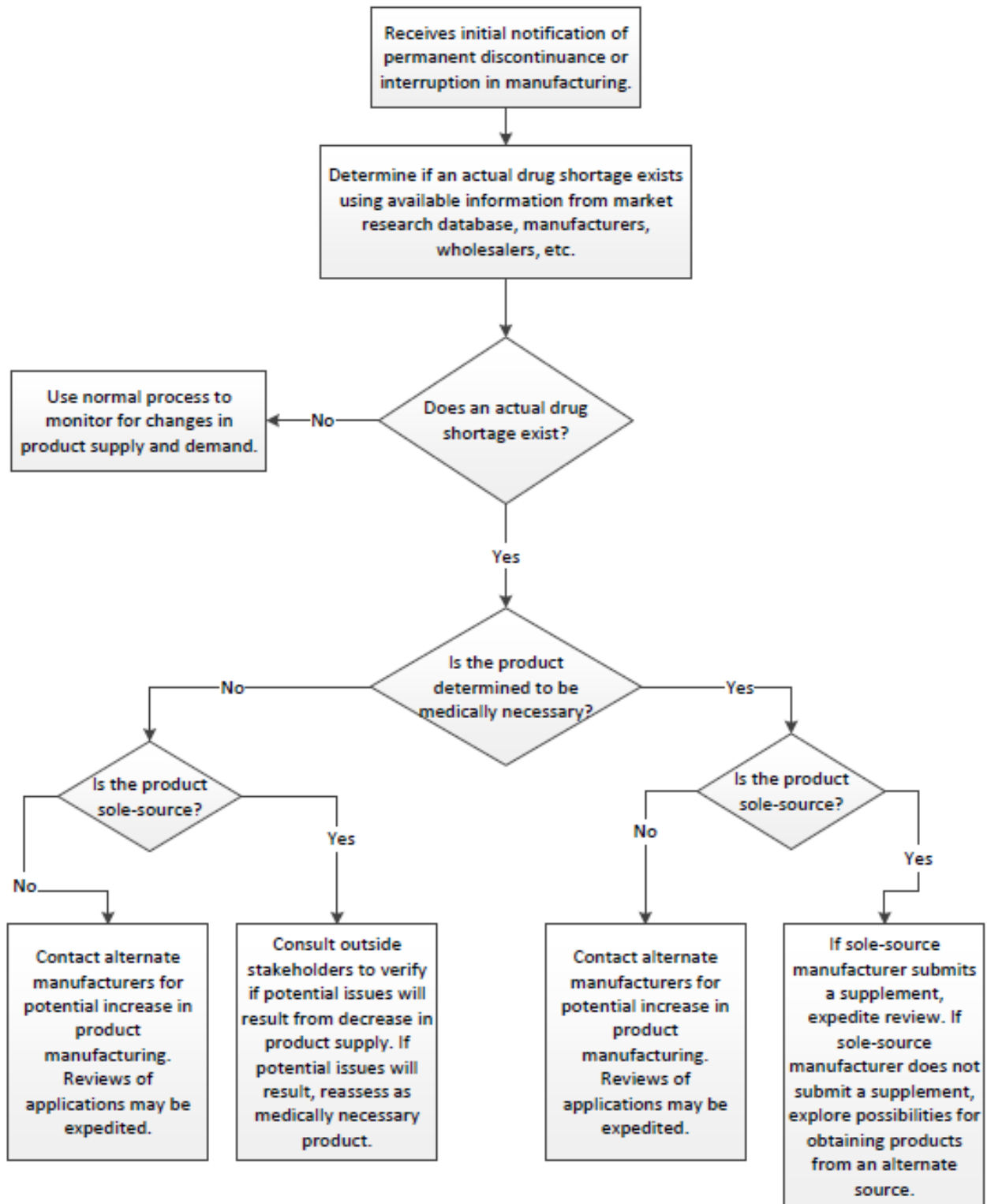
MANUAL OF POLICIES AND PROCEDURES

CENTER FOR DRUG EVALUATION AND RESEARCH

MAPP 4190.1 Rev. 4

		Background and References sections. Changed the Drug Shortage Coordinator to the CDER Deputy Director for Regulatory Programs and accordingly, the residence of the DSS. Added procedures for the Office of Biotechnology Products (OBP), ORA, and OEP. Confirmed and, when necessary, revised existing procedures. Further delineated Responsibilities and Procedures sections.
11/30/18	3	Based on CDER reorganization, added CDER Office of Pharmaceutical Quality (OPQ) and revised and expanded other Office responsibilities, as necessary. Added OPQ Drug Shortage Coordinator (DSC). Removed ONDQA Team Leader and CDER OPS, OBP Drug Shortage Coordinator responsibilities. Renamed OCTEC to CTECS. Confirmed and, when necessary, revised existing procedures. Revised Drug Shortage Process Flowchart. Added DSS Procedure for Request for Expedited Review or Expedited Inspection. Revised DSS Procedure for Shortages of Controlled Substances and Requests for Adjustment in Drug Enforcement Agency (DEA) Quotas.
1/1/24	4	Edits to reflect changes in processes. Revised responsibilities and acronyms for renamed offices and divisions. Added CDER Office of Surveillance and Epidemiology (OSE) responsibilities. Clarified alternate sources of product are non-U.S. approved sources. CARES Act (2020) added to the REFERENCES section. Updated attachments.

ATTACHMENT 1: Drug Shortage Process Flowchart



ATTACHMENT 2: Medical Necessity Determination Form

The writable PDF Medical Necessity Determination Form appears on the [MAPPs page on FDA.gov](#), immediately below the posting for CDER MAPP 4190.1, Rev. 4. The direct link to this form is <https://www.fda.gov/media/175823/download>.

ATTACHMENT 3: Index of Acronyms

ANDA — Abbreviated New Drug Application
API — Active Pharmaceutical Ingredient
ASHP — American Society of Health-System Pharmacists
ASPR — Administration for Strategic Preparedness and Response
BLA — Biologics License Application
CDC — Centers for Disease Control and Prevention
CDER — Center for Drug Evaluation and Research
CMC — Chemistry, Manufacturing, and Controls
CMS — Centers for Medicare and Medicaid Services
CTECS — Counterterrorism and Emergency Coordination Staff
DDI — Division of Drug Information
DEA — Drug Enforcement Agency
DDOC — Division of Digital and Online Communications
DoD — Department of Defense
DSC — Drug Shortage Coordinator
DSS — Drug Shortage Staff
FEI — FDA Establishment Identifier
FDASIA — Food and Drug Administration Safety and Innovation Act
IND — Investigational New Drug Application
ICB — CDER Imports Compliance Branch
IP — International Programs
IRSB — Incidents, Recalls, and Shortages Branch
MCM — Medical Countermeasure
NDA — New Drug Application
NDC — National Drug Code
OC — Office of Compliance
OCD — Office of the Center Director
OCOMM — Office of Communications
ODSIR — Office of Drug Security, Integrity, and Response
OEP — Office of Executive Programs
OGD — Office of Generic Drugs
OMQ — Office of Manufacturing Quality
OND — Office of New Drugs
OPQ — Office of Pharmaceutical Quality
OPQA — Office of Product Quality Assessment
ORA — Office of Regulatory Affairs
OSE — Office of Surveillance and Epidemiology
SNS — Strategic National Stockpile