



Connecting a World of
Pharmaceutical Knowledge

DRUG SHORTAGE SURVEY

INTRODUCTION

The International Society for Pharmaceutical Engineering (ISPE) appreciates the opportunity to collaborate with health authorities and different sectors of the pharmaceutical industry in its 2013 initiative regarding the prevention and mitigation of drug shortages. As background, ISPE believes that any effort to effectively address this complex and multi-faceted public health problem (1) requires close technical collaboration and clear communication between the pharmaceutical industry and global health authorities and (2) should include an appropriate examination of the underlying technical, scientific, manufacturing, quality and compliance issues associated with a company's supply chain and related to its ability to source, manufacture, and distribute products that have resulted in the shortage of a company's specific drug. With this in mind, ISPE has limited the scope of this survey to the technical and GMP compliance related issues that may be contributing to drug shortages. We recognize that there are many other factors that may impact the supply of drugs, including regional economic factors, differing regulatory requirements, insurance programs, and government procurement procedures. And while out of scope for this survey, understanding that respondents may want to highlight these "business-related" reasons, the survey has made allowances for users to add these type of comments into the survey. As part of its report, ISPE will summarize and present these comments, and will use them to provide context and assist in crafting/defining the scope for any next steps coming out of this phase of the effort. To this end, ISPE has developed the following anonymous survey to better understand the underlying issues and possible root causes regarding drug shortages. ISPE believes that the data from this anonymous survey will provide the pharmaceutical industry and health authorities with much needed scientific data to support additional discussion and the development of different risk-based approaches to mitigate and prevent drug shortages.

DEFINITIONS

For purposes of this survey, we have defined "drug shortage" as a situation in which the total supply of an approved (by the appropriate Health Authority) drug is inadequate to meet the current or projected demand at the user level. We have defined a near miss as a situation in which a company had reason to be concerned that the total supply of an approved drug might become inadequate to meet the current or projected demand at the user level. You may wish to write down or print these definitions for reference as you take the survey.

WHO MAY PARTICIPATE

ISPE has opened this survey for both ISPE Members and non-Members in order to help ensure the survey captures the data needed to come up with solid conclusions as well as the best possible solutions needed to overcome the issues responsible for drug shortages.

NOTICE ON ANONYMITY

Participation in the survey does not require disclosure of the respondent's identity. The anonymous respondent, however, should identify whether the response is on behalf of the individual (respondent) or a company, as described in Section A of the survey.

HOW THE SURVEY INSTRUMENT WORKS

This survey is highly specialized for the pharmaceutical industry. It contains numerous lines of questioning, all aimed at helping investigators better understand the root causes of issues related to the production process that contribute to, or cause, drug shortages.

1. Your answers will determine the subsequent questions with which you are presented, i.e, the system is presenting questions that are specific to your situation from a larger item bank. Because of this you may see the progress bar at the top seem to make large jumps between some items and much smaller jumps between others.
2. Because each answer determines the next question, you cannot go back in the survey. If you make a mistake, **DO NOT CLICK THE BACK BUTTON ON YOUR BROWSER**. In that event, please click through until the end of the survey, enter the term error into the final comment box, and click finish. Then, restart the survey.
3. If you cannot finish the survey in one sitting, please **FINISH THE PAGE YOU ARE ON**. Then click Save Page and Continue Later at the bottom of the screen you are on. You will be asked for your email address so the system can email you a special restart link. You can then close your browser. Using your special restart link you can return to the survey later and begin again. When you return, you will not see the page where you left off. The system will automatically load the next set of questions that are relevant to you. Your email identity will not be saved by the system.
4. If you have questions or concerns about the functionality of the survey, please email kkos@ispe.org.

SURVEY FORMAT

The survey is divided into the following sections:

- A. General Section
- B. Underlying Causes of Drug Shortages
- C. Company Strategies to Prevent or Alleviate Drug Shortages
- D. Regulatory Bodies: Ability to Prevent/Help Avoid Drug Shortages

Section A. GENERAL INFORMATION

This section seeks to gather information that will help ISPE identify correlations between the respondent's answers and (a) title (b) functional area/scope of responsibilities and (c) product characteristics. We know many respondents can provide multiple perspectives to this issue. For example, you may currently represent multiple functional areas or work at a company that manufactures multiple product types. To help us better identify the issues contributing to drug shortages (as well as potential solutions to help avoid them), please select one perspective for your answers to the survey. For example, if your company manufactures both sterile and non-sterile drugs, pick one product type and answer the survey on that basis. NOTE: You may complete the survey multiple times. Each set of survey responses should represent a different perspective (e.g. different shortage incidents or near misses, company versus individual point of view, sterile versus non-sterile, etc.).

Question A-1

Are you answering the survey: (choose one)

1. As an individual
2. On behalf of your company

Question A-2

How many years of experience do you have in pharmaceuticals?

1. 0-5 years
2. 6-10 years
3. 11-15 years
4. 16-20 years
5. More than 20 years

Question A-3

What is the functional area that best describes the area of your key responsibilities?

1. Quality
2. Production/Manufacturing
3. Regulatory Affairs
4. Development Scientist (Chemist/Microbiologist)
5. Professional/Consultant
6. Sales
7. Other

Question A-4

What is your current job level?

1. Vice President or above (Key Decision Maker)
2. Director, Associate Director (Key Responsible Party)
3. Sr. Manager, Manager, Team Leader/Production Supervisor/Project Manager (Key Influencer)
4. Associate/Analyst (Functional Contributor)
5. Subject Matter Expert (SME)
6. Other _____

Question A-5

Select the ONE category that best describes your company

1. Pharmaceutical/Biotech Manufacturer (Not a CMO)
2. Generics Manufacturer
3. Contract Manufacturer
4. API/Excipient Supplier
5. API/Excipient Distributor
6. Equipment Manufacturer
7. Professional Services Provider
8. Other (Describe) _____

Question A-6

How many employees does your company have in total (not just at your site)?

1. 100 or fewer
2. 101-500
3. 501-2000
4. 2001-10,000
5. 10,001 or more

Question A-7

Approximately what are your company's annual sales?

1. Below \$ 1 BN
2. Between \$ 1 BN and \$ 5 BN
3. Between \$ 5 BN and \$ 10 BN
4. Between \$ 10 BN and \$ 30 BN
5. Above \$ 30 BN
6. I don't know/NA

Question A-8

A drug shortage is defined as a situation in which the total supply of a drug approved by the appropriate health authority is inadequate to meet the current or projected demand at the user level. Have you or your company been impacted by a drug shortage?

1. Yes, my company has experienced one or more actual drug shortages or near misses. **Go to Section B on page 6**
2. No, my company has not been affected by a drug shortage, but I (or someone close to me) has been affected by a shortage as a patient **Go to Question A-9**
3. No, my company has not been impacted because we have a dedicated program to prevent shortages **Go to Section C on Page 20**
4. No, my company has not been impacted but we don't have a dedicated program to prevent shortages. **Thank you for your time. Your survey is complete.**

Question A-9

Who do you know that has been affected as a patient by a drug shortage?

1. Myself
2. A close family member
3. A friend, acquaintance or co worker
4. Other

Question A-10

What type of product was in short supply?

1. Sterile
2. Non-sterile
3. Other

Question A-11

What role did the product play in the patient's health?

1. Life-sustaining or life-preserving (e.g., an oncology drug)
2. Management of a long-term or chronic health issue but not life sustaining (e.g., a drug for managing hypertension or depression)
3. Treatment of an acute but short term illness (e.g., an antibiotic)
4. Preventive (e.g., an inoculation or birth control product)
5. Quality of life (e.g. a hair growth preparation or cosmetic)
6. Other

Question A-12

How did the patient learn about the shortage (Select all that apply)?

1. Prescribing professional or staff
2. Pharmacist
3. Media (internet, newspaper, television)
4. Official notice mailed to the patient
5. Word of mouth
6. Just figured it out when it wasn't on the shelf
7. Other

Question A-13

Was a substitute available?

1. Yes
2. No

Question A-14

What was the outcome for the patient?

1. It is too soon to tell
2. No negative effect
3. Inconvenienced, but health was not compromised
4. Health condition worsened or recovery time was lengthened
5. Death

Question A-15

Please provide any additional information you think would be helpful in our understanding of how drug shortages impact patients:

Question A-16

Does your company have a dedicated program to prevent drug shortages?

1. Yes **Proceed to Question A-17**
2. No **Thank you, your survey is complete**
3. Not sure **Thank you, your survey is complete**

Question A-17

How long has the program been in place? What was the impetus for creating/implementing the program?

Go to Section C on page 20

Section B. UNDERLYING CAUSES OF DRUG SHORTAGES

Part B-1. In the previous section you told us about your company's history with drug shortages and/or near misses. Now we want to explore those events more thoroughly to better understand what sorts of things are common when drug shortages happen - and when they can be avoided as well. From this point forward, please select ONE (1) drug shortage or near miss with which your company has been involved - the most significant one - and answer the questions on the basis of that set of events.

Question B1-1

I am answering this survey based on:

1. An actual drug shortage at my company
2. A drug shortage we avoided - a near miss

Question B1-2

How long ago did the shortage or near miss occur?

1. Three years or less
2. More than three years

Question B1-3

When you think of the drug shortage or near miss, in what region of the world was the principal plant located?

1. Africa and Middle East [Go to Question B1-5](#)
2. Asia Pacific [Go to Question B1-5](#)
3. EU and Eastern Europe [Go to Question B1-5](#)
4. Latin America [Go to Question B1-5](#)
5. North America (except USA) [Go to Question B1-5](#)
6. USA [Go to Question B1-4](#)

Question B1-4

Has your company been impacted by a drug product being placed on the US FDA drug shortage list?

1. Yes
2. No
3. Unsure/don't know

Question B1-5

Does your company have a program dedicated to preventing drug shortages?

1. Yes, and it pre-dates our shortage or near miss
2. Yes, and we started it as a consequence of our shortage or near miss
3. We are in the process of creating/implementing such a program
4. No
5. Other

Question B1-6

For the drug shortage or near miss that is the basis of your survey responses, please provide a detailed description of the event and likely root cause(s). (You need not reveal the name of the drug):

Question B1-7

For the shortage or near miss that is the basis of your survey responses, is the product:

1. Sterile [Go to Question B1-8](#)
2. Non-sterile [Go to Question B1-18 on page 8](#)

Question B1-8

What type of sterile product did your company manufacture?

1. Only finished drug product [Go to Question B1-9](#)
2. Only active pharmaceutical ingredient (API) [Go to Question B1-10](#)
3. Both API and finished drug product [Go to Question B1-11](#)

Question B1-9

What type of finished drug product was/is it?

1. Small molecule
 2. Large molecule
- [Now go to Question B1-14 on page 8](#)

Question B1-10

What type of API was/is it?

1. Small molecule
 2. Large molecule
- [Now go to Question B1-14 on page 8](#)

Question B1-11

What material most likely contributed most to the actual drug shortage or near miss?

1. API [Go to Question B1-12](#)
2. Finished drug product [Go to Question B1-13](#)

Question B1-12

What type of API was involved?

1. Small molecule
 2. Large molecule
- [Now go to Question B1-14 on page 8](#)

Question B1-13

What type of finished drug product was involved?

1. Small molecule
2. Large molecule

[Now go to Question B1-14](#)

Question B1-14

What method did your company use to produce the sterile API/drug product involved in the drug shortage?

1. Terminal sterilization
2. Aseptic processing of sterilized unit components

[Go to Question B1-15](#)

[Go to Question B1-17](#)

Question B1-15

What type of terminal sterilization?

1. Moist heat sterilization
2. Irradiation
3. Ethylene oxide

Question B1-16

What type of sterilization cycle?

1. Overkill method
2. Bioburden based cycle

[Now go to Section B, Part 2 on page 10.](#)

Question B1-17

Were your sterilized unit components

1. Manufactured under traditional aseptic controls
2. Manufactured using advanced control technologies, including Restricted Access Barrier Systems (RABS) and Blow-Fill-Seal systems

[Now go to Section B, Part 2 on page 10.](#)

Question B1-18

For your company's drug shortage or near miss, what type of non-sterile drug product/API did your company manufacture?

1. Only finished drug product
2. Only active pharmaceutical ingredient (API)
3. Both API and finished drug product

[Go to Question B1-19](#)

[Go to Question B1-20](#)

[Go to Question B1-21](#)

Question B1-19

What type of finished product was involved?

1. Small molecule
2. Large molecule

[Now go to Section B, Part 2 on page 10, read the definitions, and then proceed to Question B2-15 on page 16.](#)

Question B1-20

What type of non-sterile API was involved?

1. Small molecule
2. Large molecule

Now go to Section B, Part 2 on the following page. Read the definitions, and then proceed to Question B2-15 on page 16.

Question B1-21

Which non-sterile material likely contributed the most to your company's drug shortage or near miss?

1. API [Go to Question B1-22](#)
2. Drug product [Go to Question B1-23](#)

Question B1-22

What type of non-sterile API was involved?

1. Small molecule
2. Large molecule

Now go to Section B, Part 2 on the following page. Read the definitions, and then proceed to Question B2-15 on page 16.

Question B1-23

What type of non-sterile drug product was involved?

1. Small molecule
2. Large molecule

Now go to Section B, Part 2 on the following page. Read the definitions, and then proceed to Question B2-15 on page 16.

Section B. UNDERLYING CAUSES OF DRUG SHORTAGES

Part B-2. The second part of this section will attempt to identify the root causes of drug shortages related to your company's manufacture and testing systems, as defined below.

- Quality System – defined as the system that assures overall compliance with cGMPs and internal procedures and specifications. The system includes the quality control unit and all of its review and approval duties (e.g., change control, reprocessing, batch release, annual record review, validation protocols, and reports, etc.).
- Facilities and Equipment System – defined as the system that includes the measures and activities which provide an appropriate physical environment and resources used in the production of the drugs or drug products.
- Materials System – defined as the system that includes measures and activities to control finished products, components (including water or gases) that are incorporated into the product, containers and closures.
- Production System – defined as the system that includes measures and activities to control the manufacture of drugs and drug products including batch compounding, dosage form production, in-process sampling and testing, and process validation.
- Laboratory Control System – defined as the system that includes measures and activities related to laboratory procedures, testing, analytical methods development and validation or verification, and the stability program.
- Packaging and Labeling System – defined as the system that includes measures and activities that control the packaging and labeling of drugs and drug products.

Reminder:

- If you are answering this survey based on a sterile drug shortage or near miss, continue to **Question B2-1** on the following page.
- If you are answering this survey based on a non-sterile drug shortage or near miss, begin with **Question B2-15** on page 16.

Question B2-1

Please allocate 100 points to the issue(s) that you believe contributed most to your company's sterile drug shortage or near miss:

ISSUE	POINTS
Quality	
Component related (from third party)	
Raw material related (from third party)	
Active pharmaceutical ingredient (from third party)	
Non-quality issue at your company (e.g., mechanical failure, software failure)	
Related to health authority inspection at your company or a CMO (including voluntary shutdown)	
Related to product registration or approval issue at your company or a CMO (including compliance issues with marketing authorization conformance; conflicting requirements for products across different markets)	
Capacity issues (including lack of capacity from unforeseen demand) at your company or a CMO	
Business-related decisions (e.g., lower levels of contingency stock, product line discontinuation, consolidation of manufacturing sites at your company)	
Consolidation in the pharmaceutical industry, leading to few alternatives for supplying products	
Outsourcing with its added complexity, potentially leading to greater variability in supply chain models	
Supply chain disruptions as a root cause (e.g., carrier, transport, warehouse)	
Increased manufacturing complexity at your company	
Reliance on non-qualified manufacturers (e.g. compounding facilities)	
Other/Unknown (e.g., conflicting requirements for products for different markets)	
Total (Note: the electronic survey will total automatically and will require you to reach exactly 100 points. Please ensure that your total here equals 100 so that you can transfer it exactly to the electronic system.)	

Question B2-2

Whether or not you selected quality as a contributing cause to your company's drug shortage or near miss in the previous item, do you believe quality issues are relevant factors in the shortage?

1. Yes **Continue to the following page, read the instructions and begin with Question B2-3**
2. No **Go to Section C on page 20**

QUALITY AS A CONTRIBUTING FACTOR IN DRUG SHORTAGES.

We are now going to ask you a series of questions concerning the various quality systems that may play a role in drug shortages. We realize all of the items may not apply in every situation - and that some items may seem repetitive. In order to gather the most helpful information, and to maximize the ways we can analyze the co-existence or interrelated nature of these issues, we have had to structure the survey in this manner. Please choose the most appropriate answers for the situation at your company. If the answer you would give is not listed, please choose other and fill in your answer. If the issue does not apply to your situation, please check N/A.

Question B2-3

QUALITY SYSTEM. Which one of the following areas likely contributed the most to the drug shortage or near miss? (Please read all options before responding and select the option that is most applicable.)

1. Inadequate review of information indicating possible product contamination or adverse quality/efficacy risks to patients (safety)(For example: periodic product evaluations, complaints or rejected lots)
2. Inadequate review of discrepancy or failure investigations
3. Inadequate review of trends reports/summaries of quality indicators (For example: stability failures, product rejects)
4. More than one of the above areas in combination
5. Something else (For example, inadequate personnel training/qualification, data integrity concerns)
6. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible.

Question B2-4

FACILITIES AND EQUIPMENT SYSTEM. Please choose one of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that is most applicable.)

1. Facilities Issue [Go to Question B2-5 below](#)
2. Equipment Issue [Go to Question B2-6](#)
3. N/A [Go to Question B2-9](#)

Question B2-5

When you consider your facilities issue, which of the following areas likely contributed the most to the drug shortage or near miss?

1. Cleaning and maintenance
2. Facility layout or compliant design
3. Some combination of the above areas
4. Other

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible.

[Now go to Question B2-9](#)

Question B2-6

What type of equipment issue did you have? (Please choose the one (1) type of equipment problem that likely contributed most to the drug shortage or near miss at your company.)

- | | |
|---|---------------------------|
| 1. Production equipment | Continue to Question B2-7 |
| 2. Container/closure processing equipment
(such as depyrogenation equipment) | Now go to Question B2-9 |
| 3. Support utilities | Now go to Question B2-8 |
| 4. Other | Now go to Question B2-9 |

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible.

Question B2-7

Please choose the one (1) type of production equipment that likely contributed most to the drug shortage or near miss at your company.

1. Aseptic processing equipment
2. Stopper washer
3. Capping equipment (vials)
4. Post-fill visual inspection/automated inspection equipment
5. Sterilizers
6. Lyophilizers
7. Isolators
8. Restricted Access Barrier System (RABS)
9. Blow-Fill-Seal (BFS) Technology
10. Reactor, centrifuge, dryer, mill (to aseptically manufacture sterile bulk API)
11. Other

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible.

Now go to Question B2-9

Question B2-8

Please choose the one (1) type of support utilities problem that likely contributed the most to the drug shortage at your company.

1. Water system
2. HVAC
3. Other

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible.

Now go to Question B2-9

Question B2-9

MATERIALS SYSTEM. Please choose one of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that is most applicable.)

1. Processed gas
2. Pre-washed/ready to sterilize closures
3. Microbiological and endotoxin testing of component, container and closures
4. Verification of container and closures
5. Container and closure integrity
6. Other
7. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible.

Question B2-10

PRODUCTION SYSTEM. Please choose one (1) of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that is most applicable.)

1. Media fills or process simulations
2. Sterile filtration (aseptic processing)
3. Sterilization and depyrogenation of containers, closures and processing equipment
4. Lyophilization
5. Sealing of vials
6. Terminal sterilization
7. Parametric release of terminally sterilized drug product
8. Inspection of injectable products
9. Personnel (e.g., gowning, training, aseptic techniques)
10. Environmental and personnel monitoring
11. Other
12. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible.

Question B2-11

PRODUCTION SYSTEM. Please choose one of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that is most applicable.)

1. Inadequate batch records (for example, missing or incomplete records)
2. Nonconformance to established in-process controls, tests or specifications?
3. Control system for implementing changes in processes?
4. Process validation?
5. Other (for example, inadequate training/qualification of personnel)
6. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible.

Question B2-12

PRODUCTION SYSTEM: For any of the issues identified in the prior two questions, were similar problems observed at your company during development or technology transfer?

1. No
2. Yes
3. Uncertain (e.g., older products without robust development data)
4. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible

Question B2-13

LABORATORY CONTROL SYSTEM. Please choose one (1) of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that is most applicable.)

1. Sterility Testing
2. Limulus amoebocyte lysate (LAL) testing, including product specific validation
3. Environmental monitoring
4. Personnel monitoring
5. Efficacy of disinfectants, including assessment of the suitability, efficacy and limitations of the disinfecting agents used in the controlled area, production equipment and laboratories
6. Identifying microorganisms, including procedures that require identification of organisms found in positive sterility tests, media fills, and environmental monitoring samples as specified by your company
7. Microbiological media, including the preparation, sterilization and growth promotion testing of the media used in performing tests
8. Biological Indicators (BI) and biological cultures used in sterilization validation studies
9. Other(s)
10. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible

Question B2-14

PACKAGING AND LABELING SYSTEM. Please choose one (1) of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that most applies.)

1. Control system for implementing changes in the packaging or labeling operations
2. Investigation of discrepancies
3. Inadequate control of packaging and labeling operations
4. Other (for example, inadequate training/qualification of personnel)
5. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible

Now go to Section C on page 20.

Question B2-15

Please allocate 100 points to the issue(s) that you believe contributed most to your company's non-sterile drug shortage or near miss:

ISSUE	POINTS
Quality	
Component related (from third party)	
Raw material related (from third party)	
Active pharmaceutical ingredient (from third party)	
Non-quality issue at your company (e.g., mechanical failure, software failure)	
Related to health authority inspection at your company or a CMO (including voluntary shutdown)	
Related to product registration or approval issue at your company or a CMO (including compliance issues with marketing authorization conformance; conflicting requirements for products across different markets)	
Capacity issues (including lack of capacity from unforeseen demand) at your company or a CMO	
Business-related decisions (e.g., lower levels of contingency stock, product line discontinuation, consolidation of manufacturing sites at your company)	
Consolidation in the pharmaceutical industry, leading to few alternatives for supplying products	
Outsourcing with its added complexity, potentially leading to greater variability in supply chain models	
Supply chain disruptions as a root cause (e.g., carrier, transport, warehouse)	
Increased manufacturing complexity at your company	
Reliance on non-qualified manufacturers (e.g. compounding facilities)	
Other/Unknown (e.g., conflicting requirements for products for different markets)	
Total (Note: the electronic survey will total automatically and will require you to reach exactly 100 points. Please ensure that your total here equals 100 so that you can transfer it exactly to the electronic system.)	

Question B2-16

Whether or not you selected quality as a contributing cause to your company's non-sterile drug shortage or near miss in the previous item, do you believe quality issues are relevant factors in the shortage?

1. Yes **Proceed to Question B2-17**
2. No **Go to Section C on page 20**

Question B2-17

QUALITY SYSTEM. Which one (1) of the following areas likely contributed the most to the drug shortage or near miss? (Please read all options before responding and select the option that is most applicable.)

1. Inadequate review of information indicating possible product contamination or risks to patients (For example: periodic product evaluations, complaints or rejected lots)
2. Inadequate review of discrepancy or failure investigations
(For example: initial positive sterility tests and endotoxin and media fill failures and regardless of final disposition; failures that occurred during validation or revalidation or sterilization/depyrogenation processes; investigations involving media fills/process simulations)
3. Inadequate review of trends reports/summaries of quality indicators (For example: environmental monitoring trend data; personnel monitoring trend data; summary of water system results)
4. Inadequate review of change controls for critical utilities
(For example: sterilizers, lyophilizers, depyrogenation equipment, aseptic processing line, water systems, air-handling systems)
5. Other (For example, inadequate personnel training/qualification)
6. More than one of the above areas in combination
7. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible.

Question B2-18

FACILITIES AND EQUIPMENT SYSTEM. Please choose one (1) of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that is most applicable.)

1. Facilities Issue [Go to B2-19](#)
2. Equipment Issue [Go to B2-20](#)
3. N/A

Question B2-19

FACILITIES AND EQUIPMENT SYSTEM. When you consider your facilities issue, which of the following areas likely contributed the most to the drug shortage or near miss?

1. Cleaning and maintenance (for example, environmental monitoring)
2. Facility layout (for example, non-compliant design)
3. Other (for example, training/qualification of personnel; disaster (flood/fire))
4. Some combination of the above areas

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible

Now go to B2-22

Question B2-20

What type of equipment issue did you have? (Please choose the one (1) type of equipment problem that likely contributed most to the drug shortage or near miss at your company.)

- | | |
|--|-------------|
| 1. Equipment qualification (for example, inadequate maintenance or design) | Go to B2-22 |
| 2. Cleaning procedure(s) or cleaning validation | Go to B2-22 |
| 3. Issue(s) with control system for implementing changes in the equipment | Go to B2-22 |
| 4. Support utilities | Go to B2-21 |
| 5. Other | Go to B2-22 |

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible

Question B2-21

Please choose the one (1) type of support utilities problem that likely contributed the most to the drug shortage at your company.

1. Water system
2. HVAC
3. Other

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible

Now go to B2-22

Question B2-22

MATERIALS SYSTEM. Please choose one of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that is most applicable.)

1. Components (for example, inadequate testing or validation of suppliers test results)
2. Water and process gas (for example, inadequate validation, operation or maintenance)
3. Containers and closures
4. Some combination of the above
5. Other (for example, inadequate training/qualification of personnel)
6. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible

Question B2-23

PRODUCTION SYSTEM. Please choose one (1) of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that is most applicable.)

1. Inadequate batch records (for example, missing or incomplete records)
2. Nonconformance to established in-process controls, tests, or specifications
3. Control system for implementing changes in processes
4. Process validation
5. Other (for example, inadequate training/qualification of personnel)
6. Other
7. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible

Question B2-24

PRODUCTION SYSTEM: For any of the issues identified in the prior question, were similar problems observed at your company during development or technology transfer?

1. No
2. Yes
3. Uncertain (e.g., older products without robust development data)

Question B2-25

LABORATORY CONTROL SYSTEM. Please choose one (1) of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that is most applicable.)

1. Control system for implementing changes in the laboratory operations
2. Investigation of discrepancies
3. Analytical methods or procedures
4. Out-of-specification (OOS) procedures
5. Other (for example, inadequate training/qualification of personnel)
6. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible

Question B2-26

PACKAGING AND LABELING SYSTEM. Please choose one (1) of the following areas that likely contributed the most to the drug shortage or near miss at your company. (Please read all options before responding and select the option that most applies.)

1. Control system for implementing changes in the packaging or labeling operations
2. Investigation of discrepancies
3. Inadequate control of packaging and labeling operations
4. Other (for example, inadequate training/qualification of personnel)
5. N/A

Note: When you enter your answers into the electronic platform, clicking one of the above choices will present a free text box in which you will be asked to describe the issue and possible root cause(s) in as much detail as possible

Now proceed to Section C on the following page.

Section C. COMPANY STRATEGIES TO PREVENT OR ALLEVIATE DRUG SHORTAGES

Now we would like to know about the preventative measures, metrics, and organizational processes at your company that help maintain oversight and possibly prevent drug shortages.

- A. If your company has never had a shortage or near miss, please answer the following items with your company's general approach to preventing drug/product shortages in mind. When we ask about specific processes or strategies, please tell us what is in place at the present time.
- B. If you have completed earlier items regarding a specific drug shortage or near miss, please tell us what was in place at the time of the shortage or near miss. If you are unsure about an item or it does not apply to your company, please answer N/A. Rate the importance of each item from your own point of view, i.e., in your opinion as an industry professional, how important is the item or attribute in preventing drug shortages?

Question C-1

What level of staff within the company has been given the authority to address or prevent future drug shortages?

1. Vice President or above
2. Director or Associate Director
3. Sr. Manager or Manager (or Team Leader/Production Supervisor/Project Manager)
4. Associate/Analyst
5. Subject Matter Expert (SME)
6. Other

Question C-2, part 1

Company Quality Policy Status	No	Partial	Yes	
	1	2	3	Unsure or N/A
Strong Quality Systems that ensure compliance to manufacturing regulations are in place	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Avoiding drug shortages is stated as part of the corporate goals	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Incentives that are tied to these goals are in place	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Strong Quality Systems and GMP Inspection track records are in place	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Strong communication with Regulatory Authorities to help resolve potential issues occurs promptly when needed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-2, part 2

Company Quality Policy Status	Importance in Preventing Drug Shortages			
	Not Important	Important	Very Important	Unsure or N/A
Strong Quality Systems that ensure compliance to manufacturing regulations are in place	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Avoiding drug shortages is stated as part of the corporate goals	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Incentives that are tied to these goals are in place	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Strong Quality Systems and GMP Inspection track records are in place	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Strong communication with Regulatory Authorities to help resolve potential issues occurs promptly when needed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-3, part 1

Corporate Management Review and Governance	No	Partial	Yes	
	1	2	3	N/A
Company leaders are committed to working closely with regulatory bodies, and they alert (or are willing to alert) regulators to potential drug shortages in advance so solutions can be identified	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Metrics are in place to quickly detect and address potential drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Periodic monitoring is in place at the senior executive level to identify potential issues	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Corporate goals are associated with preventing drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-3, part 2

Corporate Management Review and Governance	Importance in Preventing Drug Shortages			
	Not Important	Important	Very Important	Unsure or N/A
Company leaders are committed to working closely with regulatory bodies, and they alert (or are willing to alert) regulators to potential drug shortages in advance so solutions can be identified	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Metrics are in place to quickly detect and address potential drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Periodic monitoring is in place at the senior executive level to identify potential issues	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Corporate goals are associated with preventing drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-4, part 1

Company Resource Management	No	Partial	Yes	
	1	2	3	Unsure or N/A
Sites are adequately staffed, i.e., the number of personnel and their ability to identify and correct issues that may lead to drug shortages meet the need	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Dedicated resources are focused on preventing drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Processes are in place to adequately and accurately predict demand for the company's products	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
There are dedicated personnel to detect and resolve (and report if necessary) drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Incentives are tied to efforts to alleviate drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-4, part 2

Company Resource Management	Importance in Preventing Drug Shortages			
	Not Important	Important	Very Important	Unsure or N/A
Sites are adequately staffed, i.e., the number of personnel and their ability to identify and correct issues that may lead to drug shortages meet the need	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Dedicated resources are focused on preventing drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Processes are in place to adequately and accurately predict demand for the company's products	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
There are dedicated personnel to detect and resolve (and report if necessary) drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Incentives are tied to efforts to alleviate drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-5, part 1

Cross-Functional Communication	No	Partial	Yes	
	1	2	3	Unsure or N/A
Processes and mechanisms are in place to anticipate the potential for drug shortages (increased demand, market withdrawal of a competing product, etc.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Processes are in place to make sure various functional groups (marketing, manufacturing, distribution) can work together to identify and resolve drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Periodic training occurs across functional groups to help better identify the potential for drug shortages and trigger the steps needed to resolve issues	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-5, part 2

Cross-Functional Communication	Importance in Preventing Drug Shortages			
	Not Important	Important	Very Important	Unsure or N/A
Processes and mechanisms are in place to anticipate the potential for drug shortages (increased demand, market withdrawal of a competing product, etc.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Processes are in place to make sure various functional groups (marketing, manufacturing, distribution) can work together to identify and resolve drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Periodic training occurs across functional groups to help better identify the potential for drug shortages and trigger the steps needed to resolve issues	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-6, part 1

Supply Chain Operations	No	Partial	Yes	
	1	2	3	N/A
The ability to quickly react to potential shortages (due to increased demand) and increase manufacturing capacity exists	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
There is redundancy in manufacturing operations that can be used to expand manufacturing capacity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Agreements are in place with suppliers that specifically include goals and incentives geared towards reducing the chances of a drug shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Strong relationships exist with contract manufacturers capable of making up the capacity needed to address a potential shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-6, part 2

Supply Chain Operations	Importance in Preventing Drug Shortages			
	Not Important	Important	Very Important	Unsure or N/A
The ability to quickly react to potential shortages (due to increased demand) and increase manufacturing capacity exists	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
There is redundancy in manufacturing operations that can be used to expand manufacturing capacity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Agreements are in place with suppliers that specifically include goals and incentives geared towards reducing the chances of a drug shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Strong relationships exist with contract manufacturers capable of making up the capacity needed to address a potential shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-7, part 1

Information Systems	No	Partial	Yes	
	1	2	3	Unsure or N/A
IT Systems are in place to help identify potential risks that could result in a drug shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
IT Systems are in place to help prevent or mitigate risks of drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
IT Systems are in place to help identify alternative solutions to drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-7, part 2

Information Systems	Importance in Preventing Drug Shortages			
	Not Important	Important	Very Important	Unsure or N/A
IT Systems are in place to help identify potential risks that could result in a drug shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
IT Systems are in place to help prevent or mitigate risks of drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
IT Systems are in place to help identify alternative solutions to drug shortages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-8, part 1

Supplier/CMO Management	No	Partial	Yes	
	1	2	3	N/A
Company has the ability to identify an alternate, qualified supplier or Contract Manufacture that can help manufacture materials needed to overcome shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Company builds supplier agreements so the firms partners are held responsible for notifying it of any potential shortages in material that may cause a shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Company has the ability to select partners that have their own contingency plans to help make up production when there is a risk of not being able to meet demand	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-8, part 2

Supplier/CMO Management	Importance in Preventing Drug Shortages			
	1	2	3	N/A
Company has the ability to identify an alternate, qualified supplier or Contract Manufacture that can help manufacture materials needed to overcome shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Company builds supplier agreements so the firms partners are held responsible for notifying it of any potential shortages in material that may cause a shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Company has the ability to select partners that have their own contingency plans to help make up production when there is a risk of not being able to meet demand	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question C-9

What actions/steps has your company taken to mitigate the negative impact of a drug shortage - whether the shortage was your own or that of another firm? (Select all that apply):

1. Published a list of therapeutic alternatives
2. Provided advance notice of the shortage to help make sure enough time is given to find therapeutic alternatives
3. Quickly identified partners that can help manufacture quantities needed to overcome the shortage
4. Re-entered the market to manufacture a drug where another company has notified the public of a shortage
5. Other (describe)

Question C-10

Please provide your thoughts and ideas regarding additional steps companies can take to address root cause issues and critical success factors to reduce the rate of drug shortages (e.g., other mitigation strategies including specific training, increased management oversight, dedicated resources, etc). Give a detailed description where possible.

Question C-11

What activities, protocols, or interventions do not work to prevent a drug shortage? Provide a detailed description where possible and explain how you know it doesn't (or wouldn't) work.



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Section D: REGULATORY BODIES AND THEIR ABILITY TO PREVENT/HELP AVOID DRUG SHORTAGES

In 2011, FDA was able to help prevent 195 drug shortages. The Agency’s ability to prevent shortages has been greatly facilitated by increased early notifications from manufacturers and the requirement signed into law (FDASIA) that they be required to do so. In Europe, EU legislation currently requires mandatory pre-notification by Marketing Authorisation Holders (MAHs) of disruption of supply in the case of permanent or temporary cessations, and for manufacturers of medicines in the case of any defect that could lead to an abnormal restriction in supply.

Question D-1

In your opinion what has been your experience regarding regulators’ ability to help avoid/mitigate a potential drug shortage issue by helping to execute/facilitate the following activities:

	Poor		Acceptable		Excellent	Unsure or N/A
Expedite filings/approval of applications	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Apply discretion/flexibility related to dealing with quality and/or compliance issues	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Help address manufacturing issues identified during inspections so production can resume	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Identify opportunities to keep manufacturing operations running e.g., with additional interim controls to address GMP issues	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Quickly approve new production lines to increase capacity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Review post-filing data that can be used to help justify decisions (e.g. agree to extend expiration dates, modification to manufacturing process, site change, etc)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Search overseas for drug to help make up for supply deficiency	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ask other companies to increase production	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ability to provide timely input on investigations. For example, where a company shares with the agency a major investigation, timely review of the investigation can avert a drug shortage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Question D-2

Have any recent legislative actions or other changes by regulatory agencies served to help improve communications between your company and the regulators?

1. Yes
2. No
3. Unsure

Question D-3

In its recent Reflection Paper, the EMA is proposing to “Promote better and proactive risk management by Marketing Authorisation Holders (MAHs) by requiring submission by all MAHs of a risk-analysis of their manufacturing process identifying any weaknesses and, depending on the severity, provide a contingency plan and proposals to strengthen the identified weaknesses.” What is your opinion of this proposal?

Question D-4

If your company produces generic drugs, is your company participating in the U.S. FDA’s Accelerated Recovery Initiative?

1. Yes
2. No
3. Unsure
4. We don’t produce generic drugs

Question D-5

Would it be useful for other countries to adopt initiatives similar to ones introduced by the FDA and EMA to help reduce drug shortages?

1. Yes
2. No
3. Maybe

Question D-6

Please describe other technical/quality/compliance steps that you think either industry or health authorities should make to further reduce the potential for drug shortages.

Question D-7

Now that you have completed the entire survey, is there any additional information you would like to share to help us better understand the situation at your company? (For example, if any of your answers would have changed had you been able to go backward in the survey, tell us here. If there are things about which we didn't ask you think were/are important to factors to consider, please fill it in here.)

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