POLICY AND PROCEDURES

OFFICE OF THE CENTER DIRECTOR

Drug Shortage Management

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PURPOSE

This MAPP establishes CDER's procedures for notification, evaluation, and management of drug[1] shortage situations for all CDER products including those studied or marketed under investigational new drug applications (INDs), 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).

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).

[1] Refers to all drug and biological products regulated by CDER.

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 shortage, in support of the 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 the 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 6 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 includes new drug shortages provisions.
- On February 12, 2013, FDA requested comments in 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 procedures for helping to prevent or mitigate shortages, and FDA's strategy for strengthening those procedures. Recommended stakeholder actions to help prevent or mitigate shortages are also outlined.
- On October 31, 2013, FDA issued a proposed rule, *Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products*, which proposes to implement certain sections of the FD&C Act as amended by FDASIA. The DSS is required to submit to Congress an annual report on drug shortages and FDA's efforts to address them.

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 has 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, 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).
- In accordance with Title X of FDASIA, 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 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.
- 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, health care professionals, and patients.
- When the DSS has confirmed an actual drug shortage exists, the DSS will post this information on the Drug Shortage Website.

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, (Amended 2013), Sec. 506 C.
4. FDA, 2013, Strategic Plan for Preventing and Mitigating Drug Shortages.
5. FDA, 2012, Center for Drug Evaluation and Research, MAPP 5240.1: Requests for Expedited Review of Supplements to Approved ANDAs.
6. FDA, 2014, Center for Drug Evaluation and Research, MAPP 5240.3: Prioritization for Review of Original ANDAs, Amendments and Supplements.
7. FDA, 2012, Office of Regulatory Affairs, FMD 15, Product Shortage Communication
8. FDA, 2012, Draft Guidance for Industry: Notification to FDA of Issues that May Result in a Prescription Drug or Biological Product Shortage.

9. 78 CFR 29. February 12, 2013

RESPONSIBILITIES

The DSS Drug Shortage Coordinator will:

- Supervise the DSS activities.
- Provide guidance on policy-level issues related to shortages, as requested.
- Provide guidance on shortage management when a shortage involves more than one OND office, and as needed.

The DSS will (see Drug Shortage Process Flowchart and Attachment 1 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. Examples of situations in which manufacturers should or must notify the DSS of a potential drug shortage or discontinuation are stated in *Guidance for Industry: Notification to FDA of Issues that May Result in a Prescription Drug or Biological Product Shortage*. Notice should be reported at least six months in advance, or as soon as practical. If applicable, shortages and discontinuances also should be reported to the review office or division that regulates the application.
- Verify that an actual 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 electronic 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 medical countermeasure (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 that have defined drug shortage management responsibilities and procedures and other FDA offices, industry, and outside entities, as needed, to develop a risk versus benefit profile for impacted products and a drug shortage management plan.
- Post shortage issues, and significant discontinuation information on CDER's Drug Shortage Web site, when provided by firms.
- Communicate information to the appropriate stakeholders both within and outside of the Agency from first report to resolution.
- Monitor each drug shortage situation until resolution.

- Manage and update information in the drug shortage database. Information contained in this database includes current shortages, pending issues, resolved shortages, averted shortages, and information requests.
- Ensure the Drug Shortage Web page on the FDA Web site contains the most current information at all times. Information on this Web site includes current drug shortages, resolved situations, and discontinuances.
- Maintain the public email account accessed through the CDER Drug Shortage Web site. Respond to drug shortage inquiries received through the DSS email account (drugshortages@fda.hhs.gov) or by phone to 888-INFOFDA (888-463-6332) or 301-796-3400.
- Submit to Congress an annual report on drug shortages and FDA's efforts to address them.
- Provide CDER's Office of Communications (OCOMM) with materials, as appropriate.

CDER OND Director will:

- Provide staff to work with the DSS when drug shortage situations involve shortages of innovator products and no or not enough generic products available to meet demand. The appropriate OND Office Directors, Division Directors, Team Leaders, Medical Officers, and Project Management specialists will coordinate to manage the shortage.

OND Office Directors will:

- Serve as points of contact for shortage situations involving drugs regulated by their offices.
- Provide guidance to OND staff on policy-level issues relating to shortages.
- Collaborate with other OND Office Directors, regarding review issues, if the shortage involves more than one OND Office.
- Appoint a lead division when a shortage involves two divisions in an office.
- Review, edit, and sign Health Hazard Evaluations (HHEs) when requested by CDER OC.

OND Division Directors will:

- Serve as points of contact for shortage situations involving drugs within their divisions.
- Collaborate with other Division Directors when the shortage involves multiple divisions.
- Identify the appropriate staff to address the situation.
- Review, edit, and sign Medical Necessity Determination forms, as needed.

- Review, edit, and sign HHEs if CDER OC requests this determination.
- Facilitate and coordinate tracking of required data elements for the DSS Annual Report to Congress.

OND Team Leaders and Medical Officers will:

- Provide guidance to the team or participants in the required area of expertise to develop and carry out a management plan for the shortage situation.
- Complete the HHE. Obtain Division- and Office-level clearance when requested by CDER OC. Send the completed HHE form to OC and the DSS.
- Complete the Medical Necessity Determination form when requested by the DSS. Obtain the necessary clearance, and return the form to the DSS.

OND Project Managers will:

- Communicate all shortage information to the appropriate team members, OND Office Directors, and Division Directors.
- Update the DSS on shortage related team activities.
- Schedule internal and external meetings as necessary, provide meeting minutes, and enter the minutes into the electronic document archiving system for INDs, NDAs, or BLAs.
- Monitor the completion of the Medical Necessity Determination form and the HHE, when used. Provide copies to the requestor and file the completed forms in the appropriate electronic document archiving system.
- Manage the documentation for IND, NDA, and BLA regulatory actions associated with shortage activities of the team.

CDER Office of New Drug Quality Assessment (ONDQA) Team Leaders will:

- Provide expertise on shortage management involving chemistry, manufacturing, and controls (CMC) issues.
- Serve as the DSS liaison to all ONDQA personnel involved in a shortage situation.
- Work with team members to facilitate resolution of shortages that involve CMC issues.

CDER OC will:

- Participate in any compliance and regulatory discussions with industry when compliance actions, recalls, or drug withdrawals are under discussion and involve a potential drug shortage.
- Consult with the DSS prior to 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 cause or exacerbate a shortage, OC will work with the DSS and other appropriate offices to evaluate the risks, unless there is imminent risk of serious adverse health consequences or death to humans. Appropriate offices could include the Office of Manufacturing and Product Quality (OMPQ); Office of Unapproved Drugs and Labeling Compliance (OUDLC); and the Imports Exports Compliance Branch (IECB) within the Office of Drug Security, Integrity and Recalls (ODSIR). Such consults are requested through the Recalls and Shortages Branch (RSB).

- Request a medical necessity determination through the DSS regarding drugs with compliance-related issues that could lead to a shortage. RSB will communicate the medical necessity and shortage information to all involved parties in OC.
- Request and process HHEs from OND clinical divisions, as needed.
- Exercise appropriate enforcement discretion for distribution of products that would otherwise violate the FD&C Act.
- Provide feedback on issues such as additional testing, Dear Healthcare Provider (DHCP) letter review, or consultant oversight on a firm's proposal to distribute a violative or out of specification batch or product units for drugs deemed to be medically necessary but at risk for potential drug shortage.
- Assist in identification of alternate drug sources for drugs in shortage, as needed.
- Initiate, facilitate, and monitor products from alternate sources related to drug shortages, when necessary.
- Provide registration and listing guidance to alternate drug source firms providing foreign drugs to alleviate a shortage.
- Inform FDA's Office of Regulatory Affairs (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.
- Track the number of expedited inspections completed for the DSS Annual Report to Congress.

OC, Office of Drug Security, Integrity and Recalls (ODSIR), Recalls and Shortages Branch (RSB) will:

- Coordinate all OC participation in drug shortage situations. For situations involving compliance and regulatory actions, the RSB is the point of contact for and supports the DSS by coordinating OC program actions for managing a shortage.

CDER Office of Generic Drugs (OGD) will:

- Facilitate resolution of regulatory and scientific issues related to generic drugs in shortage.

- Apprise the DSS of all ANDA approvals and discontinuances of drugs in shortage and MCM drugs.
- Notify the DSS when a medical necessity determination for a generic drug is needed.
- Consult with the DSS with regards to expediting an ANDA or a supplement to an ANDA in order to alleviate a shortage situation.

OGD Director will:

- Appoint an OGD Drug Shortage Coordinator.

OGD Drug Shortage Coordinator will:

- Provide guidance and expertise on generic drugs involved in shortage situations.
- Coordinate with DSS in situations involving generic drug products.
- Serve as the liaison to generic manufacturers for shortage resolution.
- Track required data elements for the DSS Annual Report to Congress.

OCOMM Director will:

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

CDER Office of Communications (OCOMM) will:

- Forward drug shortage inquiries received through the Division of Drug Information (DDI) email and voicemail accounts to the DSS.
- Provide assistance to the DSS in responding to inquiries regarding known shortage issues.
- Assist with development and dissemination of information regarding shortages.
- Assist with postings on the Drug Shortage Web site.

OCOMM DDI Coordinator will:

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

OCOMM DOC Coordinator will:

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

CDER Office of Pharmaceutical Science (OPS), Office of Biotechnology Products (OBP) Drug Shortage Coordinator will:

- Work with OBP leadership and staff to provide expertise on shortage management involving CMC issues for biologics and protein products.

- Serve as the DSS liaison to all OBP personnel involved in a shortage situation.
- Work with team members to facilitate resolution of shortages that involve CMC issues.
- Track required data elements for the DSS Annual Report to Congress.

CDER Office of Counter-Terrorism and Emergency Coordination (OCTEC) will:

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

CDER Office of the Center Director (OCD), Executive Operations staff will:

- Coordinate clearance of documents requiring the DSS input.

The 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, FDA.
- Consult with the DSS. Obtain clearance on shortage press releases and talk papers as needed.
- Obtain signatures on correspondence relating to shortages that require Center-level clearance.

OEP, International Programs (IP) Coordinators 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 exist 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 the DSS and IECB of potential shortage situations due to product being held at a port. Work through the DSS or IECB (which may consult with the DSS) to determine CDER recommendations for such shipments.
- Facilitate the entry process for drugs from alternate sources to alleviate drug shortages.
- Track required data elements for the DSS Annual Report to Congress.

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 is 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.

Health Hazard Evaluation (HHE): A formal determination of patient safety (risk-benefit) related to the drug in question. This determination is requested by the Office of Compliance (OC), through the RSB, completed by the division or divisions with subject matter expertise in the drug, provided to OC and the DSS, and filed in the electronic document archive. HHEs are essential to the path forward in a drug shortage situation, as they are a key component in making a risk-benefit decision weighing the risks associated with a given product defect against the benefit of maintaining availability.

Medical Countermeasure (MCM): Biologic and pharmaceutical products to prevent and mitigate the health effects of chemical, biological, and radiation/nuclear threats.

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 IND drugs may be considered medically necessary. Patient inconvenience 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).

Non-HHS Stakeholders: Individuals or organizations located outside of Health and Human Services with a specific interest in drug shortage management. Examples of non-HHS Stakeholders include the DoD and the American Society of Health-System Pharmacists.

Strategic National Stockpile (SNS): A federal 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 Centers for Disease Control and Prevention (CDC).

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 1358, FDASIA, Strategic Plan for Mitigating and Preventing Drug Shortages, and the proposed rule, *Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products*, 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.

ATTACHMENT 1: Detailed Drug Shortage 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 verify if 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 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 Office of Compliance action and the potential for a resulting drug shortage, when applicable. This profile will be established with input from the DSS and any related 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 demand for product 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 to the market.

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

- Contact CDER OEP, 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 the healthcare professional letter, and 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 manufacturing and testing sites, and inspectional histories. Include the relevant regulatory authority.
- Batch records, Certificates of Analysis, tests, and release specifications for the batch(s) 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 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.

Request for Adjustment in Drug Enforcement Agency (DEA) Quotas:
When the DSS determines a potential or actual shortage involves a request for an adjustment in applicable quotas made by the Active Pharmaceutical Ingredient (API) or final dosage manufacturer of a schedule II product, the DSS will:

1. Determine if the shortage notification is related to Drug Enforcement Agency (DEA) quota allocation.
2. If this shortage notification is related to a DEA quota allocation, request that the API or finished dosage manufacturer of the schedule II product provide the date the quota request was officially submitted to the DEA, the outcome of that

request, and if an additional quota was not granted, the expected month of the product shortage.

3. Review schedule II products to determine if the information currently posted on the Drug Shortage Web site identifies the current market supply and the potential for additional or future shortage.
4. Contact the DEA and provide information related to the potential or actual shortage and the current market impact if the API or finished dosage manufacturer's quota request is partially granted by the DEA.
5. Contact the DEA to communicate the manufacturer's need for additional quota modifications when the DSS determines the increased quota is needed to prevent or address a shortage, or if the API or finished dosage manufacturer's total quota request was denied by the DEA.
6. If the shortage situation is further aggravated by the denial of additional quota, post the DEA quota letter denying the manufacturer's total quota request on the Drug Shortage Web site.
7. Submit a formal request to the DEA to increase the quota allocation if the finished dosage manufacturer sends a notification to the DSS requesting additional quota, but has not requested the additional quota from the DEA.
8. Post the denial letter on the Drug Shortage Web site if the formal FDA request to the DEA to increase the quota allocation is denied.

MCM Drug shortages:
When a potential or actual shortage of an MCM drug is reported, DSS will:

- Notify OCTEC of all potential or actual shortages and discontinuances related to drugs with known MCM uses or that involve the SNS.

  Note: Information on this group of drugs may not be posted on the CDER Drug Shortage Web site because of national security considerations.

- Enter MCM drug shortage information in the Drug Shortage database.

Compounding Facilities and Repackaging:
When CDER OC becomes aware of specific risks or actions that may lead to disruptions in supply from facilities that compound or repackage drugs, the DSS is consulted to provide an assessment of the impact.

The DSS will review the drugs made at the audited facility and the risks related to the facility. The DSS will:

1. Notify CDER OC if the drugs on the list 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. State in their evaluation

that the DSS understands that actions may need to be taken due to the risks observed at the compounding facilities.

3. Continue to use all the tools available under FDA's current authority to address the identified potential shortages.

The DSS does not have data for compounding facilities compounding or repackaging drugs. Compounding data not available to the DSS include the market share, volumes produced and distributed, or the specific facilities served by compounding pharmacies or for which compounders are producing specific drug products. For all of these reasons, the DSS is only able to provide an assessment of the commercially manufactured products currently in shortage.

DSS Web site 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 Web site, which is updated daily, focuses on products that are medically necessary and in current short supply. DSS does not post products until they are in shortage. This is to avoid worsening any shortage. All information is verified with manufacturers.

Removal of postings from the "Current Drug Shortages" section of the Drug Shortage Web site and placing of information in the "Resolved Drug Shortages" section of the Drug Shortage Web site occurs when the DSS determines a shortage has been resolved based on drug supply information from sponsor(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 Web site and the date of the resolution.
- Any relevant information related to the shortage resolution.

Updates to the "Drugs to Be Discontinued" 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, and contact information for the manufacturer of the drug.
- The date of the notification and posting.
- Any relevant information related to the discontinuation.

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.

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 WL
   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 manufacture).

2. Brief summary of the potential impact that the violations found could have on product quality or safety (if applicable) …product specific or site specific findings or violations

3. Recommended action (regulatory action CDER/OC is likely to approve), and whether such action will likely stop, or is intended to stop production

4. Timing of action

5. Firm 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 number

   b. How many lots are impacted? What is the quantity per lot?

   c. When were the affected lots distributed? How much product is on the market?

   d. Is replacement product available? If not, when is the next batch being manufactured, and when would it be available to the market?

   e. Does the firm manufacture the product at another site or on another line, and if so, does that site or line have the capability to increase production?

   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 IMS 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

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 ☐ ONDQA
☐ OGD ☐ Clinical Division ☐ OBP

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 New Drug Quality Assessment (ONDQA); the Office of Generic Drugs (OGD); and 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. **How many lots are impacted? Quantity per lot?** *(If applicable)*

5. **When were the affected lots 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 IMS 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:**

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
DDI — Division of Drug Information
DEA — Drug Enforcement Agency
DHCP — Dear Healthcare Provider
DOC — Division of Online Communications
DoD — Department of Defense
DSS — Drug Shortage Staff
FEI — FDA Establishment Identifier
FDASIA — Food and Drug Administration Safety and Innovation Act
HHE — Health Hazard Evaluation
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
OCTEC — Office of Counterterrorism and Emergency Coordination
ODSIR – Office of Drug Security, Integrity, and Recalls
OGD — Office of Generic Drugs
OMPQ — Office of Manufacturing and Product Quality
OND — Office of New Drugs
ONDQA — Office of New Drug Quality Assessment
OPS — Office of Pharmaceutical Science
ORA — Office of Regulatory Affairs
OUDLC — Office of Unapproved Drugs and Labeling Compliance
RSB — Recalls and Shortages Branch
SNS — Strategic National Stockpile