Report 6 of the Research Committee for International Pharmaceutical Distribution of the Federation of Japan Pharmaceutical Wholesalers Association

The Research Committee for International Pharmaceutical Distribution
of the Federation of Japan Pharmaceutical Wholesalers Association

May 25, 2023

Global Pharmaceutical Supply Chains and Risks Posed to Maintaining a Stable Drug Supply in Japan

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Executive Summary

Background and Objective

As a result of the COVID-19 pandemic and the internationalization of pharmaceutical procurement, risk management for safeguarding a stable drug supply has become a global issue. The Research Committee for International Pharmaceutical Distribution of the Federation of Japan Pharmaceutical Wholesalers Association (JPWA) performed a survey to obtain insights regarding future risk management for safeguarding a stable drug supply in Japan based on measures taken in the United States and Europe.

Results

After conducting a review of the literature and interviews of pharmaceutical wholesaler associations in the United States, Europe, and the United Kingdom, the following points were identified:

- Causes of drug shortages: **It has been pointed out that the supply of low-margin drugs tends to be in shortage in the United States and Europe.** There is little incentive for pharmaceutical companies to manufacture low-margin products, and this causes a withdrawal of such products from the market.
- Procurement of generic active pharmaceutical ingredients (API): In the United States, the high dependence on foreign sources of supply is an issue, similar to Japan. On the other hand, in Europe, APIs can be produced locally within the region, and given the robust export performance, there isn't an immediate need to accelerate domestic production.
- Reporting lines: **Both in the United States and Europe, public agencies have set up** and manage **reporting lines on drug shortages**.
- **Adjustment of the supplied quantity of scarce items in the market: Both in the United States and Europe, such adjustments are to be made by pharmaceutical wholesalers.**
- Attitude towards the pharmaceutical industry: Both in the United States and Europe, clear engagement with the pharmaceutical industry by the state and on a regional level can be observed, but in Japan the attitude towards the pharmaceutical industry is ambiguous.

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Proposals

Based on the above results, we would like to make the following three proposals:

1. From the viewpoint of preventing drug shortages: Necessary to review the national health insurance (NHI) drug price scheme
   Current issues related to stable drug supplies in Japan are attributed to shipment suspension measures due to deviations from the manufacturing quality standards. However, it must be recognized that drug shortages in other countries that are caused by profitability issues can also occur in Japan**. It would be beneficial to establish a sustainable drug pricing system that prioritizes the steady supply of all pharmaceutical drugs, including generics.**

2. The first measure to be taken for handling drug shortages in the future: Creation of a reporting line
   It's crucial to consider **setting up a centralized system for tracking these shortages**.

3. The second measure to be taken for handling drug shortages in the future: Evaluation of the role of pharmaceutical wholesalers
   According to a survey of Japanese pharmaceutical wholesalers (conducted in April 2022), Japanese pharmaceutical wholesalers spent 19% of their total time for handling products for which shipment is adjusted for product shortage due to safety issues (shipment adjusted products, hereafter). As of February 2023, shipment adjustment products account for **approximately 50%** of all handled items (based on packaging units. **It's beneficial to implement socio-economic structures that recognize the role of pharmaceutical wholesalers in ensuring the sustainability of drug supplies.**

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Background and Objective of This Report

- Background
  - As a result of the COVID-19 pandemic, API procurement has become a major issue not only in Japan but also globally.
  - In Japan, the handling of products for which shipment is adjusted due to manufacturing quality issues is a great burden.

    → The perspective of risk management for safeguarding a stable drug supply becomes essential for drug supply chains.

- Objective

  To obtain insights regarding future risk management for safeguarding a stable drug supply in Japan based on measures taken in the United States and Europe.

- Survey method

  We sent questionnaires to and conducted hearings with the US Healthcare Distribution Alliance (HDA), the European Healthcare Distribution Association (GIRP), and UK Healthcare Distribution Association (HDAUK) from September to December 2022. In addition, we reviewed public documents such as the literature and websites disclosed as of 2022 and 2023.

Definition of the Term "Drug Shortage"

In this report, the term “shortage” of drugs is used as described below in accordance with the definition by the WHO:

Definition of Shortage
A “shortage” occurs when the supply of medicines, health products and vaccines identified as essential by the health system is considered to be insufficient to meet public health and patient needs. This definition refers only to products that have already been approved and marketed.

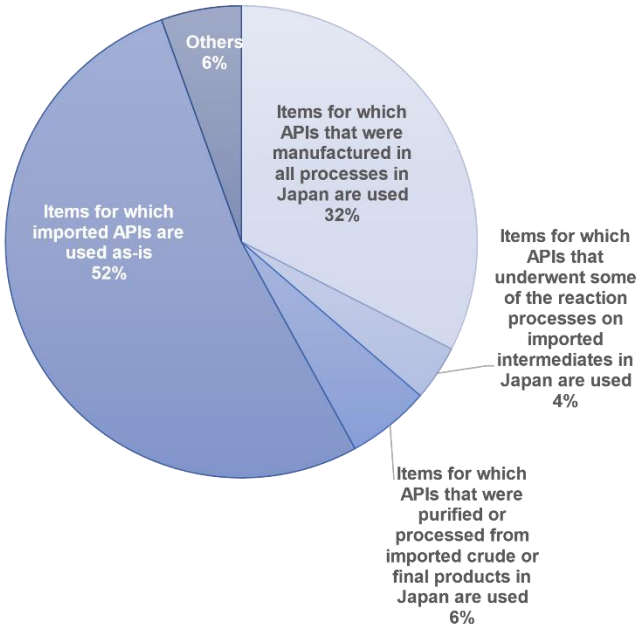
Note: Definition of Stockout
The complete absence of the medicine, health product or vaccine at the point of service delivery to the patient

Source: Meeting Report: Technical Definitions of Shortages and Stockouts of Medicines and Vaccines

Challenges of Drug Manufacturing in Japan

In Japan, generic API supplies depend heavily on foreign supply sources, and in particular the proportion of APIs that are procured in specific countries, such as China, South Korea, and India, is high.

Procurement status of APIs for generic drugs that are listed in the NHI Drug Price Standard (Based on the shipment value)



Source: Report of a survey on the roadmap for promoting the use of generic drugs (March 2022)

Procurement countries of APIs or crude/final products for generic drugs and proportion based on the purchase amount

API

Country name	Proportion (%)
China	23.5
South Korea	22.3
Italy	13.2
India	11.5
Spain	5.4
France	3.0
Hungary	3.0
Taiwan	3.0
Germany	2.5
US	2.5
UK	1.8
Israel	1.4
Poland	1.0
Czechia	0.9
Swiss	0.9
Mexico	0.8
Finland	0.4
Canada	0.4
Singapore	0.3
Slovenia	0.2
Netherlands	0.2
Others	1.8
Total	100.0

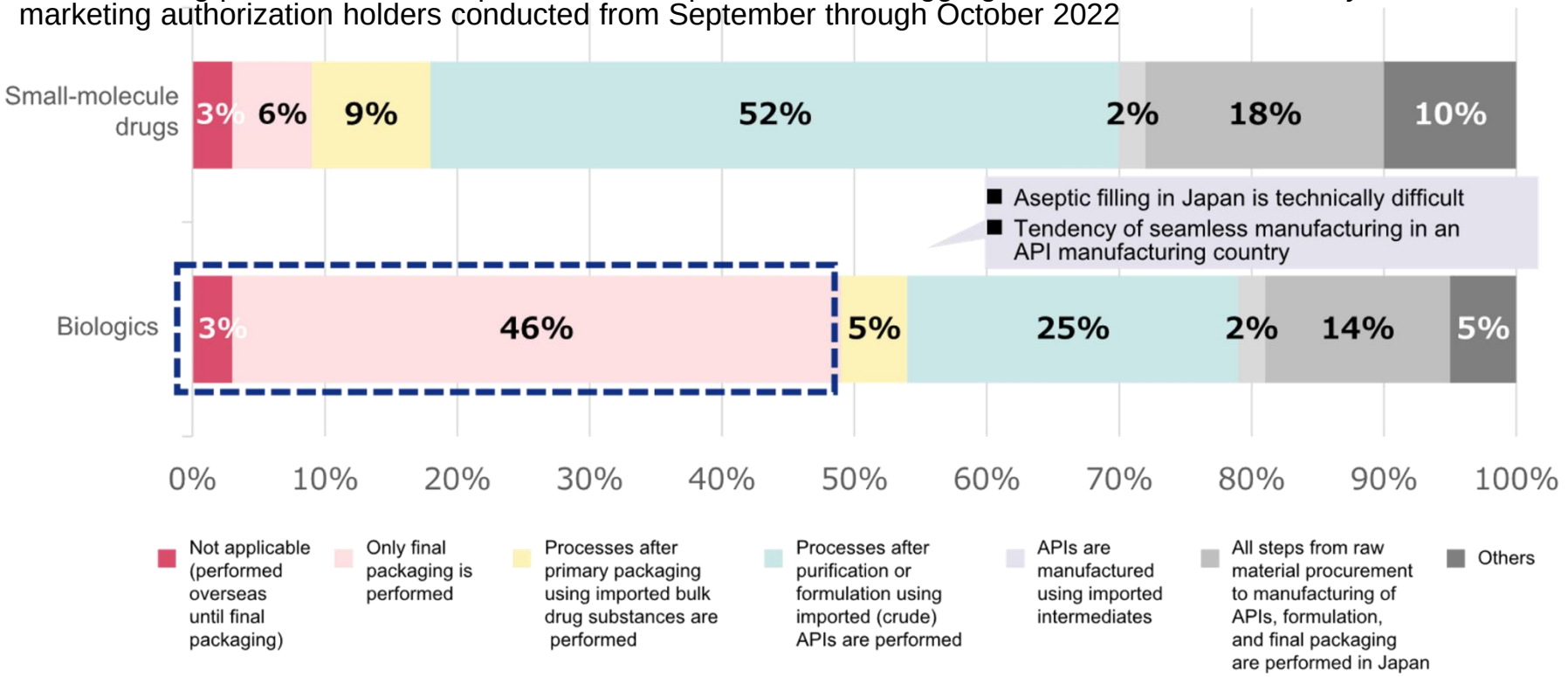
Crude or final product

Country name	Proportion (%)
China	48.9
South Korea	15.5
India	14.8
Italy	11.8
Germany	1.4
Hungary	0.8
Taiwan	0.8
US	0.8
Spain	0.7
Poland	0.4
France	0.2
Canada	0.2
Israel	0.2
Thailand	0.1
Others	3.4
Total	100.0

Challenges of Drug Manufacturing in Japan

Regarding the manufacturing process of Category B and C of stable supply medicines, the proportion of drugs that are entirely manufactured in Japan is 18% for small-molecule drugs and 14% for biologics.
For biologics, mostly only final packaging is performed in Japan.

Situation regarding Category B and C of stable supply medicines
Manufacturing processes that are performed in Japan. Data were aggregated the results of a survey of 220 marketing authorization holders conducted from September through October 2022



Source: A survey on the actual situation regarding pharmaceutical and medical device supply chains (a project commissioned in 2022 by the Policy Planning Division for Pharmaceutical Industry Promotion and Medical Information Management; Health Policy Bureau; Ministry of Health, Labour and Welfare)

Current Situation regarding Drug Shortages (US)

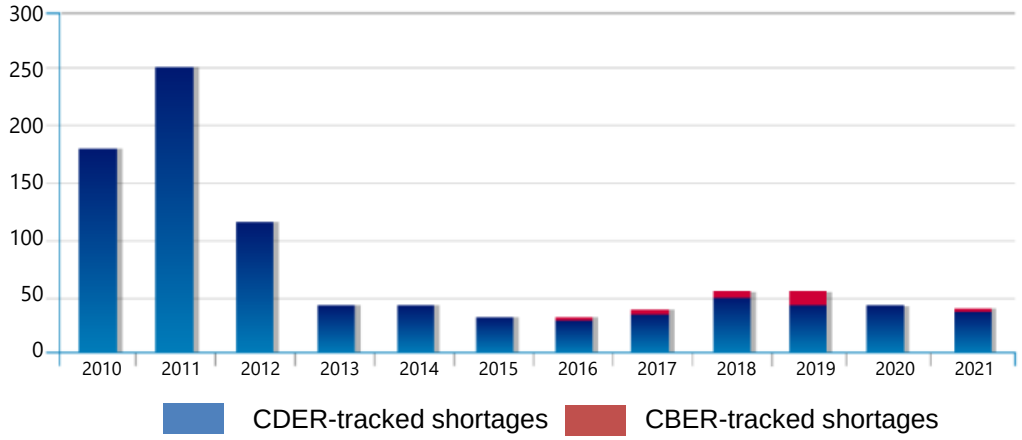
Main measures taken in the United States against drug shortages (1)

In response to the significant drug shortages experienced in 2011, national initiatives were launched to address this issue. Manufacturers are now required to notify the FDA in advance if they intend to discontinue or interrupt the production of a drug. Consequently, the FDA implemented a system to mitigate drug shortages.

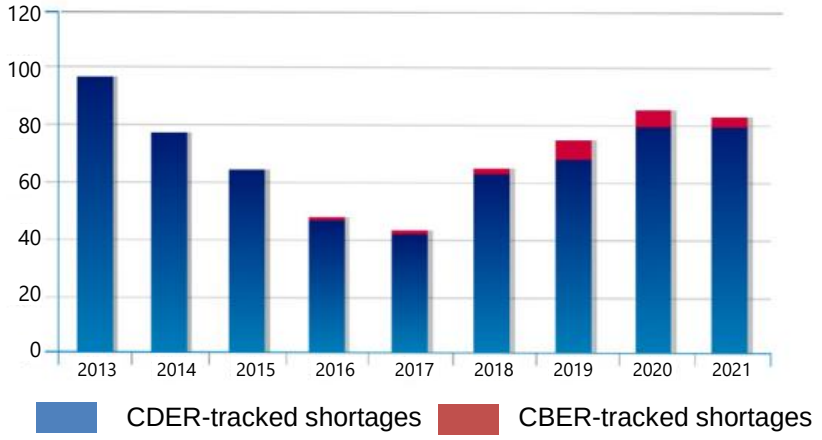
●	October 2011	White House	Executive Order 13588 The FDA received the order to take preventive measures in response to the serious drug shortages.
●	July 2012	U.S.	Enactment of the Food and Drug Administration Safety and Innovation Act (FDASIA) It was stipulated that drug manufacturers must notify the FDA at least six months in advance when the manufacturing of a drug is permanently discontinued or temporarily interrupted.

Current Situation regarding drug shortages (US)

Number of New Drug Shortages Per Calendar Year, 2010 to 2021



Number of Ongoing Drug Shortages Per Calendar Year, 2013 to 2021



Source: Drug Shortages for Calendar Year 2021

FDA: US Food and Drug Administration, CDER: Center for Drug Evaluation and Research, CBER: Center for Biologics Evaluation and Research

Current Situation regarding Drug Shortages (US)

Main measures taken in the United States against drug shortages (2)

In response to legislative appeals, a task force on drug shortages was established, involving collaboration with government entities including the FDA. This task force aimed to pinpoint the underlying causes of drug shortages and devise strategies for their prevention and mitigation.

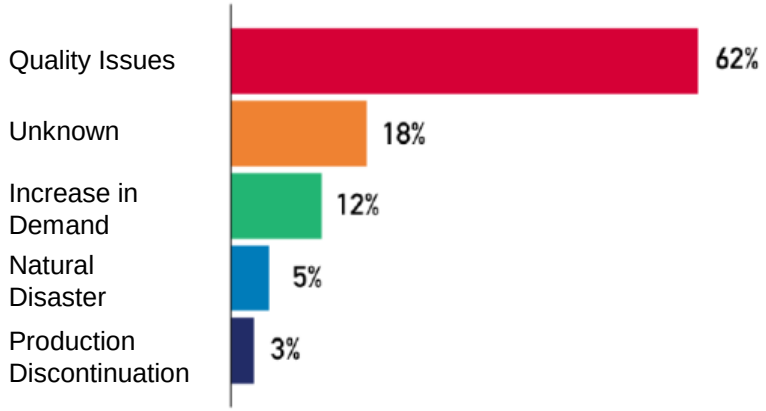
●	October 2019	FDA	A report on the root causes of drug shortages and potential solutions (Drug Shortages: Root Causes and Potential Solutions) was published (updated in February 2020)

Analysis of drug shortages

The 163 drug shortages from 2013 through 2017 were analyzed.

- 63% were injectable drugs, and 67% were off-patent drugs (the median time since initial approval: 35 years).
- 62% of all drug shortages were caused by manufacturing or quality issues.
- Approximately 53% of all drug shortages occurred after a sudden drop in revenues or the drug price.
- For 18% of all drug shortages, the drug price increased after the drug had been in short supply, and for 30%, the sales volume returned to pre-shortage levels.
- Regarding drugs that were in short supply, three pharmaceutical companies per item did not sell such drugs even though these drugs had received approval.

Percentage of Drugs Newly in Shortage by Reason, Calendar Years 2013-2017



Three root causes of drug shortages

- Lack of incentives to produce less profitable drugs
- Market does not recognize and reward manufacturers for mature quality management systems
- Logistical and regulatory challenges make it difficult for the market to recover after a disruption

Recommendations for enduring solutions

- Create a shared understanding of the impact of drug shortages and the contracting practices that may contribute to them
- Create a rating system to incentivize drug manufacturers to invest in achieving quality management system maturity
- Promote sustainable private Sector contracts

Source: Drug Shortages: Root Causes and Potential Solutions

Current Situation regarding Drug Shortages (US)

Main measures taken in the United States against drug shortages (3)

The COVID-19 pandemic has revealed the vulnerability of the US drug supply chains. Immediately after taking office, President Biden ordered to review the supply chains for four critical products, including pharmaceutical products and APIs.

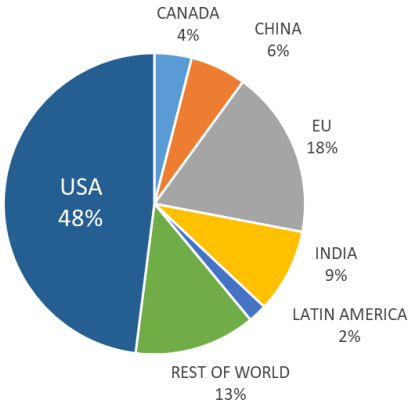
● February 2021	White House	Executive order to strengthen the resilience of US supply chains for critical products and materials: Order to review the supply chains for four designated critical items, including pharmaceutical products
● June 2021	White House	A report on resilient supply chains and revitalization of American manufacturing (Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth) was published.

Review of pharmaceutical and API manufacturing locations

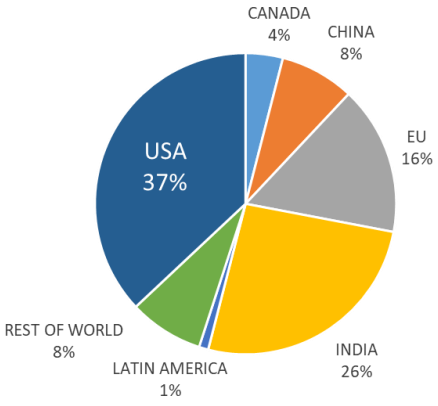
It was found that in particular the supply of APIs for generics is highly dependent on foreign supply chains.

Location of final product manufacturing base (as of March 2021)

All products

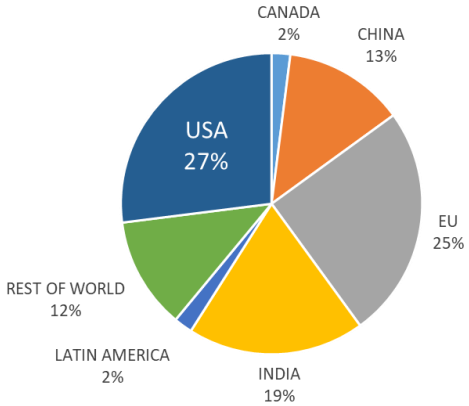


Generics

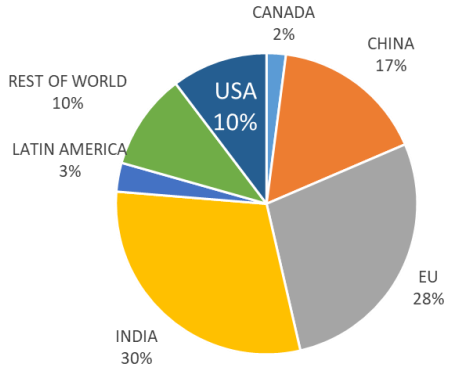


Location of API manufacturing base (as of March 2021)

All products



Generics



API: Active pharmaceutical ingredient

Source: Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth

Current Situation regarding Drug Shortages (US)

Main measures taken in the United States against drug shortages (4)

Following the findings of a report drafted per an executive order, the establishment of a task force dedicated to strengthening supply chains was unveiled. The mandate included safeguarding the economic security of four critical products, pharmaceutical products being one of them. In 2022, actions were initiated to identify APIs sourced from China with the aim to procure them either domestically or from allied nations.

●	June 2021	White House	The establishment of a task force for building resilient supply chains (Supply Chain Disruptions Task Force) was announced.

Actions the Biden-Harris Administration will immediately take

1. Support domestic production of critical medicines
   - The Department of Health and Human Services (HHS), under the Defense Production Act (DPA) and building on current public-private partnerships, will establish a public-private consortium for advanced manufacturing and onshoring of domestic essential medicines production.
   - The consortium's first task will be to select 50-100 critical drugs, drawn from the Food and Drug Administration's essential medicines list, to be the focus of an enhanced onshoring effort.
   - HHS will make an initial commitment of approximately $60 million from the Defense Production Act appropriation in the American Rescue Plan to develop novel platform technologies to increase domestic manufacturing capacity for API.
2. Secure an end-to-end domestic supply chain for advanced batteries
3. Invest in sustainable domestic and international production and processing of critical minerals
4. Partner with industry, allies, and partners to address semiconductor shortages

HHS: US Department of Health and Human Services
Source: Fact Sheet: Biden-Harris Administration Announces Supply Chain Disruptions Task Force to Address Short-Term Supply Chain Discontinuities
https://www.uscc.gov/annual-report/2022-annual-report-congress

Current Situation regarding Drug Shortages (Europe)

Main measures taken in the EU against drug shortages (1)

The European Medicines Agency (EMA) establishes the Task Force on the Availability of Authorised Medicines for Human and Veterinary Use and it is functioned as a supply and availability hub within the EU. It develops strategies and work plans for improving availability of medicines and coordinates the EU-wide situation.

Measures taken for ensuring the availability (access to medicines)

●	December 2016	HMA/ EMA	The Task Force on the Availability of Authorised Medicines for Human and Veterinary Use was created. Scope of application: Drugs that received approval but are not marketed Drugs that received approval and are marketed, but are not available due to supply issues
●	November 2020	EC	The Pharmaceutical Strategy for Europe was formulated.
●	December 2020	HMA/ EMA	The European Medicines Agencies Network Strategy to 2025 was formulated.

EU: European Union, EMA: European Medicine Agency, HMA: Heads of Medicines Agencies,
EC: European Commission, EEA: European Economic Area
Source: https://www.ema.europa.eu/en/human-regulatory/post-authorisation/availability-medicines

Current Situation regarding Drug Shortages (Europe)

Main measures taken in the EU against drug shortages (2)

As a result of the COVID-19 pandemic, the vulnerability of the availability of drugs and supply chains in the EU was brought to light, and the EC performed a study on drug shortages.

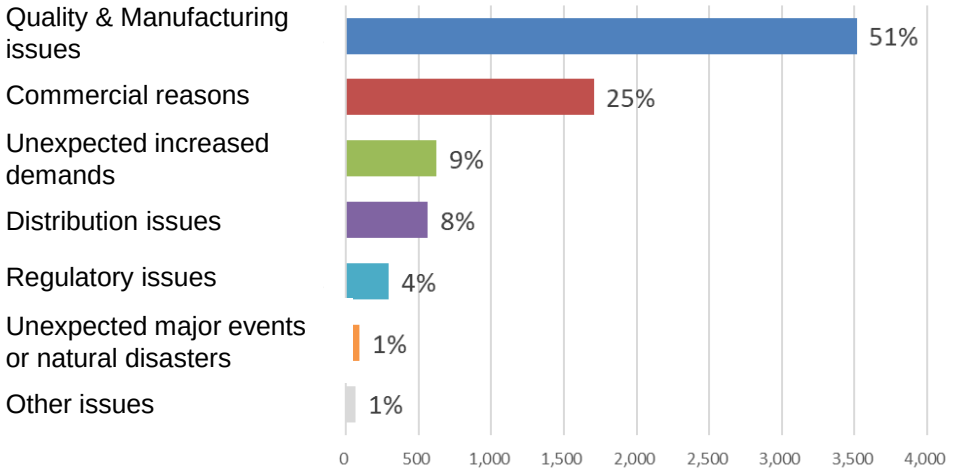
●	December 2021	EC	A study on drug shortages in the EU and the EEA (Future-proofing pharmaceutical legislation - study on medicine shortages) was published.

Analysis of drug shortages

Drug shortages in 22 countries from 2007 through 2020 were analyzed.

- Drug shortage notifications had been increasing since 2007, but started to decrease in 2020 after reaching its peak in 2019.
- Most shortages occur locally.
- Shortages were observed for old off-patent products and low-profit generic drugs.
- For 94% of drugs that were in short supply, the total sales volume in affected countries remained above 20% of one year prior.
- The average shortage period was three months, but shortage periods varied widely.
- 33% of drugs that were in short supply were drugs that are listed in the WHO Essential Medicines List.
- For 80% of drugs that were in short supply, alternative drugs were available.

Reported root causes of medicine shortages



Analysis of the causes of drug shortages

- Approximately 50% of all drug shortages were caused by quality and manufacturing issues.
- The available information is insufficient to quantify the importance of outsourcing of pharmaceutical production (including the production of APIs) and of parallel distribution as potential risk factors for shortages.

Source: Future-proofing pharmaceutical legislation – study on medicine shortages

Current Situation regarding Drug Shortages (Europe)

Main measures taken in the EU against drug shortages (3)

In the updated European industrial strategy of May 2021, the EC identified APIs as one of six strategic areas for economic security measures.
Both France and Germany are making strides towards domestic production of essential medicines.
As of March 2022, the EMA has intensified its monitoring of drug shortages. Concurrently, manufacturers are now mandated to register their Industry Single Point of Contact with the EMA.

Economic security initiatives

● May 2021	EC	Update of the new European industrial strategy Six strategic areas (raw materials, batteries, APIs, hydrogen, semiconductors, and cloud and edge technologies) were determined.

Action taken on drug supply issues due to public health emergencies or major events

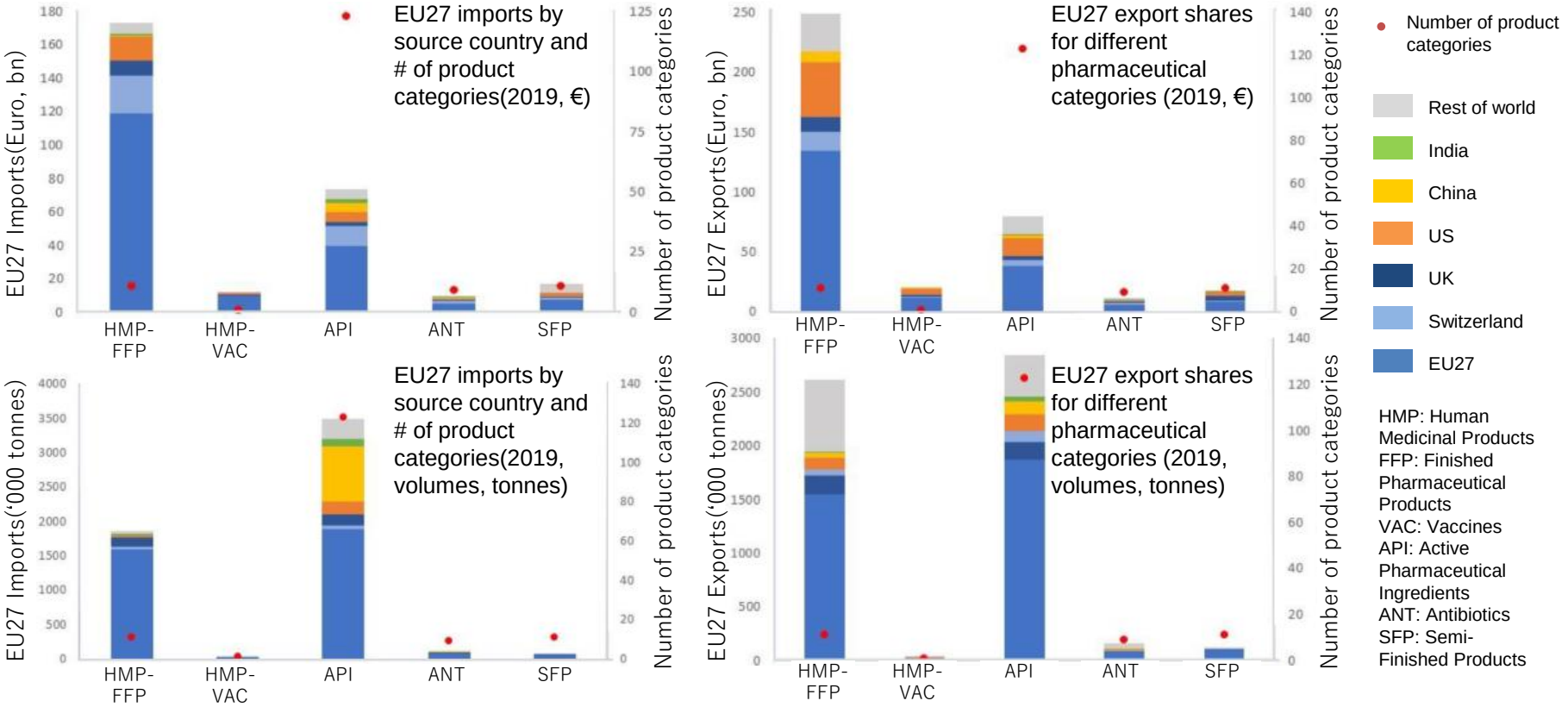
● March 2022	EC	Assignment of new legal authority to the EMA to monitor and mitigate drug shortages Monitor drug shortages that can lead to potential crisis situations. Report shortages of critical medicines and coordinate responses of EU countries in crisis situations Establish and maintain a platform for monitoring drug shortages in Europe (until the beginning of 2025)
● Until September 2022	EMA	In the EU, all manufacturers need to register their Industry Single Point of Contact on supply and availability (i-SPOC) with the EMA.

Updating the 2020 Industrial Strategy
https://www.ema.europa.eu/en/human-regulatory/post-authorisation/availability-medicines

Current Situation regarding Drug Shortages (Europe)

Reactions to the new European industrial strategy
In May 2021, the ECIPE published results of an analysis of the manufacturing and import/export of pharmaceutical products in 27 EU countries. The report shared the view that exports of the EU's pharmaceutical industry, including exports of APIs, are strong but that the 27 EU countries need to be cautious about the policy to reduce their dependence on imports because it may affect the trade policies of other countries.

Analysis of import/export of medicinal products in 27 EU countries (by category and country)



ECIPE: European Centre for International Political Economy
International EU27 pharmaceutical production, trade, dependencies and vulnerabilities: a factual analysis

Drug Shortage Reporting Lines

Both in the United States and the EU, pharmaceutical manufacturers are required by law to notify the supervisory authorities within a certain period of time before the manufacturing of a product is discontinued or suspended. In addition, a list of drugs that are in short supply is published on the agencies' websites.

US

- **Requirement for manufacturers**

  Under the Food and Drug Administration Safety and Innovation Act (FDASIA), signed into law on July 9, 2012, FDA requires manufacturers of most prescription drugs that are life-supporting, life-sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition (whether approved or unapproved) to notify FDA of a permanent discontinuance or temporary interruption in manufacturing that is likely to lead to a meaningful disruption in supply of the drug in the United States, including the estimated shortage duration and shortage reason. A notice required shall be submitted at least 6 months prior to the date of the discontinuance or interruption. FDA sends a non-compliance letter to firms that fail to notify the Agency in accordance.

- **Database：Current and Resolved Drug Shortages and Discontinuations Reported to FDA**

  FDA recommends notifying FDA of potential supply issues if a problem occurs at any stage of manufacturing so that it can help address the problem. FDA will review and post on the website if it finds that it does not meet the demand of the overall market. Database is updated daily.

EU

- **Requirement for marketing authorisation holder**

  In accordance with article 23(a) of Directive 2001/83/EC, if the product ceases to be placed on the market of a Member State, either temporarily or permanently, the marketing authorisation holder shall notify the competent authority of that Member State. Such notification shall, other than in exceptional circumstances, be made no less than two months before the interruption in the placing on the market of the product. The marketing authorisation holder shall inform the competent authority of the reasons for such action.

- **EMA shortage catalogue**

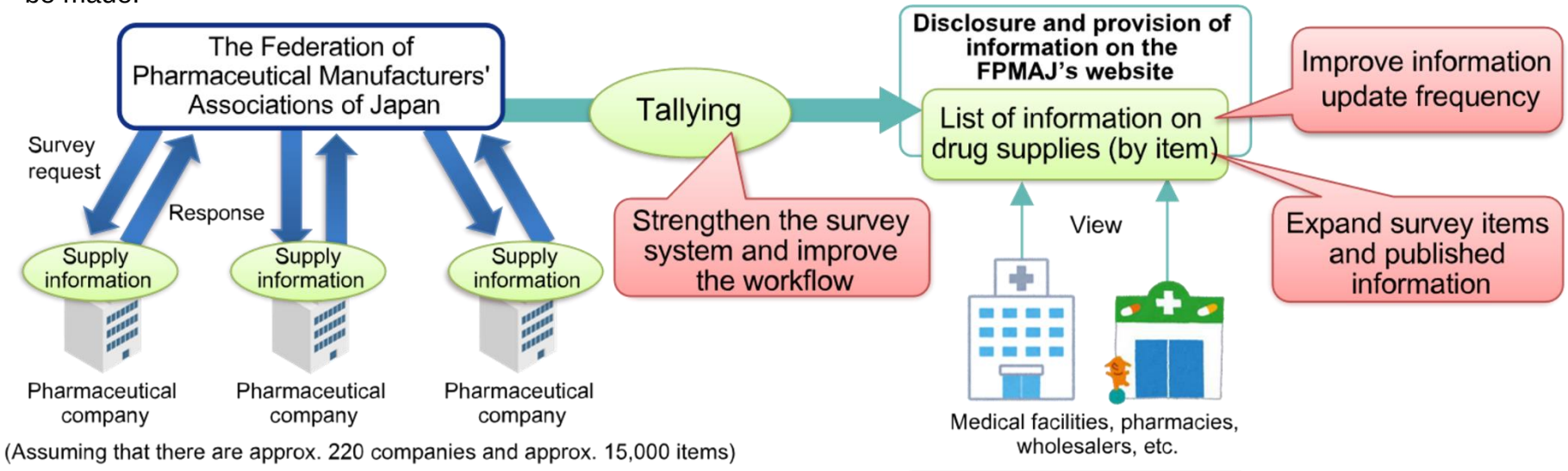
  EMA assesses medicine shortages that affect or are likely to affect more than one EU Member State. Database is updated daily.

Source: US: https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm
EU: https://www.ema.europa.eu/en/human-regulatory/post-authorisation/availability-medicines/national-registers-shortages#ema-shortages-catalogue-section

Drug Shortage Reporting Lines

In Japan, supply instabilities of ethical drugs continue. To obtain an accurate picture of the supply situation, an emergency research project for obtaining information on ethical drug supplies is scheduled to be conducted in fiscal 2023.
In addition, under the amended Infectious Disease Act and the Medical Care Act, regulations on reporting and publicizing information on the supply of pharmaceutical products to the government agency will be enforced in fiscal 2024, and preparations and formulation of guidelines will start from fiscal 2023.

Fiscal 2023 Emergency research project for obtaining information on ethical drug supplies
Regarding the survey on the ethical drug supply status that is conducted by the Federation of Pharmaceutical Manufacturers' Associations of Japan (FPMAJ), the frequency of this survey will be increased from once every three months to once a month, the survey system will be strengthened, and the workflow will be improved. In addition, other improvements, such as shortening the time until its publication and expanding survey items and disclosed information, will be made.



Source: Materials for the 7th conference on measures to secure stable supplies of ethical drugs

Drug Shortage Reporting Lines in the United States and the EU

No. of items that are in short supply (based on the no. of ingredients) according to each country's reporting line

No. of items that are in short supply (based on the no. of ingredients)

	No. of ingredients
US	116
France	219
Germany	175
EU	15
Japan (for reference)	518

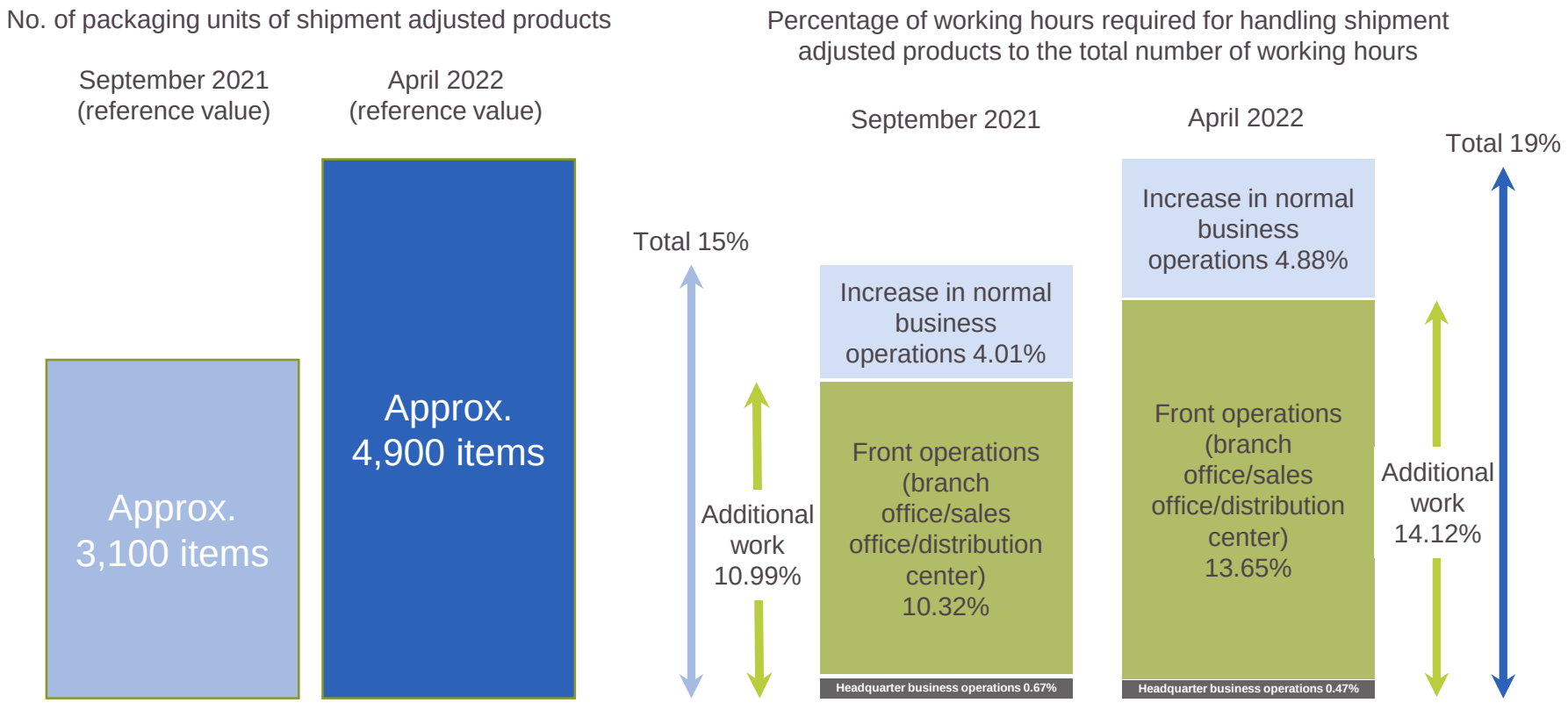
Note: The number of items that are in short supply in Japan was determined based on the results of a survey on the supply status that was performed by the FPMAJ in February 2023.

Source:
US
https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm
Extracted "current drug shortages" Accessed on February 18, 2023
France
https://ansm.sante.fr/S-informer/Informations-de-securite-Ruptures-de-stock-des-medicaments
"Delivered" status was deleted Accessed on February 9, 2023
Germany
https://www.bfarm.de/DE/Arzneimittel/Arzneimittelzulassung/Arzneimittelinformationen/Lieferengpaesse/_functions/Filtersuche_Formular.html?nn=11296612
Accessed on February 9, 2023
EU
https://www.ema.europa.eu/en/human-regulatory/post-authorisation/availability-medicines/national-registers-shortages#ema-shortages-catalogue-section
Accessed on March 25, 2023

Role That Pharmaceutical Wholesalers Play for Safeguarding a Stable Drug Supply

Concerning stable drug supplies, the roles of governments and regulatory bodies in both the United States and Europe primarily involve consolidating information and liaising with manufacturing firms on production. In these regions, private pharmaceutical wholesalers adjust the quantity of supplies to the market. A survey of Japanese pharmaceutical wholesalers indicated that they allocate 19% of their overall time managing products with adjusted shipments (as of April 2022).

Survey on additional work to be done by pharmaceutical wholesalers for handling shipment adjusted products



Source: Survey on additional work to be done by pharmaceutical wholesalers for handling shipment adjusted products

Discussion

- **Causes of drug shortages**

  Both in the United States and Europe, public agencies have conducted surveys on the current status of drug shortages and underlying causes, and as a result it was pointed out that low-margin products tend to be in short supply.

- **Reporting mechanisms**

  Public agencies in both the United States and Europe have established and oversee reporting mechanisms for drug shortages. While the specifics of these reporting systems vary by country, they typically include the expected duration of the shortage, its underlying cause, and occasionally alternatives to the unavailable product. This underlines the importance of centralized information sharing on drug shortages to maintain market stability.

- **Acknowledgment towards the pharmaceutical industry**

  A pronounced commitment to engage with the pharmaceutical industry is evident at both the national and regional levels in the United States and Europe.
  In the U.S., there's heightened concern over shortages of generic APIs, mirroring the situation in Japan. The U.S. strategy emphasizes sourcing scarce APIs from military allies, including Japan, while also ramping up domestic API production. This approach stems from recognizing such shortages as a national security risk, and the U.S. is resolved to meet set deadlines to address this issue.
  Europe, with its extensive production facilities, has achieved a balance between drug imports and exports, making drug self-sufficiency a viable goal.
  In contrast, Japan lacks a comprehensive acknowledgment of its domestic pharmaceutical sector. Only regulatory bodies and industry insiders are tuned into the looming supply crisis. It's vital for Japan to forge a unified vision regarding the extent to which sustainable drug supplies should be protected for the benefit of its pharmaceutical industry and the population at large.

Proposals

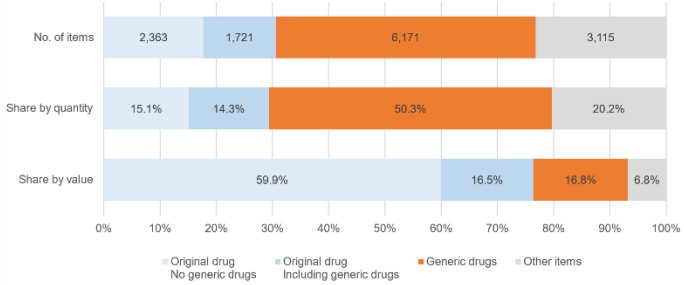
- **From the viewpoint of preventing drug shortages: Necessary to review the national health insurance (NHI) drug price scheme**

  The main causes of drug shortages are non-manufacturing related factors (e.g., a rapid increase in demand, natural disasters, political instability, and a shortage of APIs and devices), compliance-related issues, technical quality issues, and manufacturing-related factors (e.g., discontinuation of manufacturing based on the management's judgment). The latter factor is assumed to be directly or indirectly related to the profitability of items that are in short supply.

  The surveys conducted in the United States and Europe revealed that low-priced and low-margin products tend to be in short supply. Current shipment adjustments in Japan are caused by shipment suspension measures due to manufacturing quality deviations, and it is not known whether there is a direct relationship with profitability. On the other hand, the price of long-listed products and generic drugs continues to fall since 2018 due to annual price revisions (including revisions due to a consumption tax hike in 2019), and according to a survey by the Japan Generic Medicines Association, a pharmaceutical company in Japan saw no profits in 220 out of 779 items. It must be recognized that drug shortages in other countries that are caused by profitability issues can also occur in Japan.

  Based on the number of items and quantity, generic drugs account for more than half all drugs, and thus play an important role for maintaining public health. Regarding NHI price revisions in 2023, a temporary and exceptional recalculation of unprofitable items was performed for responding to price rise caused by inflation, it would be beneficial to establish a consistent drug pricing system that prioritizes the steady supply of all pharmaceutical drugs, including generics.

No. of generic drug items, share by quantity, and share by value



Other items: Pharmacopoeia-listed drugs, Kampo extracts, herbal medicines, biologics (e.g., vaccines and blood products), pharmaceutical products that received approval before 1967, etc.

Source: Overview of NHI drug price revisions in 2022

Proposals

- **A proposed solution to address drug shortages: 1. Establishing a central reporting mechanism**

  Presently, Japan lacks a centralized, real-time system to monitor drug shortages. Information on shipping adjustments is dispersed among pharmaceutical wholesalers, medical institutions, and pharmacies. This decentralization leads to inefficiencies in information dissemination. Disparities in market data can sometimes even exacerbate shipping adjustments.
  Given the increasing intricacies of pharmaceutical supply chains, it's almost inevitable that we'll witness more drug shortages in the future. It's crucial to consider setting up a centralized system for tracking these shortages. Drawing insights from international models could provide invaluable guidance in this endeavor.

- **A proposed solution to address drug shortages: 2. re-evaluating the role of pharmaceutical wholesalers**

  In the context of drug shortages in the United States and Europe, public agencies predominantly negotiate with pharmaceutical manufacturers and adapt regulations to preempt shortages. However, when shortages occur, the onus largely falls upon the pharmaceutical wholesalers to manage and address them.
  Initial assumptions suggested that the shipping adjustments, which began in early 2021, would stabilize between January and March 2022. Contrary to expectations, the number of adjusted items surged, and by February 2023, nearly 50% of all items (calculated by packaging units) experienced these adjustments. An April 2022 survey revealed that Japanese pharmaceutical wholesalers dedicated about 19% of their total work hours (primarily for MS) to balance demand and supply. At that point, approximately 30% of all items required shipment adjustments.
  Recognizing the pivotal role pharmaceutical wholesalers play in maintaining drug supply continuity, it's beneficial to implement socio-economic structures that recognize the role of pharmaceutical wholesalers in ensuring the sustainability of drug supplies.

* Source: DrugShortage.JP