独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

Regulatory updates in Japan

日本藥品·醫療器械等監管更新

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國際部經理
田中 大祐

5 October 2023
11th Joint Conference of Taiwan and Japan on Medical Products Regulation

2023年10月5日
第十一屆台日醫藥交流會議

Today's contents

1. Environment surrounding Japanese Pharma and Medical Device industry.
2. Recent Drug & Medical Device Development Support
3. Activities with Asian Countries
4. After pandemic and challenges
5. PMDA Oversea Office

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Changes in the environment surrounding the pharmaceutical and medical device industries (1)

1. Technological advances and expansion of digital health

- Expansion of preventive and pre-emptive medicine, personalised medicine (regenerative medicine, genomic medicine), AI drug discovery, etc.
- Expansion of the scope of use of big data and disease registries
- Dynamic change in modalities from small molecules to biotechnology, gene therapy, etc.

2. Changes in domestic systems and pharma markets

- Further population decline and ageing in Japan
- Growth rate of the Japanese pharmaceutical market generally flat to slightly declining
- Changes in domestic pharmaceutical and medical insurance systems (e.g. rationalisation of regulations, cost-effectiveness)
- Structural shift in the pharmaceutical market: replacement of long-term listed products (less than 20%) with patented products (more than 60%)
- Expansion of the market for speciality drugs such as anticancer drugs, infectious diseases, immunological diseases, etc.
- Expansion of generic drugs use

Changes in the environment surrounding the pharmaceutical and medical device industries (2)

3. Changing global competitive environment

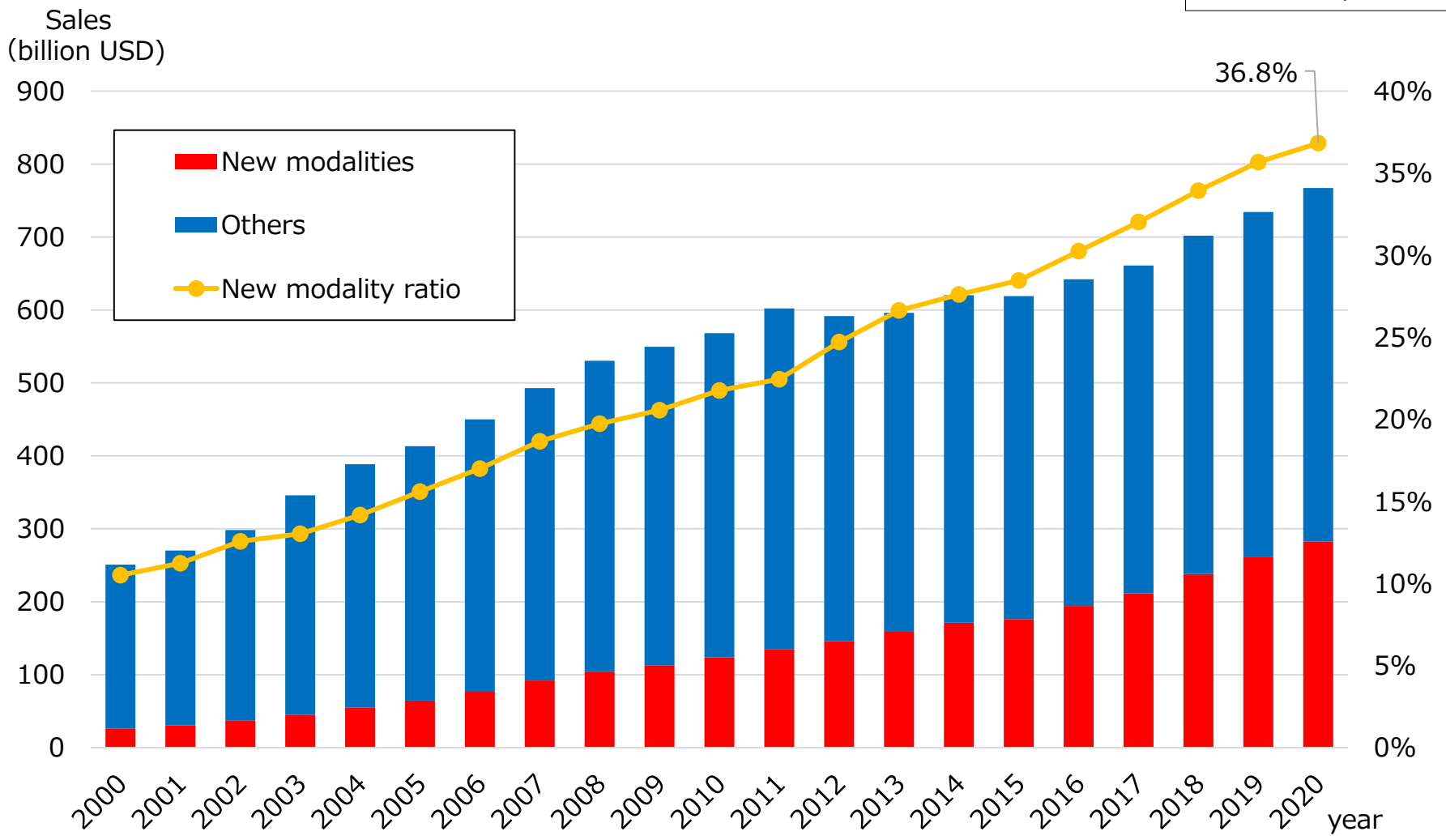
- Continuous growth of the world's population and rapid ageing of the population.
- Global pharma markets are expanding due to expansion in the US, China, whilst European markets are flat and growth in emerging markets is slowing
- **Rise of biopharma ventures**
- Expansion of Asian markets, e.g. India, Southeast Asian countries

4. Changes in disease structure in Japan

- With the ageing of the population, the number of patients with lifestyle-related diseases in Japan is on the rise, and the number of patients is also increasing worldwide, especially in developing countries.
- The number of dementia patients worldwide is increasing in line with the growth of the ageing population
- Addressing unmet medical needs

New Modalities Global Pharmaceutical Sales Trends

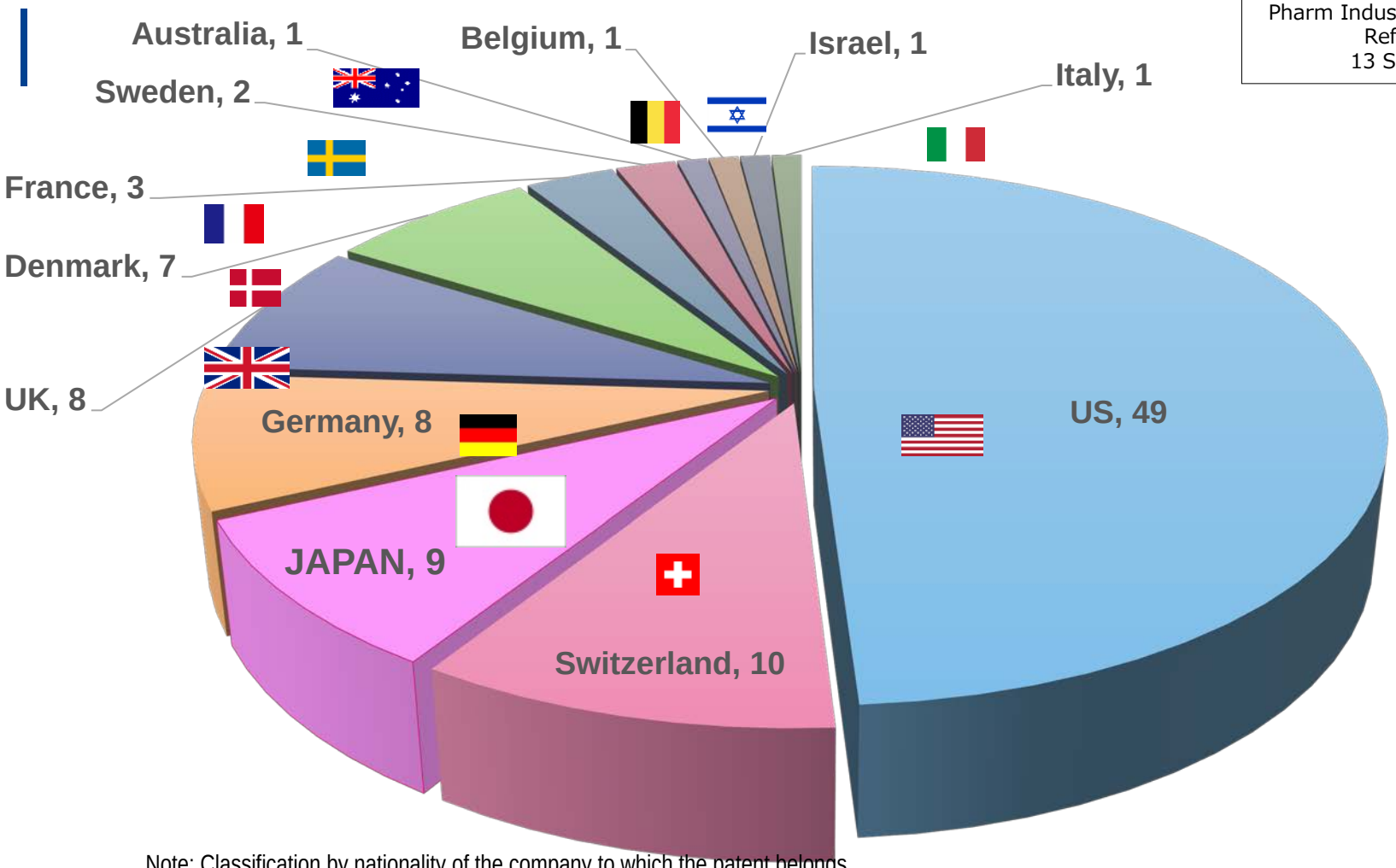
MHLW
Pharm Industrial Vision 2021
Reference
13 Sep 2021



Source: prepared by the Pharmaceutical Industry Policy Institute based on EvaluatePharma (as of February 2021).

Country origin comparisons of the top 100 global sales of ethical drugs (2019)

MHLW
Pharm Industrial Vision 2021
Reference
13 Sep 2021



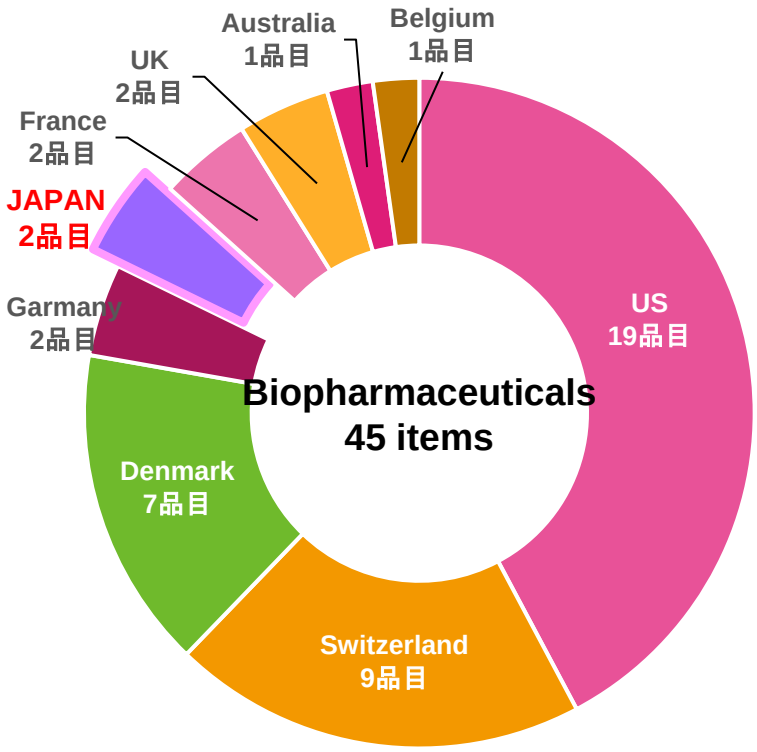
Note: Classification by nationality of the company to which the patent belongs.
The top 100 products in terms of sales in 2019, broken down by originating company nationality.
Source: copyright©2021 IQVIA. IQVIA World Review Analyst 2019, IQVIA Pipeline & New Product Intelligence, EvaluatePharma, Clarivate Analytics Cortellis.
Compiled by the Pharmaceutical Industry Policy Institute based on Competitive Intelligence (All rights reserved).
Source: Institute of Pharmaceutical and Industrial Policy, Policy Research News No. 61 (November 2020).

Breakdown of the number of medicines by nationality of the top 100 drug generators in global sales

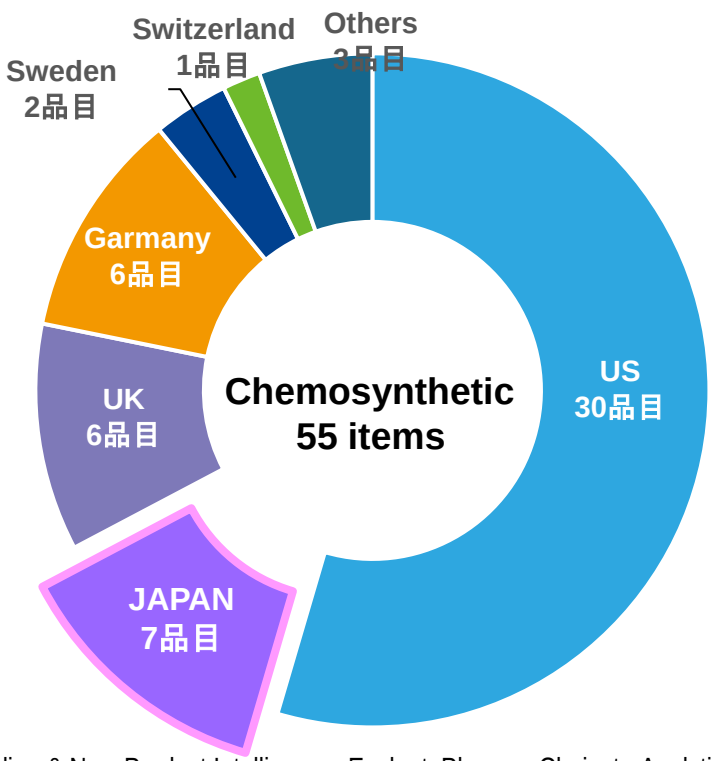
MHLW
Pharm Industrial Vision 2021
Reference
13 Sep 2021

- 10% of the world's top 100 ethical drugs originate from Japan
- On the other hand, Japan's share of biopharmaceuticals is small compared to Europe and the US
- The challenge is to increase the number of biopharmaceuticals originating from Japan.

Biopharmaceuticals



Chemosynthetic



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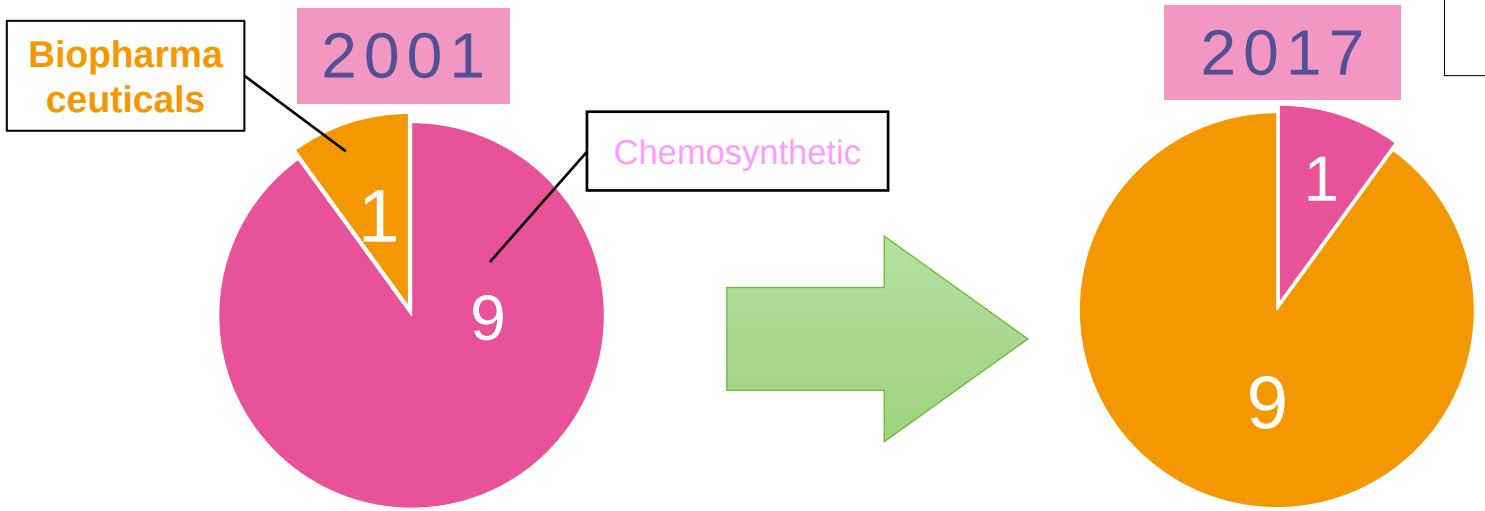
Compiled by the Pharmaceutical Industry Policy Institute based on Competitive Intelligence (All rights reserved).
Source: Institute of Pharmaceutical and Industrial Policy, Policy Research News No. 61 (November 2020).

Changes in drug discovery trends (Top 10 global sales)

MHLW
Pharm Industrial Vision 2021
Reference
13 Sep 2021



	Products	Indication	Company	Sales (million USD)
1	ｿﾞｺｰﾙ(ﾘﾎﾟﾊﾞｽ)	高脂血症薬	ﾒﾙｸ	6,670
2	ﾘﾋﾟﾄｰﾙ	高脂血症薬	ﾌｧｲｻﾞｰ	6,449
3	ｵﾒﾌﾟﾗｰﾙ/ﾌﾟﾘﾛｾﾞｯｸ	抗潰瘍剤PPI	ｱｽﾄﾗｾﾞﾈｶ	5,684
4	ﾉﾙﾊﾞｽｸ	降圧剤Ca拮抗剤	ﾌｧｲｻﾞｰ	3,582
5	ﾒﾊﾞﾛﾁﾝ/ﾌﾟﾗﾊﾞｺｰﾙ	高脂血症薬	三共/BMS	3,509
6	ﾌﾟﾛｸﾘｯﾄ/ｴﾌﾟﾚｯｸｽ	腎性貧血	J&J	3,430
7	ﾀｹﾌﾟﾛﾝ	抗潰瘍剤PPI	武田薬品/TAP	3,212
8	ｸﾗﾘﾁﾝ/D	抗ヒスタミン剤	ｼｪﾘﾝｸﾞ・ﾌﾟﾗｳ	3,159
9	ｾﾚﾌﾞﾚｯｸｽ	Cox2阻害剤	ﾌｧﾙﾏｼｱ	3,114
10	ｼﾞﾌﾟﾚｷｻ	精神分裂病薬	ｲｰﾗｲ・ﾘﾘｰ	3,087

		Products	Indication	Company	Sales (million USD)
	1	ﾋｭﾐﾗ	関節ﾘｳﾏﾁ	ｱｯﾋﾞｨ/ｴｰｻﾞｲ	18,923
★	2	ｴﾝﾌﾞﾚﾙ	関節ﾘｳﾏﾁ	ｱﾑｼﾞｴﾝ/ﾌｧｲｻﾞｰ/武田	8,234
	3	ﾚﾌﾞﾗﾐﾄﾞ	多発性骨髄腫	ｾﾙｼﾞｰﾝ	8,191
★	4	ﾘﾂｷｻﾝ	非ﾎｼﾞｷﾝﾘﾝﾊﾟ腫	ﾛｼｭ	7,528
★	5	ﾚﾐｹｰﾄﾞ	関節ﾘｳﾏﾁ	J&J/ﾒﾙｸ/田辺三菱	7,172
★	6	ﾊｰｾﾌﾟﾁﾝ	乳がん	ﾛｼｭ/中外製薬	7,126
★	7	ｱﾊﾞｽﾁﾝ	結腸・直腸がん	ﾛｼｭ/中外製薬	6,795
	8	ｱｲﾘｰｱ	加齢黄斑変性症	ﾘｼﾞｪﾈﾛﾝ/ﾊﾞｲｴﾙ/参天製薬	6,291
★	9	ｵﾌﾟｼﾞｰﾎﾞ	悪性黒色腫他	BMS/小野薬品	5,761
	10	ﾌﾟﾚﾍﾞﾅｰ	肺炎球菌	ﾌｧｲｻﾞｰ	5,693

Yellow: biopharmaceuticals, ★: venture-origin medicines

Source: MHLW, based on Pharma Future 2002 No. 136, published by Ute Brain Division, Sesidem Strategic Data Co Ltd, and Evaluate Ltd, Evaluate Pharma.

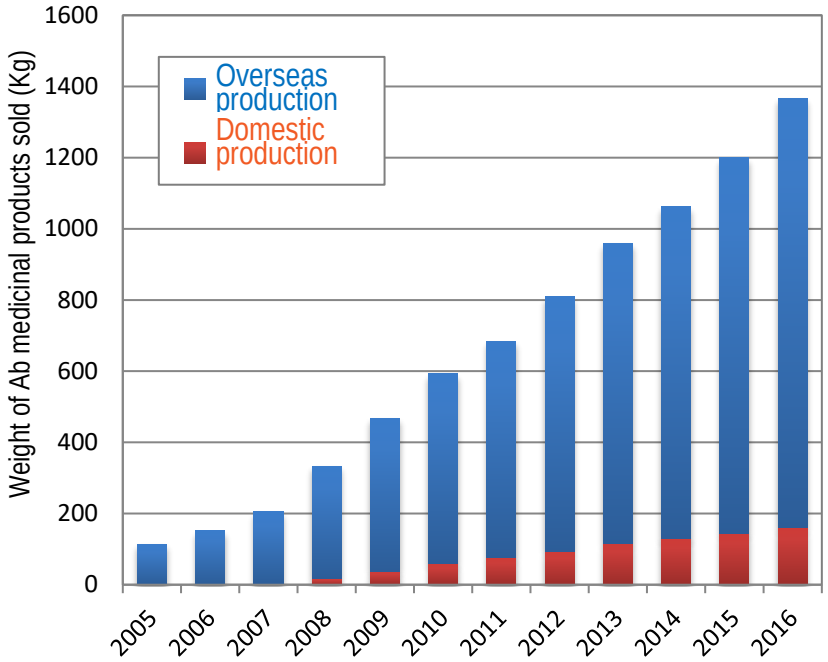
Status of sales and production of biopharmaceuticals in Japan.

MHLW
Pharm Industrial Vision 2021
Reference
13 Sep 2021

Although the number of antibody drugs sold in the country is increasing, around 90% of these are produced abroad, making the country highly dependent on overseas production sites.

Weight of antibody drugs sold by domestic and international production

<Weight>



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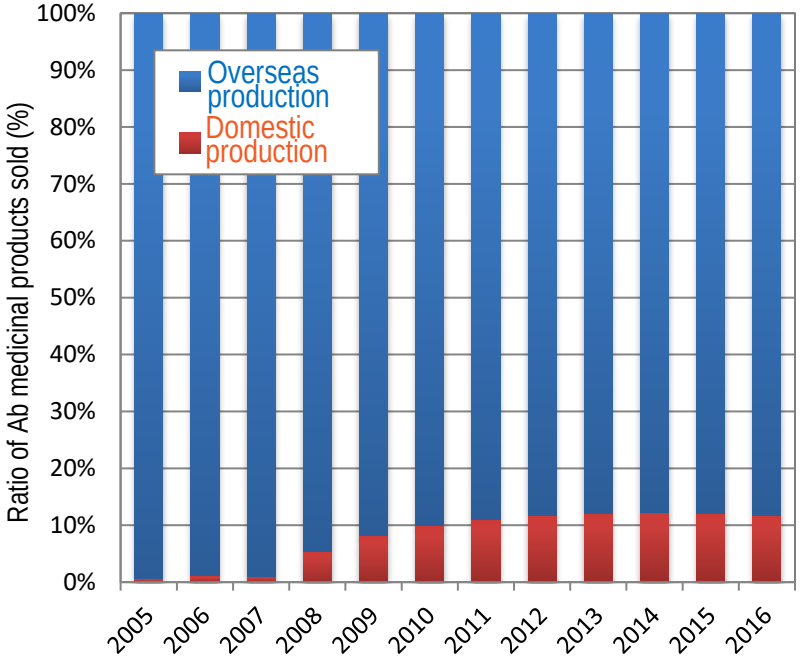
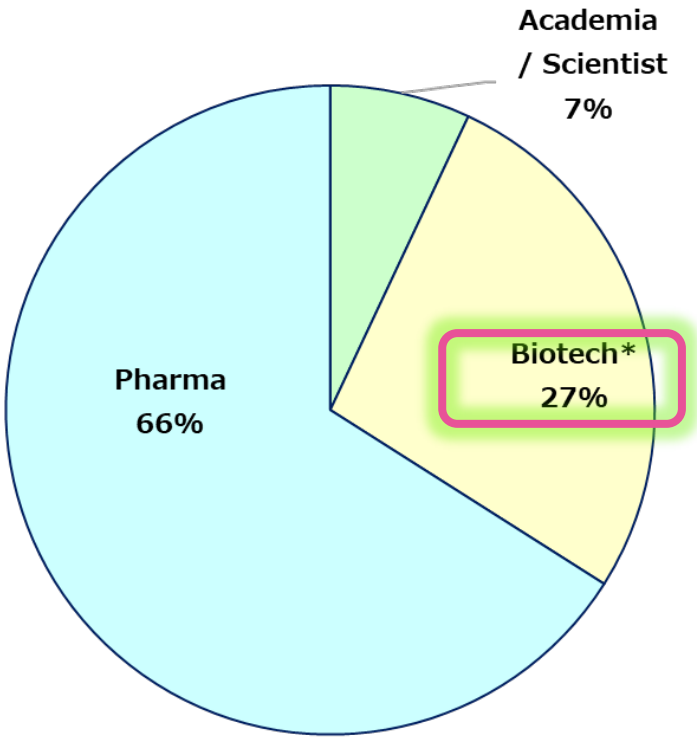


Source: copyright©2021 IQVIA. based on individual surveys conducted by IQVIA JPM March 2017 MAT and the Pharmaceutical Industry Policy Institute (all rights reserved).
Source: Institute for Pharmaceutical Industry Policy Research Paper Series No. 71 (March 2018).

Recent drug development trend

Classification of global top sales products by origin organisation in 2017

MHLW
Pharm Industrial Vision 2021
Reference
13 Sep 2021



	Academia / Scientist	Biotech*	Pharma
USA	5	23	22
JAPAN	1		11
Switzerland		1	10
UK		1	6
Germany			7
Denmark			5
France		1	1
Belgium		1	
Sweden			2
Italy			
Israel	1		
Luxembourg			1
Netherland			1

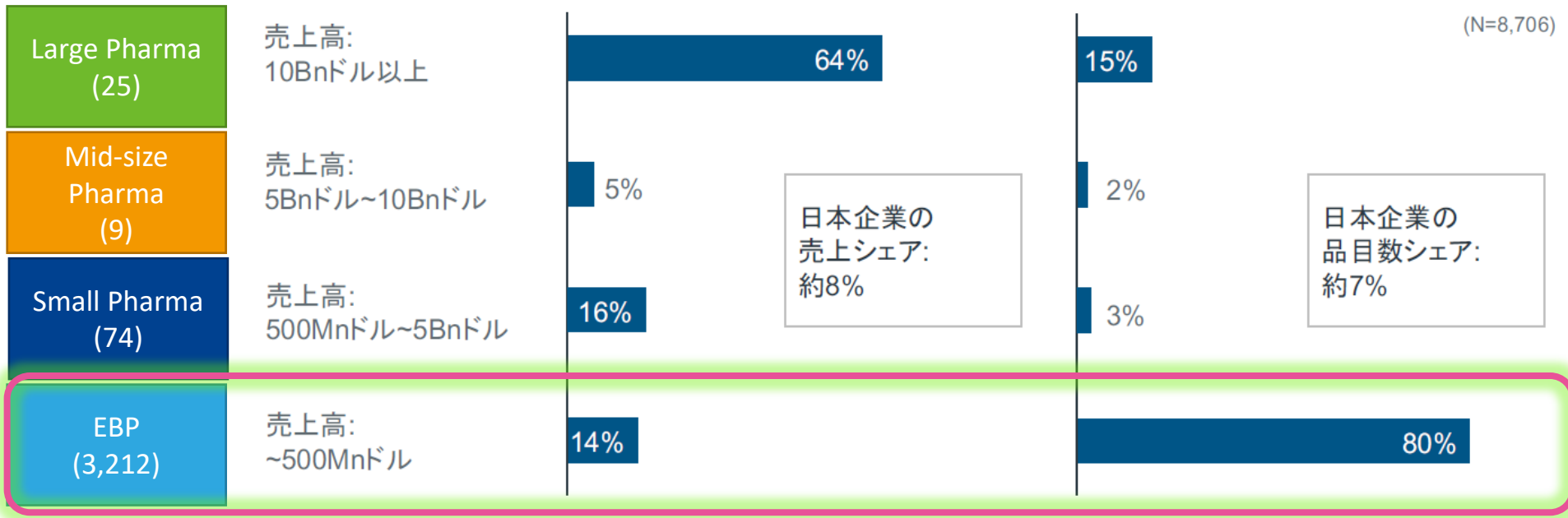
*Biotech: A company that is developing novel pharmaceutical products. They typically have very few marketed products and the products they are developing are generally NMEs/BLAs.

2017年売上上位100品目の特許帰属組織の種別による分類 (EvaluatePharma)
出所：Copyright© 2021IQVIA. IQVIA World Review Analyst 2017, IQVIA Pipeline & New Product Intelligence、Thomson Innovation、Pharmaprojects、EvaluatePharmaに基づき、医薬産業政策研究所にて作成（無断転載禁止）

Recent drug development trend

EBP's share of pharmaceutical sales and number of products under development

MHLW
Pharm Industrial Vision 2021
Reference
13 Sep 2021



- 日本では新興バイオファーマの存在感が低い (アメリカでは新薬承認数の半分以上を新興バイオファーマの創製品が占める)
- 日本企業は低分子領域の開発品では**10%**近いシェアをもつが、新モダリティ領域の開発品では**3%**程度のシェアにとどまる

(出所) IQVIAデータをもとにIQVIA分析

IQVIA

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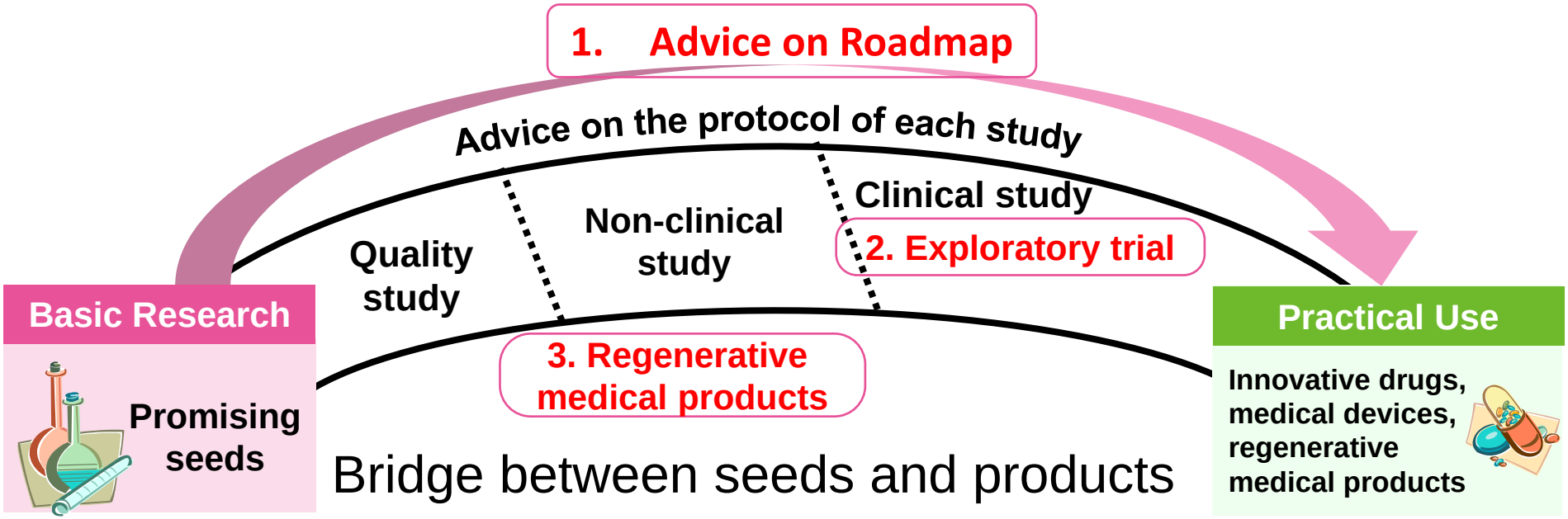
- PMDA has introduced **support systems** according to customer's need

- The environment for **new seed development** is being prepared by throughout Japan

Regulatory Science Consultation on R&D Strategy

1. Facilitate the development of medical products by developing a more reliable roadmap.
2. Accelerate the clinical trials led by academia.
3. For regenerative medical products, ensure the quality of the products and confirm the nonclinical safety before the clinical trial notification.



* In collaboration with the Japan Agency for Medical Research and Development (AMED), PMDA is proactively supporting the establishment of an exit strategy via Regulatory Science (RS) Consultation on R&D Strategy.

Outline of the RS Consultation

Category	Objective	Consultant	Style	Duration	Fee	Minutes
General Consultation	Introduction of general information on: -Consultation system -Pharmaceutical regulatory system -Related guidelines	Technical Experts	F2F / Online	20min	Free	Not shared
Pre-consultation meeting	Clarification of discussion points, consultation dossiers	Technical Experts and Reviewers	F2F / Online	30min	Free	Not shared
Consultation	Scientific discussion	Technical Experts and Reviewers	F2F / Online	Max. 2hr	Charged	Shared

PMDA offers 90% reduction to venture companies.

Please contact:

rs-contact@pmda.go.jp

SAKIGAKE (Forerunner) drugs - Designation System

<Objective>

To put innovative products into medical practice in Japan

<Criteria for designation>

1. Innovativeness - new mode of action (in principle)
2. Severity of the target disease - life-threatening or no curative therapies
3. Prominent efficacy - no existing therapies or probable significant improvement in efficacy or safety compared to existing therapies
4. Plan/System - to submit the NDA in Japan first or at the same timing* as the first NDA submission to other national regulatory authority

<Incentive>

*within 30 days

- Concierge service offered by senior review partner (PMDA)
- Priority scientific advice (PMDA)
- Pre-review in consultation (PMDA)
- Priority review (6 months)(PMDA)
- Premium drug pricing
- Extension of re-examination period

Fastest Practical Use in the world

senku_iyakuhin@mhlw.go.jp

Orphan drug – Designation System

<Objective>

To promote the R&D of the products for rare diseases to provide the patients with safe and effective medicines / medical devices as early as possible

<Criteria for designation>

1. Number of patients (any of the following has to be met)
   - Less than 50,000 in Japan
   - The target disease is one of the designated intractable diseases
2. Medical needs
   - Serious diseases with high medical needs
3. Feasibility of development

<Incentive>

- Grant-in-Aid for R&D of orphan designated drugs (NIBIOHN*)
- Tax deduction for R&D expenses
- Priority scientific consultation (PMDA)
- Priority review (PMDA)
- Premium drug pricing
- Extension of re-examination period

Promoting R&D

orphan_drug@mhlw.go.jp

*National Institutes of Biomedical Innovation, Health and Nutrition

Clinical Research Core Hospitals

Abundant experience in:
- Planning, implementation, and analysis of clinical research and trials
- Commercialisation of innovative seeds

Diverse human resources:
- Experts in clinical research and commercialisation
- Cooperation from various departments in the hospitals
- Biostatisticians and data managers
- CRC and other operational units
- Review committee bodies such as CRBs
- Staff experienced in PMDA

Support by making the most of features,

etc.

Clinical Research Core Hospitals have similar difficulties and experiences with venture companies.

"Clinical Research Core Hospitals" can provide **a range of support tailored to ventures needs**!

- National Cancer Centre Central Hospital
- Tohoku University Hospital
- Osaka University Hospital
- National Cancer Centre East Hospital
- Nagoya University Hospital
- Kyushu University Hospital
- University of Tokyo Hospital
- Keio University Hospital
- Chiba University Hospital
- Kyoto University Hospital
- Okayama University Hospital
- Hokkaido University Hospital
- Juntendo University Hospital
- Kobe University Hospital
- Nagasaki University Hospital

Public support for medical ventures

Recently public organisations support medical ventures in Japan.

Consultation Services for Ventures

InnoHub

- Provides consultation on a wide range of fields, including healthcare and life sciences
- Support the creation of innovation through the matching of consultants and supporters, as well as a consultation function that can introduce support measures from ministries, public and private funds, the private sector, etc.

Coordination

MEDISO
Medical Innovation Support Office

- Focuses on consultations on pharmaceutical regulations and the medical insurance system.
- In addition, actively provide consultation and support for developing business strategies for issues faced by medical ventures at each stage of R&D, such as IP and business management, and overseas expansion.

Coordination

Pmda

- RS Consultation, General Consultation etc.

Plus One

- Support for R&D ventures, in addition to healthcare and medical fields.
- Agreements with nine organisations to provide integrated support according to the characteristics of the supporting organisation.

Grants and Acceleration programmes

Acceleration Programmes

- IP Acceleration programme
- Pharmaceutical and Medical Venture Acceleration programme

Grants and Acceleration Programmes

- ViCLE, bridging research, projects to promote medical-engineering collaboration, etc.
- NEP, STS etc.
- START, SCORE, SUCCESS etc.

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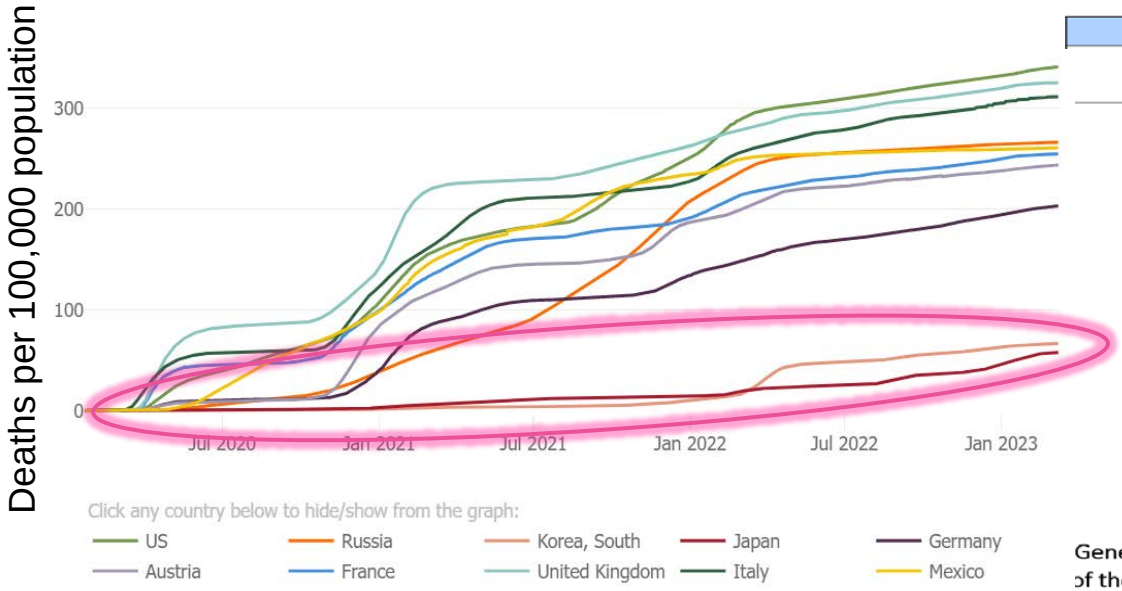
Why is PMDA committed to Asia ?

Intrinsic / Extrinsic factors in Asian

Cumulative Cases by Date



https://coronavirus.jhu.edu/data/cumulative-cases

ICH-E5

INTRINSIC		EXTRINSIC
Genetic	Physiological and pathological condition	Environmental
Gender		Climate
	Height	Sunlight
	Body weight	Pollution
	Liver	Culture
	Kidney	Socioeconomic status
	Cardiovascular functions	Educational status
		Language
	ADME	
	Receptor sensitivity	Medical practice
		Disease definition/Diagnostic
Race		Therapeutic approach
		Drug compliance
		Smoking
		Alcohol
Genetic polymorphism of the drug metabolism		
		Food habit
		Stress
Genetic diseases	Diseases	Regulatory practice/GCP
		Methodology/Endpoints

Cooperation with Asian regulators

- Asian Network Meeting (ANM)
- Symposium
- Bilateral Meeting
- Seminar

Asian Network Meeting (ANM)

➢ Objectives

- Aims to establish **a voluntary high-level network** involving Heads of Agencies to address strategic issues pertaining to the regulation of medical products in the Asia region.
- Is enabled through **the sharing of emerging trends / issues** from horizon scanning, sharing of information and best practices.
- Seeks **to synergise with other international initiatives** while avoiding duplication.

❖ This framework will

a. **contribute to convergence and harmonisation** of medical products regulation,
b. **promote regulatory efficiency and reliance**, and
c. **enable faster and seamless access** of safe, quality and efficacious medical products in Asia.

The 5th Asian Network Meeting

- Date and venue: 19 April 2023 in Tokyo (Hybrid meeting)

- Co-hosts: NMPA China, CDSCO India,
  MHLW/PMDA Japan and HSA Singapore
- Topics:
  1. Future pandemic -How to collaborate ?
  2. Efficient regulatory systems in Asia
     - How to support ?

Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC)

Established in April, 2016 to promote capacity building and human resource development through training seminars for Asian regulators.

Action Policy of PMDA-ATC

Contribute to universal health coverage in Asia through developing a foundation for regulatory harmonisation in the Asian region.

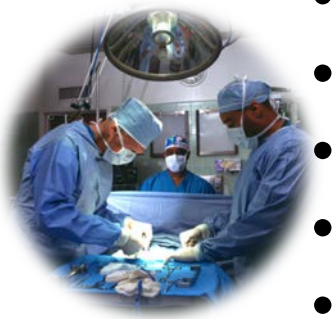
Visits sites and conducts lectures, case studies and practical trainings.

Provides trainings tailored to local needs for more people.

Invites Asian regulatory representatives and offers training seminars.

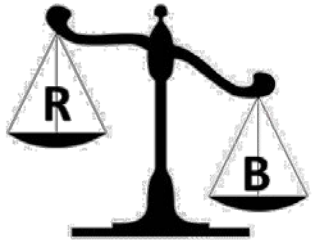
Shares Japanese knowledge and experiences in the regulation of pharmaceuticals and medical devices with Asian countries.

Contents of PMDA-ATC Training Seminars



Example

- Pediatric Review
- Quality Control (Herbal Medicine)
- Pharmaceuticals Review
- Medical Devices Review
- Multi-Regional Clinical Trial (MRCT)
- Good Manufacturing Practice (GMP)
- Pharmacovigilance



In fiscal year 2022, nine (9) Seminars open to all regulators and eleven (11) Seminars for specific countries were held.

PMDA-ATC e-Learning courses and learning videos

PMDA-ATC provides learning videos on

- Current topics such as “Measures against COVID-19”
- Overview of PMDA and its services including review, safety and relief
- Our activities to promote international regulatory harmonisation

	Contents Category
1	Review
2	Safety
3	Relief
4	Medical Device
5	GxP
6	PMDA Efforts

https://www.pmda.go.jp/english/int-activities/training-center/0003.html

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Transition from Pandemic to Endemic

➢ Infectious Disease Category Change for COVID-19

- The Infectious Diseases Control Law classifies infectious diseases into Class 1 to 5 based on their infectiousness and severity
- Measures to prevent the spread of infections differ among classes
- COVID-19 was recategorised from Class 2 to 5 on 8 May 2023.

Class 2		Class 5
Unified prevention approach requested by Government	→	Voluntary efforts (No request by government to take unified prevention measures)

❖**Terminated as of 8 May 2023**: prioritised review that was applied to COVID-19 therapeutics and vaccines

❖**Application of "Emergency Approval" will be reviewed** for future pandemic preparation.

Towards Revision of Cannabis Control Act

➢Cannabis Control Act

- Prohibit use and import of drugs made from Cannabis

❑ Medical needs for drugs manufactured from Cannabis

- **Epidiolex** (CBD oral solution for treatment of Lennox-Gastaut syndrome or Dravet syndrome) is not permitted to be used in Japan

➢Proposed amendment to the act

- To permit import, manufacture, and use of drugs made from cannabis under Pharmaceuticals and Medical Devices Act approval

Future Regulatory Actions (in short term)

- Accelerate Paediatric Drug Development
  - Provide PMDA's support for paediatric drug development plan
- Review Conditional Approval Implementation
  - Confirmation of accelerated part
- Promote Digital Transformation in the area of Clinical Trials
  - Develop Guidance to ensure data quality and reliability collected through DCTs and digital devices
- Develop Guidance for the use of RWD
  - Expand the use of RWD from pharmacovigilance to new drug review
  - Intensify the use of MID-NET (Medical Information Database NETwork)

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Initiatives to strengthen cooperation with Asian countries and the United States

- To support innovative medicines & medical devices access in Japan and Asian countries,
  - To strengthen cooperation with ASEAN countries
  - To support the promotion of regulatory harmonisation with Asian countries
  - To develop an environment for smooth clinical development
- Close collaboration between Japan, US and European regulatory authorities is essential in supporting;
  - Development of innovative medicines and medical devices
  - Regulatory review
  - Post-marketing measures.

Cooperation with Asian countries and the US, including the establishment of overseas offices in the ASEAN region and the US, in order to promote the development of and access to innovative medicines & medical devices.

PMDA Oversea Office

Establishment of Asia Office and US Office

Facilitating information exchange;

(1) between PMDA - Asian regulators

(2) between PMDA - U.S. industries as portal to Japanese regulation and market

独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

Thank you for listening !

感謝您的關注！

Daisuke TANAKA, Ph.D.
Office Director, Office of International Program
Pharmaceuticals and Medical Devices Agency, Japan

5 October 2023
11th Joint Conference of Taiwan and Japan on Medical Products Regulation

獨立行政法人
醫藥品醫療機器綜合機構

國際部經理
田中 大祐

2023年10月5日
第十一屆台日醫藥交流會議