



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-N-3272]

Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions; Public Meeting;
Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public meeting; request for comments.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is announcing a public meeting entitled "Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions." The purpose of the meeting is to give stakeholders, including health care providers, patients, manufacturers, wholesalers, pharmacists, pharmacy benefit managers, veterinarians, public and private insurers, academic researchers, and the public, the opportunity to provide input on the underlying systemic causes of drug shortages, and make recommendations for actions to prevent or mitigate drug shortages. Members of Congress have asked the Agency to examine the root causes and drivers of these shortages, and to recommend measures that will provide more enduring solutions. To this end, the Commissioner has convened an inter-Agency task force of senior Federal officials of FDA, the Centers for Medicare & Medicaid Services, the Department of Veterans Affairs, and the Department of Defense. After receiving input from stakeholders, the task force intends to provide a report to Congress regarding the root causes of drug shortages. The report will also include recommendations regarding new authorities FDA or other Federal agencies could use to help provide enduring solutions to shortages.

DATES: The public meeting will be held on November 27, 2018, from 8:30 a.m. to 4:30 p.m. Submit either electronic or written comments on this public meeting by January 11, 2019. See the SUPPLEMENTARY INFORMATION section for registration date and information.

ADDRESSES: The public meeting will be held at the Washington Marriott at Metro Center, 775 12th St., NW, Washington, D.C. 20005. The hotel's phone number is 202-737-2200.

You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before January 11, 2019. The <https://www.regulations.gov> electronic filing system will accept comments until midnight Eastern Time at the end of January 11, 2019. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2018-N-3272 for "Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions." Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its

consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Michie Hunt, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6153, Silver Spring, MD 20993, 301-796-3504.

SUPPLEMENTARY INFORMATION:

I. Background

Drug shortages are among the greatest challenges health care providers and patients face. These shortages can affect treatment options and require practitioners to make difficult decisions

that can compromise care, such as rationing supplies or using less desirable, but more readily available, alternative therapies. FDA has acted within its statutory authority to prevent and mitigate drug shortages. By working with industry and other parties, the Agency has helped to steadily reduce the number of new shortages since a peak of 251 new shortages occurred in 2011, as detailed in the Agency's "Report on Drug Shortages for Calendar Year 2017," which is available at <https://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM610662.pdf>.

Despite this success in preventing or mitigating individual cases, more can and must be done to better understand and address the underlying systemic factors that are leading to shortages of medically necessary drugs. Members of Congress have asked the Agency to examine the root causes and drivers of these shortages, and to recommend measures that will provide more enduring solutions. To this end, the Commissioner has convened an inter-agency task force of senior federal officials of FDA, the Centers for Medicare & Medicaid Services, the Department of Veterans Affairs, and the Department of Defense. After receiving input from stakeholders, the task force intends to provide a report to Congress regarding the root causes of drug shortages. The report will also include recommendations regarding new authorities FDA or other federal agencies could use to help provide enduring solutions to shortages.

II. Topics for Discussion at the Public Meeting

We are soliciting input from stakeholders concerning the adverse consequences of drug shortages, the underlying systemic causes and drivers of these shortages, and the policies and strategies that may help to prevent or mitigate them. We welcome any relevant information that stakeholders wish to share, as all factors contributing to shortages are matters of concern. We are particularly interested in stakeholder input in the following areas:

*A. Assessing the Adverse Consequences of Drug Shortages to Patients, Health Care Providers,
and the Drug Supply Chain*

1. Drug Shortages' Impact on Patients

- a. What clinical impacts have patients experienced: e.g., adverse events, treatment delays, accelerated disease progression, or worsened outcomes due to patients' using less effective or less safe alternatives?
- b. What economic impacts have patients affected by drug shortages experienced?
- c. Do drug shortages affect patients disproportionately by geographic region, age, disease or condition, socioeconomic status, or other factors? Are there specific times of year or classes of drugs that see episodic, more frequent or more severe shortages? If so, why does this happen?

2. Drug Shortages Impact on Health Care Providers

- a. What economic impacts (including increased inventory management costs, substitution of more expensive drugs for drugs in shortage, and increased liability from adverse events) have health care providers, including veterinarians, experienced because of drug shortages?
- b. Do the adverse consequences of shortages affect providers disproportionately by, for example, geographic region, clinical area, or other characteristics?

3. Drug Shortages' Impact on the Supply Chain

- a. What economic effects have shortages had on key links in the drug supply chain: e.g., wholesalers, distributors, and pharmacies?
- b. Have certain links in the supply chain been disproportionately affected by shortages? If so, which ones?

4. Do available data accurately capture the differences among shortages (e.g., their severity and duration) that may affect their clinical and economic adverse consequences? If not, what additional data would be needed to better capture these differences?

B. Identifying the Root Causes and Drivers of Drug Shortages

1. What factors affect the likelihood, severity, and duration of shortages? Are these factors mostly related to raw materials, management, and resilience of production facilities, or other factors such as contracting or market structure? Do they differ for various drugs?

2. What government policies and regulations may contribute to drug shortages, and how could these be modified to prevent or limit impacts of drug shortages?

3. How do manufacturers contribute to drug availability or shortages, including responses to shortages?

a. What factors do generic and brand manufacturers consider when making decisions about whether to seek approval for certain drugs, to produce and market a drug for which they already hold an approved new drug application or abbreviated new drug application, or to discontinue marketing a drug? How do those decisions contribute (directly or indirectly) to shortages?

b. How do manufacturers monitor for situations that may result in a drug shortage? Are there certain indicators that are monitored? If so, are the potential triggers the same for all drugs, for example brand and generic sterile injectable drugs?

c. When manufacturers recognize a potential shortage, what options do they have for averting one? How easy or difficult is it to implement these options, and how costly is it to implement them? What is the impact of government policy or regulation on these options?

d. What factors play a role in manufacturers' decisions to make capital investments to expand capacity or to modernize infrastructure?

e. When manufacturers are remediating or upgrading a facility, how can shortages related to production slowdowns and shutdowns be avoided?

4. Drug supply is controlled through contracts among manufacturers, distributors, and end users. What features of contracts used throughout the supply chain contribute to drug availability and shortages, including responses to shortages?

a. What is the effect of duration and scope (how many and what types of drug products are covered by each contract, and whether non-drug products are bundled into the contract), on drug availability or shortage?

b. How commonly do these contracts include incentives such as contingency clauses, performance requirements, failure-to-supply clauses, or restrictions on limiting downstream price increases? How large are these incentives currently? Are there institutional or informational impediments limiting greater use of such incentives or performance clauses?

c. What are the implications of markups on inventory management throughout the supply chain? How might these markups contribute to shortages, and to response to shortages?

d. How have the characteristics of contracts, and markups at different points in the supply chain, changed over the past 15 years?

e. What are the implications of these contracting provisions and their changes for the probability, severity, and duration of drug shortages?

f. How much competition exists throughout the supply chain? Over the past 15 years, have there been challenges to competition and if so, what factors are responsible for these challenges? For example, has consolidation in different parts of the supply chain created market

barriers to entry and reduced competition? If so, what effect has the reduction in competition had on drug shortages?

C. Identifying Strategies for Preventing or Mitigating Drug Shortages

1. What policies could the Federal Government adopt, and what strategies could it implement, that would reduce the likelihood, severity, and duration of shortages? Would additional authorities be necessary or helpful? For example:

a. Establish a list of "essential medicines" for use in preventing and mitigating shortages. If such a list were established, what should be the criteria for inclusion? And how should such a list be maintained and administered?

b. Provide financial incentives, such as tax credits or revised reimbursement policies: e.g., to allow additional payments for drugs in or at risk of shortage or to encourage investment to expand manufacturing capacity or to modernize aging infrastructure, to enhance process capability and variability control, or to prevent manufacturing problems that affect product availability;

c. Allow other entities (e.g., contract manufacturers) to fill gaps in supply;

d. Require risk management plans to help manufacturers prepare to respond efficiently and effectively to potential shortages;

e. Require the extension of expiration dates for drugs in shortage or at risk of shortage, where scientifically justified;

f. Revise trade policies and authorities: e.g., to allow federal purchasers to buy imported drugs or raw materials to prevent or mitigate a shortage;

g. Heighten scrutiny of proposed mergers and acquisitions that increase market concentration or the likelihood of shortages;

- h. Revise payment policies and authorities: e.g., that would be coupled with a requirement to establish contingency plans for supplying medicines that go into shortage; and
 - i. Federal investment in production capacity for essential medicines directly related to national security, emergency preparedness, and defense.
2. In designing new policies to prevent or mitigate shortages, how can the Federal Government avoid creating perverse incentives or negative cascading effects in the health care financing and delivery system? For example, how might changes to government payment and reimbursement affect the other sectors of the market?
 3. Are there lessons for the Federal Government, or practices that it can emulate, from strategies used to prevent or mitigate shortages in other commodity markets that face shortage issues?
 4. What challenges does the global nature of drug manufacturing and marketing pose for efforts to prevent shortages in the U.S. market?
 5. As drug shortages are a national problem, what are the sources of funding that can be applied to provide incentives to remedy the root causes?

III. Participating in the Public Meeting

Registration: To register for the public meeting, please visit the following website: <https://healthpolicy.duke.edu/events/drug-shortage-task-force>. Please provide complete contact information for each attendee, including name, title, affiliation, address, email, and telephone. Registration is free and based on space availability, with priority given to early registrants. Persons interested in attending this public meeting must register by Wednesday, November 21, 2018, midnight Eastern Time. There will be no onsite registration. Early registration is recommended because seating is limited; therefore, FDA may limit the number of participants from each organization. Registrants will receive confirmation when they have been accepted. If

you are unable to attend the meeting in person, you can register to view a live webcast of the meeting. The Duke-Margolis Center for Health Policy will post on its website if registration closes before the day of the public meeting.

If you need special accommodations due to a disability, please contact Sarah Supsiri at the Duke-Margolis Center for Health Policy (phone: 202-791-9561, email: sarah.supsiri@duke.edu) no later than November 20, 2018.

Streaming webcast of the public workshop: This public workshop will be webcast live. Persons interested in viewing the live webcast may register ahead of the event by visiting <https://healthpolicy.duke.edu/events/drug-shortage-task-force>. The live webcast will also be available at the website above on the day of the event without pre-registration. Archived video footage will be available at the Duke-Margolis website following the workshop.

Transcripts: Please be advised that as soon as a transcript of the public meeting is available, it will be accessible at <https://www.regulations.gov>. It may be viewed at the Dockets Management Staff (see ADDRESSES). A link to the transcript will also be available on the internet at <https://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm>.

Other Issues for Consideration: A 1-hour lunch break is scheduled, but food will not be provided. There are multiple restaurants within walking distance of the Washington Marriott at Metro Center, 775 12th St., NW, Washington, D.C. 20005.

All event materials will be provided to registered attendees via email prior to the workshop and will be publicly available at the Duke-Margolis Center for Health Policy website at <https://healthpolicy.duke.edu/events/drug-shortage-task-force>.

Dated: September 5, 2018.

Leslie Kux,

Associate Commissioner for Policy.

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