

- Toward a Bright Future as a Country with Advanced Medical Care- Recommendations for Reform of the Pharmaceutical System IV September 27, 2022

This document is intended to be widely disseminated to all parties involved in medical care and pharmaceuticals, as well as government councils and other interested parties.

We will continue to work on further fleshing out the contents of these recommendations. We hope that all parties concerned will use them as a basis to deepen the discussion on reform and contribute to the realization of a society full of hope with a bright future in health care for all Japanese people.

(The previous recommendations have been partially updated with the addition of relevant materials, and a new recommendation is appended.)

Study Group on Drug Pricing and Distribution Policies/
Academy for Pharmaceutical Future (Kusuri Mirai Juku)



For Japan to Be a Country with Advanced Medical Care

- Japan was one of the first countries in the world to introduce a universal health insurance system.
- Japanese health care was rated the best in the world (by the WHO) and the longest life expectancy was achieved.
- However, Japanese health care is now at a major turning point.
=> **In order for Japan to remain a country with advanced medical care,** it is important to take action now.

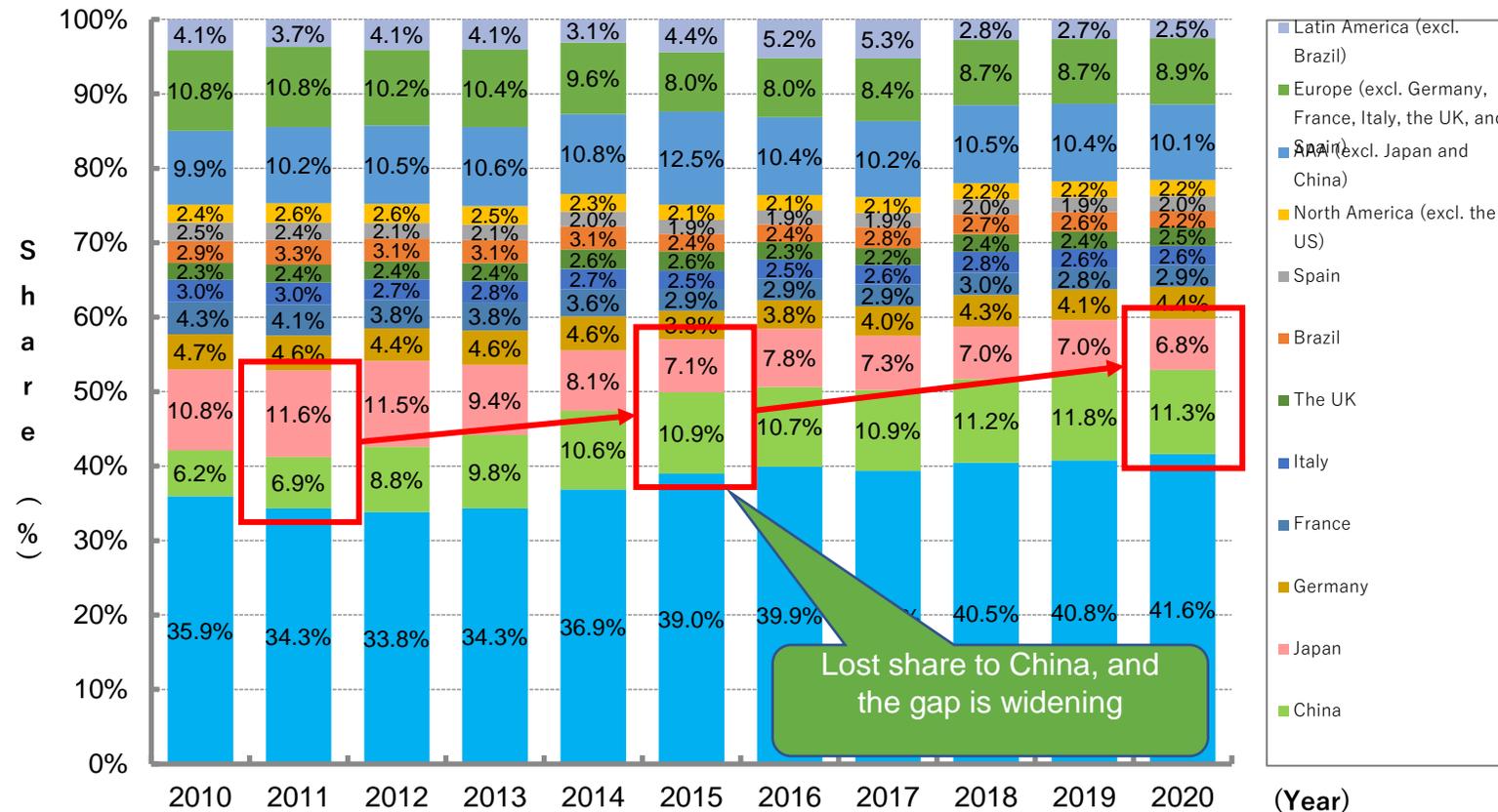
From the world, new drugs are no longer coming into Japan. Large quantities of medicines are in short supply and not available to doctors in Japan. Japan, which has made great achievements in combating infectious diseases, now relies on foreign companies for vaccines and treatments for new infectious diseases.

The medical and pharmaceutical fields now face a multitude of challenges. And we are beginning to see a risk of losing our position as a major world power.

Japan's Rank in the World Continues to Decline

- China's growth has been remarkable in recent years

Global Ethical Drug Market Share (By Region/Country)



- The Japanese pharmaceutical market was the third largest in the world.
- In 2015, Japan was overtaken by the following markets:
 - China
 - EU excluding Germany, France, Italy, the UK and Spain
 - Asia, Africa, and Australasia, excluding Japan and China

The Japanese share has further dropped due to negative growth in recent years (Japan 6.8%, China 11.3% [as of 2020]).

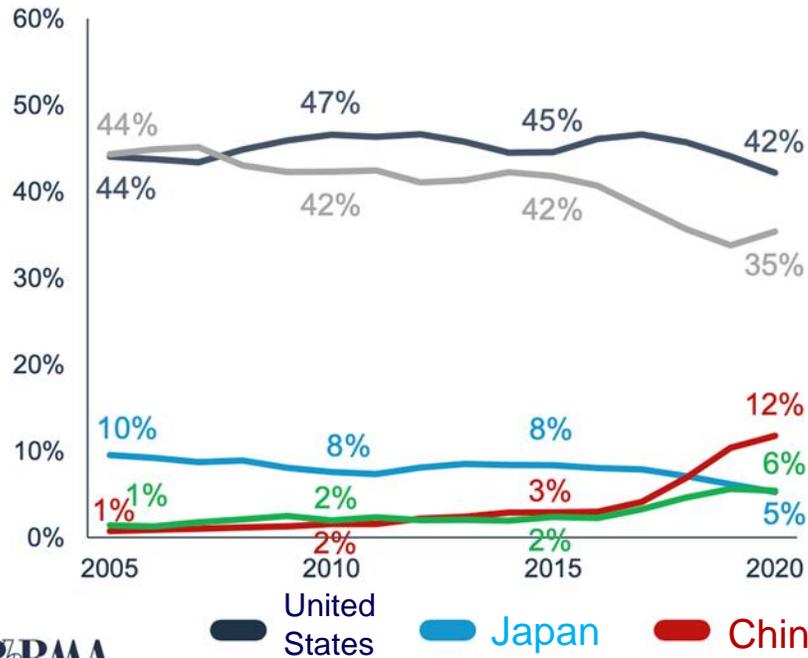
- Only Japan is projected to experience negative growth in the future (private-sector forecast).

Note: AAA stands for Asia, Africa, and Australasia
 Source: Copyright© 2022 IQVIA. Prepared by the Office of Pharmaceutical Industry Research based on IQVIA World Review, Data Period - Year 2010-2020 (All rights reserved)

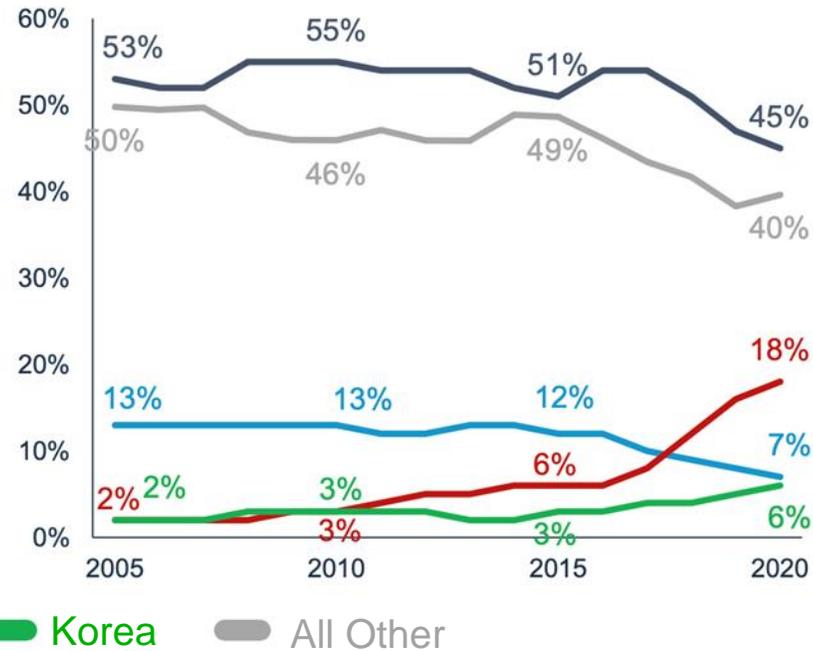
Japan's Presence in Global New Drug Development Continues to Decline - China has surpassed Japan in the new drug development pipeline

Country Share of Early-Stage Pipeline Based on Company Headquarter Location, 2015-2020

All Medicines



Oncology



- The world's drug development has been led by Japan, the US, and Europe.
- In 2015, the number of drugs developed by Japanese companies still exceeded those of China and South Korea, but the situation reversed in 2020.
- In particular, China's progress is significant, and the number of new drugs originating from Japanese companies is declining.
- Without incentives for foreign companies to develop drugs in the Japanese market, there is a risk of a serious drug lag.

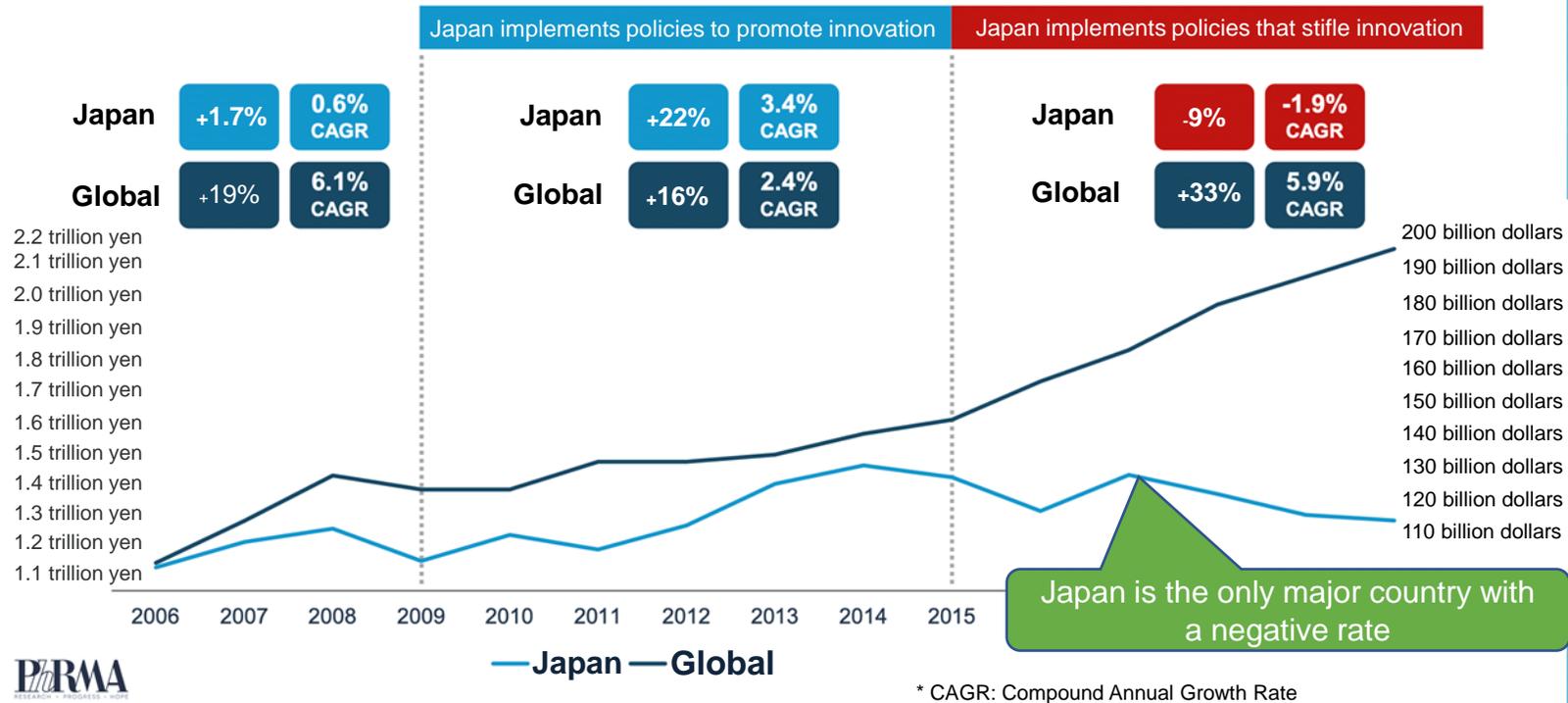


Source: IQVIA Institute for Human Data Science, Global Trends in R&D :Overview through 2020, May 2021.
* Percentage totals for each year exceed 100%, as co-developments by pharmaceutical companies based in different countries are also included.

Source: PhRMA Chairman David Ricks' press conference on January 28, 2022

In Order to Ensure World Class Treatment in Our Country, the Japanese Drug Development Environment Should Be Comparable to the Rest of the World

Policy changes over the past few years have harmed biopharmaceutical investment in Japan.



Source: Ministry of Internal Affairs and Communications, "Survey of Research and Development (2021)," Evaluate Pharma World Preview

- To launch a drug in Japan, investment in development in Japan is necessary (Japanese data is required for approval).
- Drugs are an international commodity, and companies from around the world are closely watching Japan.
- Japan is currently at a dangerous level that discourages the development of new drugs.
- In order for Japan to ensure international standards of medical care, strategies taking account of global trends are necessary.

Source: PhRMA Chairman David Ricks' press conference on January 28, 2022

Issues in the Japanese Drug Pricing System and Drug Market from a Global Perspective

- Market size continues to shrink and is now falling behind other major and developing countries
- In recent years, drug prices have fallen faster than in the past (rising in other countries. Japan is the only developed country where prices for new drugs in the patent term are falling).
- The image of a country where the government does not reflect the value of innovation in official prices is spreading.

Japan is beginning to be regarded as **a country with low priority for drug development** by the world's pharmaceutical companies.

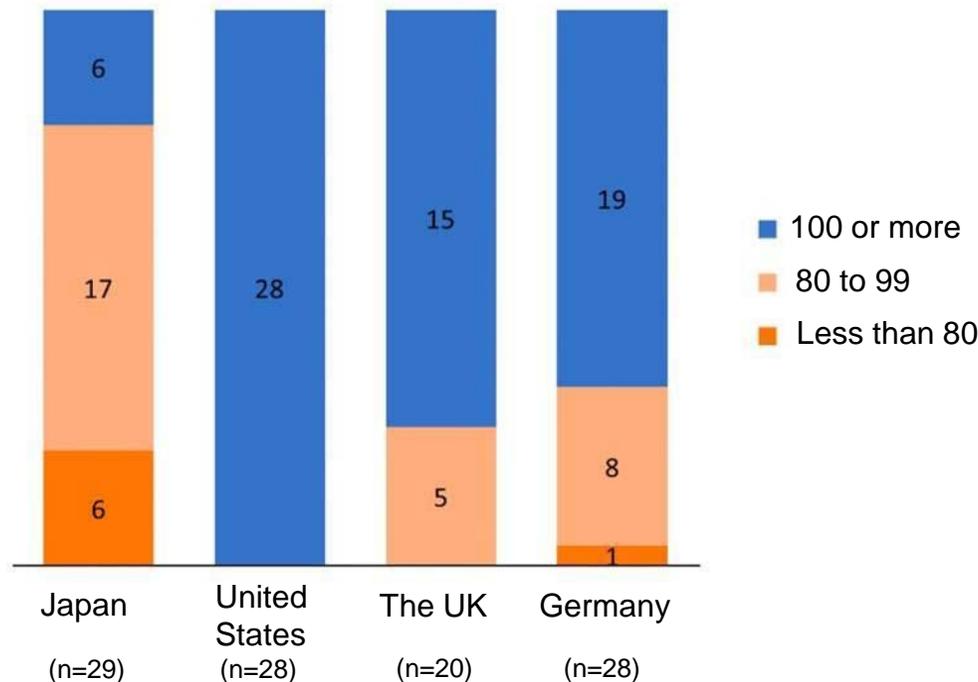
→ **Risk of a serious drug lag** (lack of access to the latest medications) **in the future** (many newly approved drugs in Europe and the US have not been introduced in Japan even after 5 years).

Price reduction during patent term



- Maintaining drug prices during the patent term is the standard in major developed countries.
- Market expansion repricing is a major disincentive to launch in Japan.

Current price level of the top 30 global sales products, with the price at the time of NHI price listing set at 100



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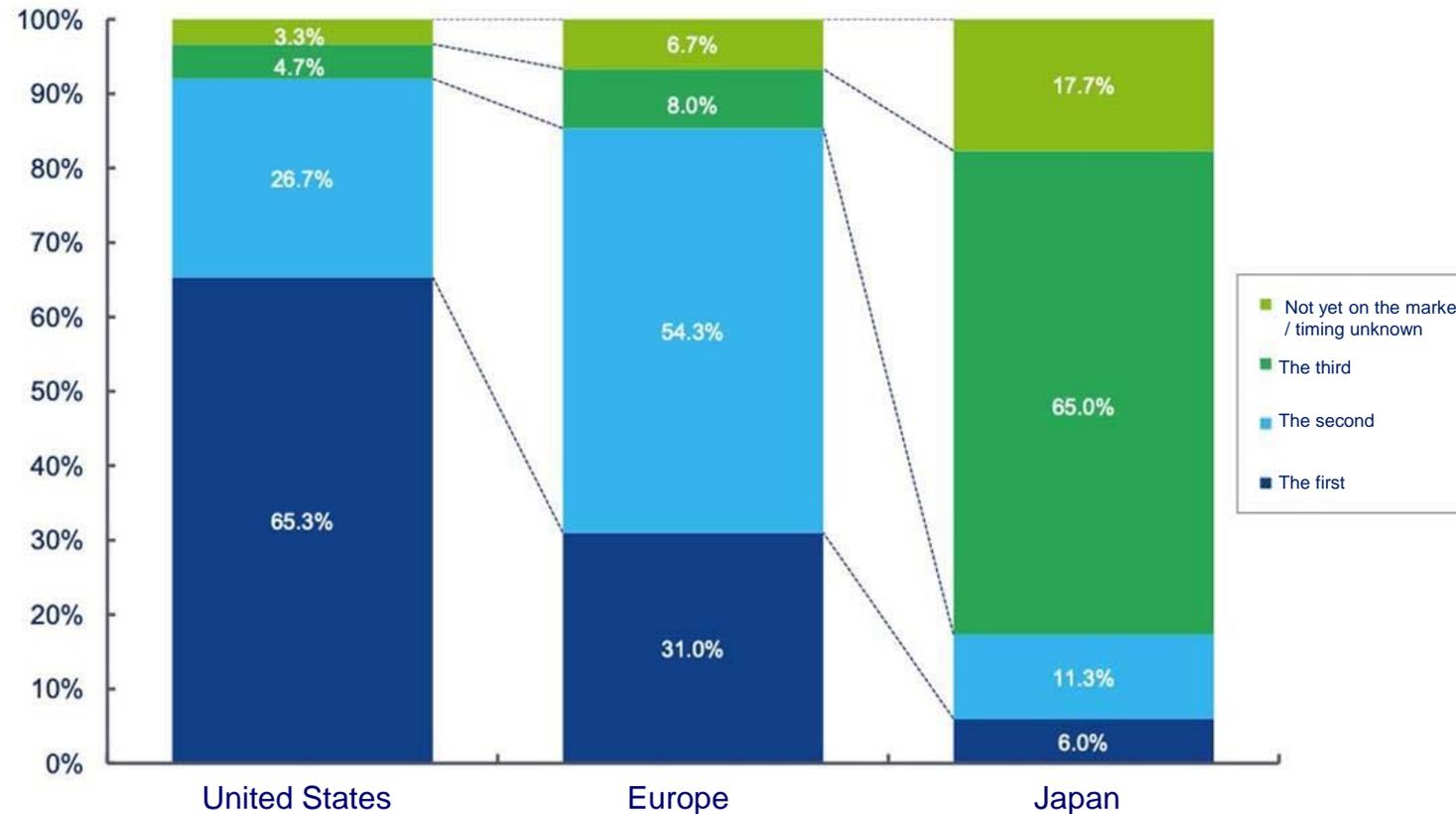
- Material from the JPMA on how “maintaining drug prices during the patent term” is viewed from a global standard.
- During the same period, the U.S. had no products with price reductions, and 70% of drugs in the U.K. and Germany were without price reductions. On the other hand, conversely, Japan lowered prices on about 80% of its drugs.
- Verification that this is how the market looks when viewed globally. Foreign companies are less likely to invest.
- These are the issues that have been raised by our Academy. The specifics are up for discussion, but the voices of the private sector should be heard.

From the material of the first Expert Panel Meeting on Distribution and Drug Pricing System for Prompt and Stable Supply of Pharmaceuticals (August 31)

Ranking of the world's top 300 medical products in terms of sales (2020) launched by Japan, the US, and Europe

OPIR
Office of Pharmaceutical Industry Research

65% of the pharmaceuticals launched in Japan come in third after those launched in the US and Europe.



Note:

1) Data on market launch as of June 2021

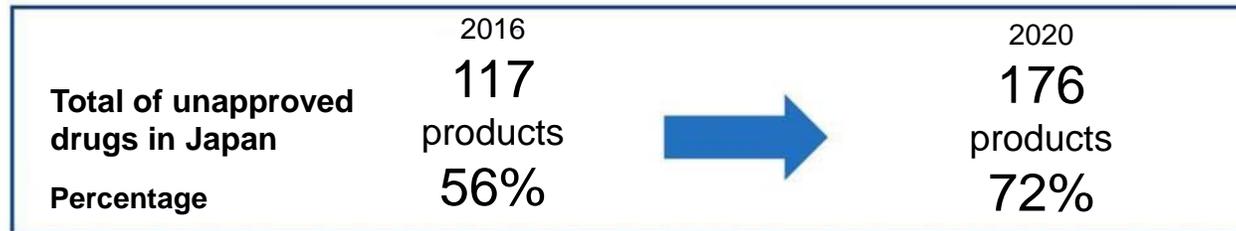
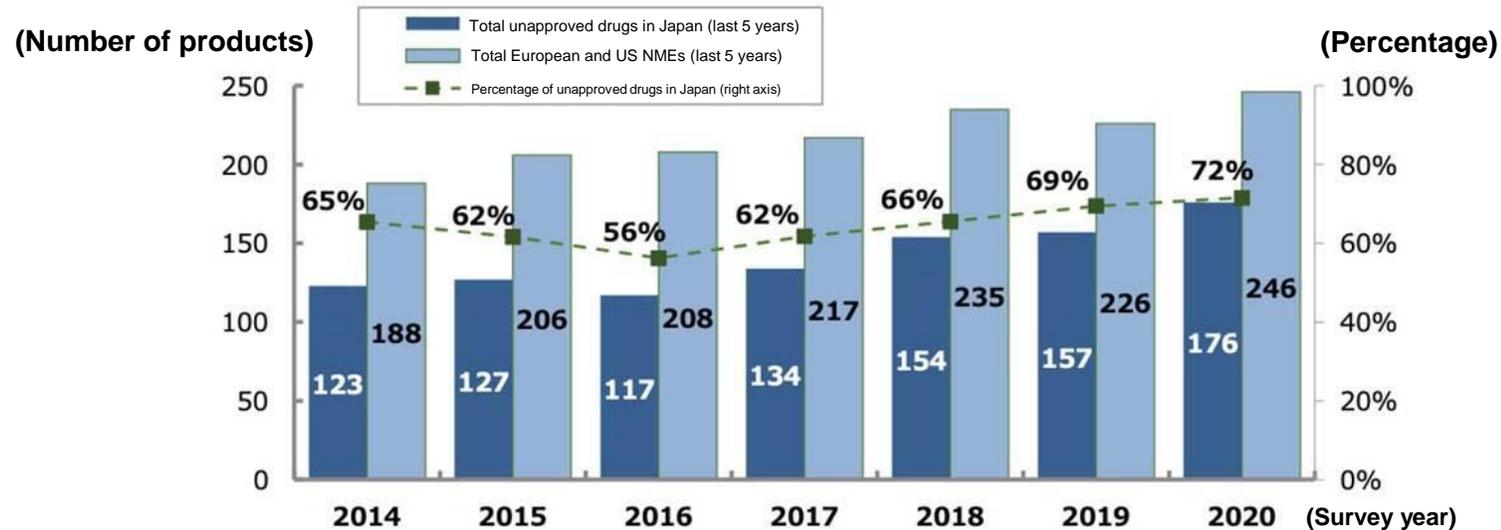
2) Europe refers to "France, Germany, Italy, Spain, Switzerland, Turkey, the United Kingdom, and other European countries" as "Europe" defined by Evaluate Pharma.

Source: Created by the Office of Pharmaceutical Industry Research based on data from Evaluate Pharma

From the material of the first Expert Panel Meeting on Distribution and Drug Pricing System for Prompt and Stable Supply of Pharmaceuticals (August 31)

January 20, 2022
Japan Pharmaceutical Manufacturers
Association Press Conference
Materials

Increase of unapproved drugs in Japan



Note 1: The number of products for each year is the number of domestic unapproved drugs for the most recent 5 years at the time of the survey.

Note 2: Percentage of unapproved drugs in Japan = Total unapproved drugs in Japan (most recent 5 years) / Total NMEs in Europe and the US (most recent 5 years)

Source: Prepared by the Office of Pharmaceutical Industry Research based on publicly available information from PMDA, FDA, and EMA.

Source: Office of Pharmaceutical Industry Research, "Drug Lag: Status and Characteristics of Unapproved Drugs in Japan," Office of Pharmaceutical Industry Research News No. 63 (July 2021)

From the material of the first Expert Panel Meeting on Comprehensive Measures to Achieve a Prompt and Stable Supply of Pharmaceuticals (September 22)

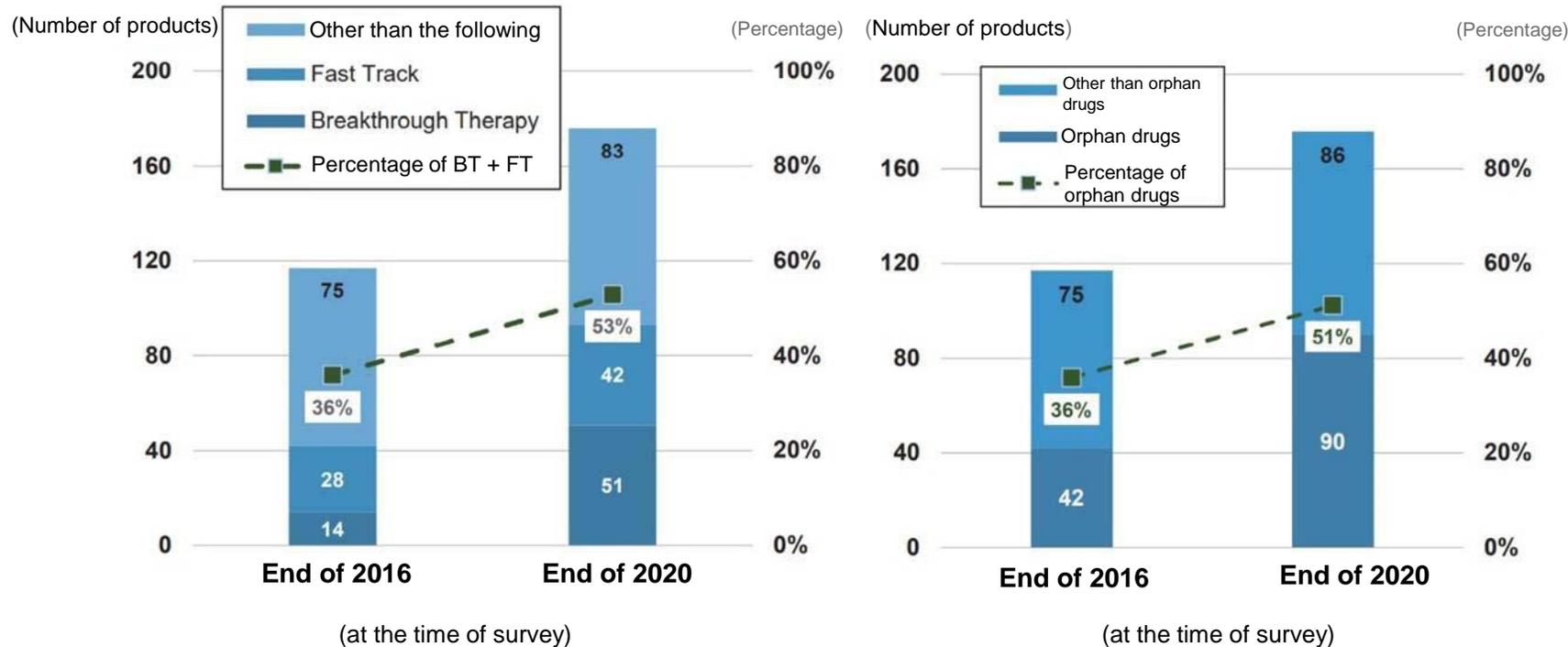
Clinical importance of unapproved drugs in Japan



Number and percentage of unapproved drugs in Japan designated for special measures in overseas pharmaceutical affairs

Fast Track or Breakthrough Therapy designation from FDA

Orphan drug designation from FDA or EMA



Academy for Pharmaceutical Future
(Kusuri Mirai Juku)

- The number of drugs identified by the FDA as Fast Track or Breakthrough Therapy has increased and now accounts for most drug lag items.
- Orphan designation (Orphan Drug Designation) shows the same trend and now is the majority.
- There is a tendency that drugs that patients are waiting for are less likely to be introduced in Japan. (Impact of the system)
- The system should be designed to take into account new modalities, start-up companies, and companies developing a small number of products.

A Look at the Domestic Pharmaceutical Industry

- Development of COVID-19 vaccines and therapeutics allows other countries to take the lead.
(In the past, Japan was on par with them in both vaccines and therapeutics for infectious diseases)
- Inability to supply ethical drugs needed by the people
(Trust in generics as being inexpensive and of good quality has been lost, and shortages have become the norm for about 8,000 items¹).
Note 1: Approximately 4,000 products (according to DrugShortage.jp)
- The performance of the pharmaceutical wholesale industry, the foundation of medical care, has been super sluggish, and bid-rigging cases have been uncovered.

Both the pharmaceutical and drug distribution industries are exhausted.

=> Nevertheless, a further market reduction of about 500 billion yen each year is being implemented as a policy

How Did This Happen?

(They say, “You are discounting, so it is only natural to lower prices.”)

- **NHI drug price reduction → price negotiation (bidding) with the price capped after the reduction → NHI survey to identify price declines → NHI price reduction as the official price, and so on.** (In recent years, there has been a change in the system to double the speed of this cycle (**introduction of annual price revisions**), which has **also doubled the rate of price declines.**)
- **The mechanism for exempting drug prices from falling to support innovation has been drastically scaled back** (it was a fiscally neutral system of maintaining prices & lowering them all at once after patent expiration → the amount maintained was suddenly halved).
- In drug distribution, short-term negotiations and uniform total discounting became even more normalized with the COVID-19 pandemic. Meanwhile, **the repetition of official price reductions and renegotiations (re- bidding) under those prices basically established a structure in which the prices of all items fell** (resulting in many unprofitable products with losses that increase the more they are made).

The government and others are discussing a proposal for a zero adjustment margin (a stricter calculation method for the price reduction of all items) and a drug cost cap system (further tightening of regulations on innovation).

Pharmaceutical Wholesalers Face Severe Deficit Structure in Orders

Nationwide application of “bulk discount pricing” increased = Structural deficit for large pharmacies (especially in rural areas)

Current status of orders incurring losses (orders whose prices are less than purchase cost + SG&A)

Orders below purchase cost + SG&A expenses (based on the number of premises)

2020-2021	Hospitals	Clinics	NHI pharmacies (20 or more outlets)	NHI pharmacies (19 or fewer outlets)
Urban areas	30%	20%	87%	45%
Representative local cities	27%	18%	85%	52%
Representative remote areas/islands	43%	8%	100%	48%

(Reference 1)
SG&A expenses for each wholesaler are:

- Urban areas 4.0%-5.9%
- Local areas 6.8%-7.3%
- Remote areas 7.1%-9.3%

(*Data from 3 of the 4 wholesalers)

(Reference 2)
Efforts are being made to compensate for losses resulting from orders received by cutting costs, charging manufacturers additional fees for returned goods, and diversifying the business. However, the profit margin is far below the average for all wholesalers (2%).

Orders below purchase cost + SG&A expenses (in value terms)

2020-2021	Hospitals	Clinics	NHI pharmacies (20 or more outlets)	NHI pharmacies (19 or fewer outlets)
Urban areas	48%	15%	86%	32%
Representative local cities	31%	17%	81%	43%
Representative remote areas/islands	67%	6%	100%	42%

Based on all data within the region in question for the four wholesalers' representative areas (sample regions).

Of the total 1.9 trillion yen in orders received by the four companies, 38% (approximately 700 billion yen) were in the red.

(Source: HIP Study Group)

Critical Situation = We Must Stop and Think Now. What perspectives are needed to do so?

- The goal of the policy should be to ensure that the necessary medicines reach the people.(Ensuring health security and stable supply of medicines)Harmonization with finances and economy is necessary.
- However, it is also essential to be in harmony with the industrial sector that creates and delivers medicines.
- Discussion is needed on how to harmonize economic and fiscal affairs with industry, and on a system that is not “fiscally driven” and does not reject the ideas of the private sector.

From these perspectives, how about creating five pillars of basic concepts?

Basic Approach to the Revision of Drug Pricing and Distribution System, and its Five Pillars

The study group will make recommendations on various related policies, especially on drug pricing and distribution policies, based on the following five pillars.

- ✓ Comprehensive and integrated policy on drug pricing and distribution that fosters a stable and sustainable industry with the goal of ensuring that the public receives the medicines they need.
(Ensuring health security and stable supply of medicines and perspective of industrial policy for this purpose)
- ✓ Open markets that are internationally harmonized and encourage innovation
- ✓ A predictable system that provides an appropriate environment for business activities.
- ✓ Maintaining the universal health insurance system (ensuring access to world-class medical care)
- ✓ A system that is in harmony with the economy and finances

→ All of the above are tasks that must be accomplished.

We must not sacrifice one for the other.

There will always be a detrimental effect on something. (Currently, harm has already occurred.)

There can be much debate on each of the subsequent policy ideas.

Therefore, the basic perspectives should be based on the consensus of the parties involved, while the discussion on each issue should emphasize dialogue with the private sector.

**Based on the above,
we present draft recommendations**

Recommendations for Drug Pricing and Distribution Reform II Revised