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**POLICY AND PROCEDURES**

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**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<sup>1</sup> shortage situations for all CDER 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 outlines the responsibilities of the CDER Drug Shortage Staff (DSS).

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<sup>1</sup> Refers to all drug and biological products regulated by CDER.

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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).

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## 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 13588, Reducing Prescription Drug Shortages. This Executive Order highlighted the serious public health threat of drug shortages and directed the FDA to take steps to further "help to prevent and reduce current and future disruptions in the supply of life saving medicines."
- On December 19, 2011, FDA published an interim final rule (IFR) in the Federal Register amending its postmarketing reporting regulations implementing certain provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act) to require manufacturers who are the sole manufacturers of certain drug products to notify FDA at least six months before discontinuance of manufacture of the products. This interim final rule modifies the term "discontinuance" and clarifies the term "sole manufacturer" with respect to notification of discontinuance requirements. The broader reporting resulting from these changes enables FDA to improve its collection and distribution of drug shortage information to physician and patient organizations and to work with manufacturers and other stakeholders to respond to potential drug shortages.
- 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. The new provisions require 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 FD&C Act, implemented by 21 CFR 314.81(b)(3)(iii) and 21 CFR 600.82(a), manufacturers must report all permanent discontinuances of and all interruptions of the manufacture of any drug that is life supporting, life sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition, including any such drug product used in emergency medical care or during surgery (excluding radiopharmaceutical products), which are likely to lead to a meaningful disruption in the supply of that drug in the United States.
- On February 12, 2013, FDA issued a Federal Register Notice (Vol. 78, No. 29) requesting comments related to drafting a strategic plan on drug shortages.
- 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

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procedures for helping to prevent or mitigate shortages, and FDA's 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. On July 8, 2015, FDA published the final rule, which became effective on September 8, 2015.

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## POLICY

- The CDER Deputy Director for Regulatory Programs serves as the Drug Shortage Coordinator for the DSS. The DSS resides in the CDER Office of the Center Director, Immediate Office.
- The DSS establishes and maintains a network of designated contacts within CDER to address drug availability issues comprehensively and proactively.
- The DSS monitors drug supply and demand, including those used as medical countermeasures (MCMs), 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 Drug Shortage Website.

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## RESPONSIBILITIES

### The DSS Drug Shortage Coordinator will:

- Supervise the DSS activities.
- Provide guidance on policy issues related to shortages.
- Provide guidance on shortage management.

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**The DSS will** (see Attachment 1 and the Procedures section for detailed procedures):

- Receive reports from all sources (including industry, other FDA offices, the ASHP and other external entities, health care professionals, and patients) related to drug shortages and discontinuations. A manufacturer must provide notice at least 6 months in advance, or as soon as practicable, but in no case later than five business days after the permanent discontinuance or interruption in manufacturing occurs. If applicable, shortages and discontinuances also should be reported to the review office or division that regulates the application.
- Verify that a shortage or discontinuation 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 drug shortage database and other available databases for drug history, information on other drugs in the same class, related CDER Office of Compliance (OC) activity, any existing medical necessity determination, and status as a critical, emergency, or MCM drug.
- Request a new or updated Medical Necessity Determination Form from the Office of New Drugs' (OND) clinical division with expertise on that drug product.
- Work with CDER offices and staff with defined drug shortage management 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 risk versus benefit profile for impacted products and a drug shortage management plan.
- Identify, review related information, and monitor the supply of products from alternate sources related to drug shortages, when necessary.
- After verifying the shortage, post shortage issues 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.<sup>2</sup>
- 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 situations, and discontinuances.
- Manage and update information on current shortages, pending issues, resolved shortages, averted shortages, and information requests in the drug shortage database.

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<sup>2</sup> 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.

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- Maintain the DSS email account (drugshortages@fda.hhs.gov) listed on the CDER Drug Shortage Website. 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, which includes FDA's efforts to address shortages, to Congress.
  - Notify CDER's Counter-Terrorism and Emergency Coordination Staff (CTECS) of issues relating to possible shortages or supply problems of any MCM drugs.
  - Provide CDER's Office of Communications (OCOMM) with materials, as appropriate.

**CDER 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 Project Managers 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.

**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 disciplines include, but are not limited to, drug substance, drug product, microbiology, biopharmaceuticals, and manufacturing sites regarding non-enforcement-related issues.
- Participate in regulatory and compliance discussions with industry that involve an actual or likely drug shortage that is related to drug quality, including facility issues.
- Immediately forward all notifications of a drug shortage or potential drug shortage received by OPQ staff to the OPQ Drug Shortage Coordinator (OPQ DSC).
- Appoint an OPQ DSC and any additional points of contact within OPQ sub-offices to act as liaisons between OPQ staff and 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 a supplement in response to an applicant's request claiming drug shortage-related reasons.
- Coordinate with the DSS for an NDA, BLA, ANDA, 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 determine if the action could cause or exacerbate a drug shortage.
  - If an active pharmaceutical ingredient (API) supplier has a discontinuance or interruption to determine whether any drug products that use the API supplier are in shortage or likely to be in shortage.
- Coordinate with 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 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 likely to be in shortage.
- Provide required data elements to the DSS for submission of the Annual Report on Drug Shortages that is submitted to Congress.

**CDER Office of Compliance (OC) will:**

- Assign a point of contact from the Recall and Shortages Branch (RSB) in OC, Office of Drug Security, Integrity, and Recalls to coordinate OC program actions for managing a shortage.
- Participate in any compliance and regulatory discussions when compliance actions, recalls, or drug withdrawals are under discussion and involve an actual or potential drug shortage.
- Consult (see Attachment 3) with the DSS, through the RSB, before any enforcement action or issuance of a warning letter to determine if the action or letter could cause or exacerbate a shortage. If it is determined an action or warning letter could lead to or

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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 RSB.

- When appropriate, evaluate the need for distribution of drug products that would otherwise violate the FD&C Act and consider exercising enforcement discretion.
- Evaluate proposed actions from a manufacturer to help prevent, mitigate, or resolve a drug shortage.
- Help identify alternate drug sources for drugs in shortage, as needed.
- Provide registration and listing guidance to firms providing alternate sources of drugs to alleviate a shortage.
- Inform FDA's ORA regarding drugs in shortage.
- Facilitate the U.S. entry process for drugs in shortage, as needed.
- Collaborate with ORA and 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.
- 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 that is related to a generic drug.
- Appoint an OGD DSC.

**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 resolve a drug shortage.
- Notify the DSS when a medical necessity determination for a generic drug is needed.
- 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 prevent, mitigate, or resolve a drug shortage.
- Immediately forward all notifications of a drug shortage or potential drug shortage to the appropriate OGD Regulatory Project Manager (RPM), the DSS, and as appropriate, the OPQ DSC.

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- 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 discontinuances of drugs in shortage.
  - Serve as the liaison to generic drug applicants and, in coordination with the OPQ DSC, with generic drug manufacturers for drug shortage issues.
  - Provide required data elements to the DSS for the Annual Report on Drug Shortages that is submitted to Congress.
  - With respect to pending ANDA applications related to a drug shortage, ensure that review of all pending applications and supplemental applications has been appropriately prioritized in accordance with OGD's MAPP regarding Prioritization of the Review of Original ANDAs, Amendments, and Supplements (MAPP 5240.3).

**CDER Office of Communications (OCOMM) Director will:**

- Appoint coordinators within OCOMM's Division of Online Communications (DOC) and Division of Drug Information (DDI) to work with the DSS.

**CDER OCOMM will:**

- Provide assistance to the DSS by responding to inquiries regarding known drug shortage issues.
- Forward new drug shortage inquiries and notifications received by DDI to the DSS.
- 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 Online Communications (DOC) 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 discontinuance information to the Center Director, CDER, 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 Office of Strategic Programs (OSP), 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 alternative 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) Coordinators will:**

- Provide shortage management expertise to FDA District Offices.
- Notify RSB of potential shortage situations discovered during inspections.
- Notify Imports Exports Compliance Branch (IECB) of potential shortage situations due to product being held at a port. IECB will work with RSB to determine CDER recommendations for such shipments.
- In conjunction with IECB, facilitate the entry process for drugs from alternate sources to alleviate drug shortages.

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**PROCEDURES**

The following steps are to be taken 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 division(s) with the requisite expertise on that drug product, if needed.
6. Collecting the same information as in steps 1 – 4, above, for acceptable alternative drug product(s), if acceptable 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:**

1. Historic national demand for product within the U.S. is not being met.
2. The manufacturer of the product and those making alternative products 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.

**Exploration of Alternative Sources:**

When a potential or actual shortage might be resolved by obtaining a drug from an alternate source, the DSS will:

- Contact CDER OSP, International Programs (i.e., OSP and 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 alternate source.
- Coordinate issuance and clearance of a Dear Healthcare Provider Letter, if known risks regarding the product should be communicated to healthcare professionals.
- Discuss shipping logistics with the alternate source, including entry information.
- Notify RSB of the product port location and entry information for communication to the district and port.
- Monitor the shortage situation. Determine when product from the alternate source is no longer needed.
- Communicate with appropriate Agency offices to ensure the proper controls are in place when product from the alternate 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 alternate 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 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 alternate source product and the U.S. marketed product in shortage).
- 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.

**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, 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.

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

When the DSS receives notification of 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 FDA 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 to facilitate the manufacturer's request to the DEA for an increase in quota. In particular, provide the DEA information related to the potential or actual shortage and the expected market impact if the manufacturer's quota request were to be denied in part or in full.
5. If the DEA denies the manufacturer's request for an increase in quota and provides the denial letter to the DSS, post the denial letter on the 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 FDA CDER Drug Shortage Website.

**MCM Drug Shortages:**

When a potential or actual shortage of an MCM drug is reported, 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 drug shortage database.

**Outsourcing Facilities:**

When CDER OC becomes aware of specific risks or actions that may lead to disruptions in supply from an outsourcing facility that compounds or repackages drugs, CDER OC will inform DSS.

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 this information on the Drug Shortage Website.

Note: The Drug Shortage Website is updated daily. DSS does not post products until they are in shortage. This is to avoid creating any shortage. All information is verified with manufacturers.

Removal of postings from the "Current Drug Shortages" section of the Drug Shortage Website and placing of information in the "Resolved Drug Shortages" section of the Drug Shortage Website occurs when the DSS determines a shortage has been resolved based on drug supply information from applicant(s) or manufacturer(s) and historical market data. This information should include:

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

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

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

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**REFERENCES**

1. The White House, 2011. Executive Order 13588, Reducing Prescription Drug Shortages.
  2. Food and Drug Administration Safety and Innovation Act, 2012, Title X.
  3. Federal Food, Drug, and Cosmetic Act, Sec. 506C.
  4. FDA, 2013, Strategic Plan for Preventing and Mitigating Drug Shortages.
  5. FDA, 2017, Center for Drug Evaluation and Research, MAPP 5240.3: Prioritization of the Review of Original ANDAs, Amendments and Supplements.
  6. FDA, 2018, 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.
  7. FDA, 2012, Office of Regulatory Affairs, FMD 15, Product Shortage Communication.
  8. Federal Register Vol. 78, No. 29. February 12, 2013.
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**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 CDER medical staff to be an appropriate substitute or there is an inadequate supply of an acceptable 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).

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 Assistant Secretary for Preparedness and Response (ASPR).

**EFFECTIVE DATE**

This MAPP is effective 30 days following 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 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 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

**MANUAL OF POLICIES AND PROCEDURES**

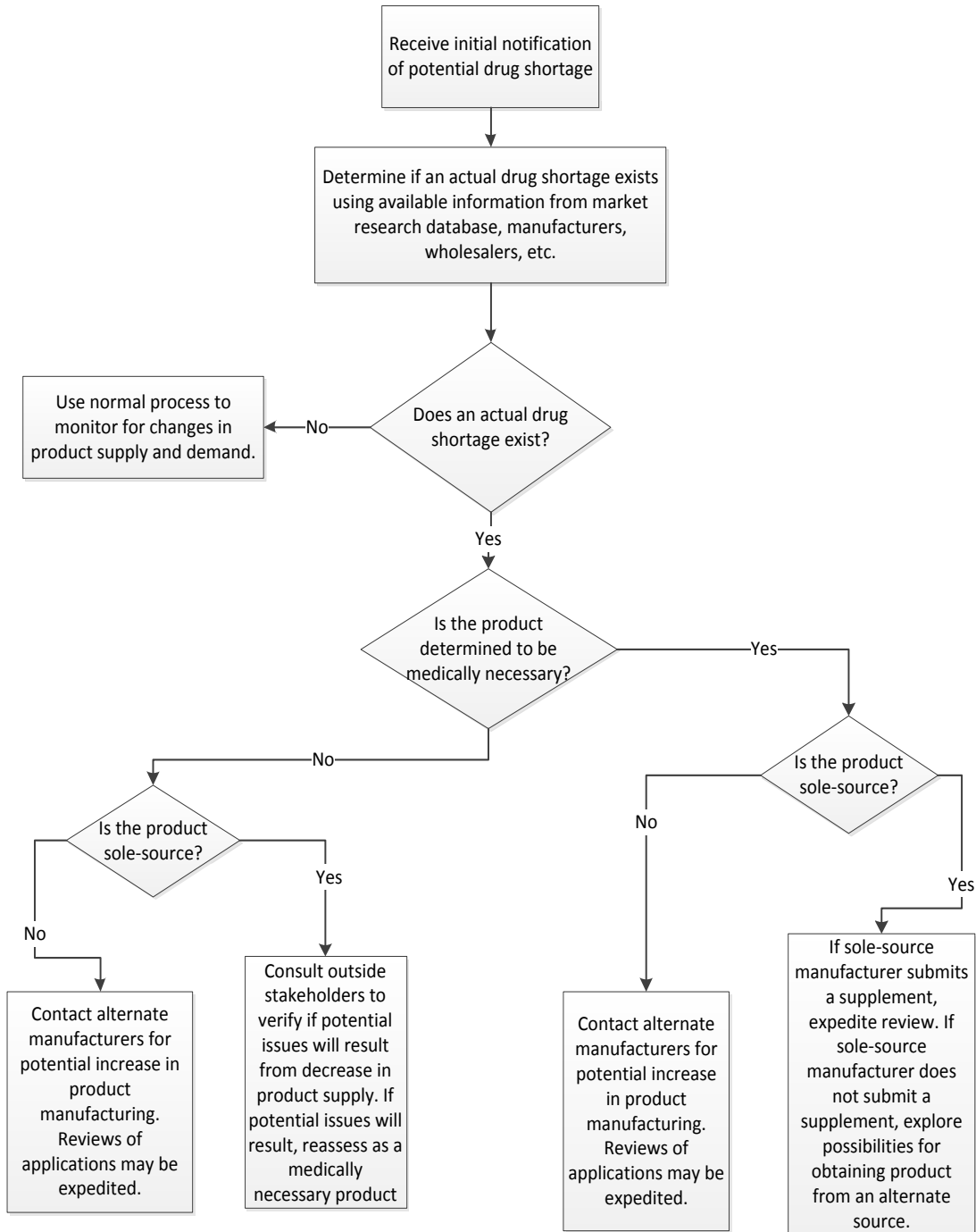
**CENTER FOR DRUG EVALUATION AND RESEARCH**

**MAPP 4190.1 Rev. 3**

	<p>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.</p>
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ATTACHMENT 1: Drug Shortage Process Flowchart



**ATTACHMENT 2: Medical Necessity Determination Form**

The writable PDF Medical Necessity Determination Form is attached to this MAPP. Click the paper clip icon, called “Attachments: View file attachments,” on the left side of this PDF document. Then select the document called “Att 2: Medical Necessity Determination Form.” Save a copy of the form to your computer’s hard drive to enter data.

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**ATTACHMENT 3: Office of Compliance Drug Shortage Consult Form**

**TO BE COMPLETED BY OFFICE OF COMPLIANCE**

1. Complete list of finished drug products and pending applications that will be impacted by the enforcement action or Warning Letter  
*Whenever possible/applicable, the list should include product name, dosage form, strength, and NDC number, as well as a list of who markets and distributes the product (i.e., identify ownership or customers for contract manufacturer).*
2. Brief summary of the potential impact that the violations found could have on product quality or safety, including product specific or site specific findings or violations, if applicable
3. Recommended action (regulatory action CDER/OC is likely to take), and whether such action will likely stop production, or if the action is intended to stop production
4. Timing of action
5. Firm FDA Establishment Identifier (FEI) and site address
6. If the consult involves expansion of a recall, provide the following information when available:
  - a. Product name, strength, NDC number, dosage form, and NDA, ANDA, or BLA number
  - b. Number of lots impacted and quantity per lot.
  - c. When affected lots were distributed and how much product is on the market.
  - d. Availability of replacement product. If replacement product is not available, when next batch is being manufactured and released.
  - e. Ability for product to be manufactured at another site or another line.
  - f. Current market information
    - i. Firm estimated burn rate
    - ii. Inventory within the firm's control
    - iii. Anticipated stock out date
  - g. Estimated time to correct the problem
  - h. Firm's plans both short and long term to resolve the problem

**TO BE COMPLETED BY THE DRUG SHORTAGE STAFF**

For each product impacted please provide the following (*may be provided as a separate document that includes the following information*):

7. Medical necessity determination (*please provide completed forms*)
8. Market share breakdown  
*When the product is also marketed by alternate manufacturers, market share of those manufacturers should be included as well.*
9. Burn rate  
*Include comments on alternate manufacturers or therapeutic alternatives with significant supply.*
10. Capacity of other firms (in a market research database or in the Orange Book) to increase production or cover market demand.  
*Prior to requesting that an alternate manufacturing firm increase production, the DSS should confirm with OC that the manufacturing site has an acceptable compliance status. OC will provide the DSS with current compliance status on alternate manufacturing firms.*
11. The DSS assessment of additional factors, including population-specific concerns (e.g., pediatric strengths), vulnerability to shortage, vulnerability of therapeutic alternatives, and feasibility (capacity and timing) of other firms to increase production or cover market demand

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**ATTACHMENT 4: Shortage Information Summary Form for Requests Initiated by the CDER Drug Shortage Staff**

**CDER Drug Shortage Staff Contact:** [Name]

**Recommendation/input needed from:**  Office of Compliance  OPQ  
 OGD  Clinical Division

**Date of request:** [Date]

**Date Office of Compliance Recommendation Needed:** [Date]

*The Drug Shortage Staff (DSS) provides the following information as background information to the Office of Compliance (OC), via the Recalls and Shortages Branch; the Office of Pharmaceutical Quality (OPQ); the Office of Generic Drugs (OGD); and OND clinical divisions when assistance is needed to alleviate, prevent, or resolve a drug shortage situation. If an office or division cannot make a recommendation or provide input by the requested date, then it should contact [Name] via e-mail [name]@fda.hhs.gov or phone [301-796-xxxx] to propose a new date.*

- 1. Firm FEI and site address**
  
- 2. Product name, strength, NDC number, dosage form, and NDA/ANDA/BLA number**
  
- 3. Reason for consult/summary** *(include what is needed from each office or division)*
  
- 4. Number of lots impacted and quantity per lot.** *(If applicable)*
  
- 5. When affected lots were distributed.** *(If applicable)*
  
- 6. Medically necessary** *(please provide completed form)*
  - Yes
  - No
  - Medically necessary by outside consult

**7. Current market information**

- a. Burn rate
- b. Market share breakdown
- c. Inventory within firm's control
- d. Anticipated stock out date
- e. When will product(s) be available to alleviate, prevent, or resolve the drug shortage? What is the FDA regulatory filing status of current product(s)?

**8. Approved suppliers: Are there alternate suppliers listed in the Orange Book that are not included in a market research database sales data?**

Yes; provide application number(s) and any status information available:

No

Comments:

**9. Pending application(s) in-house (if applicable/known):**

**10. Pending inspection(s) (if applicable/known):**

**11. Estimated duration of shortage:**

**12. Firm's short- and long-term plans to resolve shortage (attach firm proposal):**

**13. Overall Drug Shortage recommendation/assessment:**

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**Is an unapproved drug from an alternate source being proposed in order to alleviate the shortage?**

No

Yes

**a. Site information of every firm involved in the manufacturing process**

*(name, address, FEI, if available)*

- i.** Finished product
- ii.** API
- iii.** Testing
- iv.** Packaging and labeling
- v.** Other *(specify function)*

**b. Has the firm submitted an application (NDA/ANDA/BLA)?**

Yes; date of submission:

No; reason for not submitting an application or anticipated date of submission:

**c. In what countries is the product marketed?**

**d. Is the product approved in another country? If so, which countries?**

**ATTACHMENT 5: Index of Acronyms**

ANDA — Abbreviated New Drug Application  
API — Active Pharmaceutical Ingredient  
ASHP — American Society of Health-System Pharmacists  
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  
DOC — Division of 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  
IECB — Imports Exports Compliance Branch  
IP — International Programs  
MCM — Medical Countermeasure  
NDA — New Drug Application  
NDC — National Drug Code  
OBP — Office of Biotechnology Products  
OC — Office of Compliance  
OCD — Office of the Center Director  
OCOMM — Office of Communications  
ODSIR — Office of Drug Security, Integrity, and Recalls  
OEP — Office of Executive Programs  
OGD — Office of Generic Drugs  
OND — Office of New Drugs  
OPQ — Office of Pharmaceutical Quality  
ORA — Office of Regulatory Affairs  
OSP — Office of Strategic Programs  
RSB — Recalls and Shortages Branch  
SNS — Strategic National Stockpile