Advances in Pharmaceutical Regulations in Japan and the Path of the Japanese Pharmacopoeia

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Today's Topics

1. The Establishment of the Japanese Pharmacopoeia

2. Revisions of the Japanese Pharmacopoeia and Changes in Pharmaceutical Regulation

3. Current Status and Future Prospects of the Japanese Pharmacopoeia

1. The Establishment of the Japanese Pharmacopoeia

The Path of the Japanese Pharmacopoeia

- The role of the Pharmacopoeia is to note the principles regulating the quality level of pharmaceuticals supplied in our country…

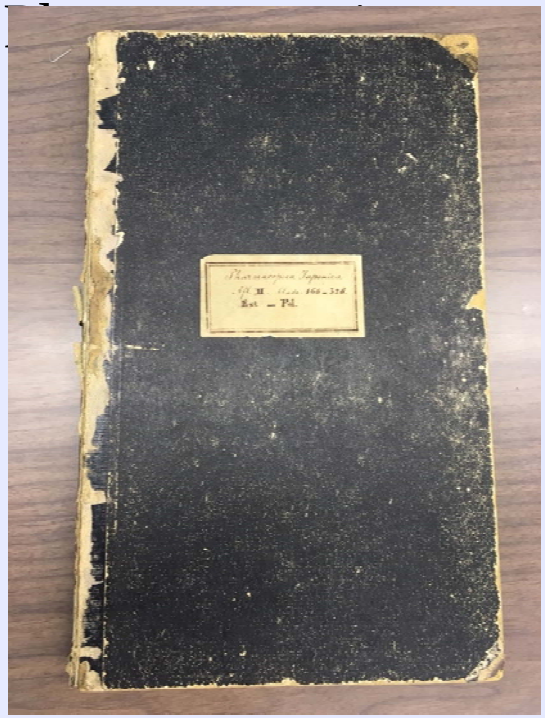
"Document on the role assigned to the Japanese Pharmacopoeia" (October 6, 1880)

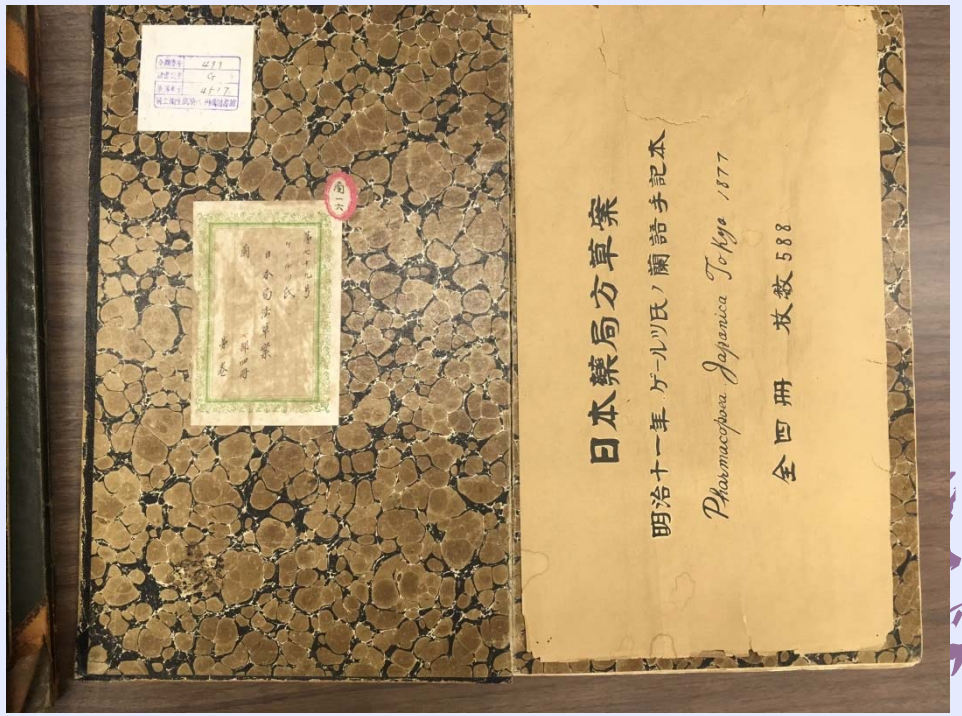
⇒ During this era, advanced countries already had their own Pharmacopoeia for drugs used and had a certain criteria established for healthcare provided. As our country did not have regulations to prepare such manuals, healthcare was in disarray as the amount of the main ingredient included in drugs with the same name differed depending on which country it was being imported from and, in some cases, fraudulent or defective products were being circulated.

(Source: "In commemoration of 100 years since the Japanese Pharmacopoeia was first published" (October 1986))

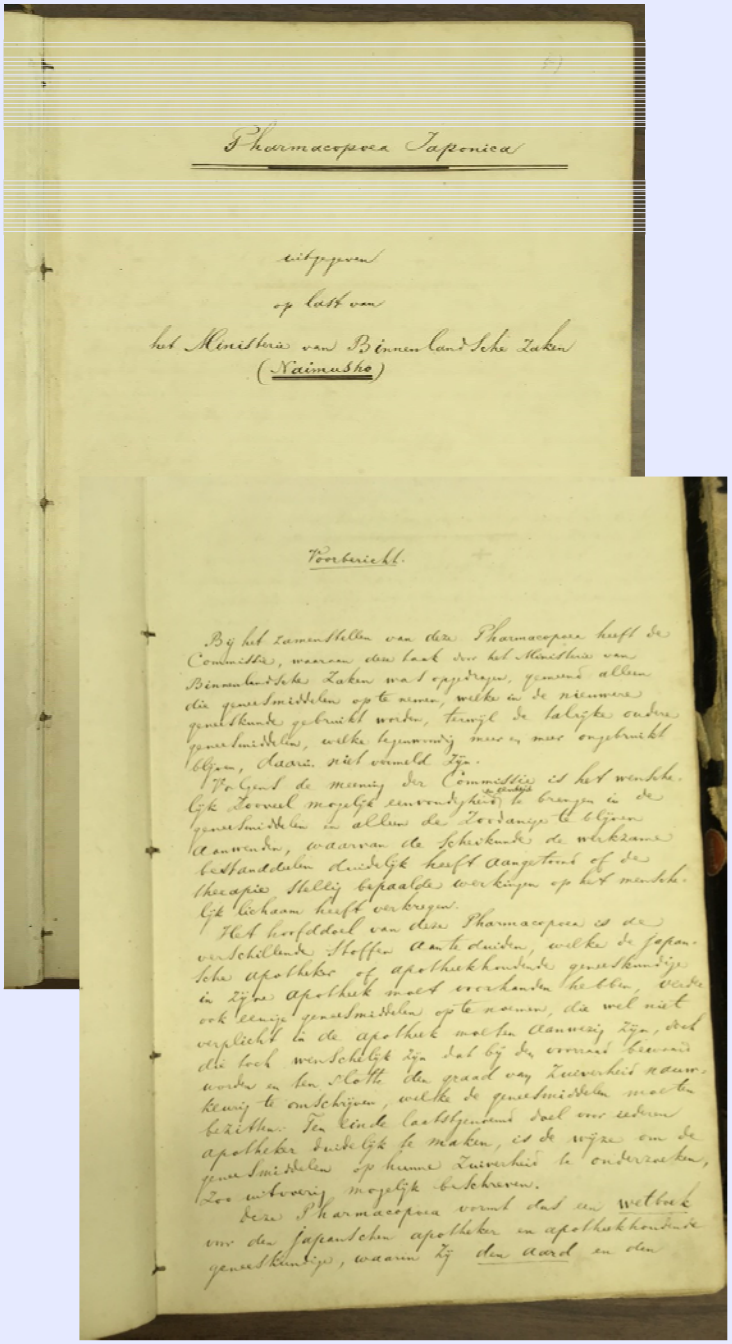
For Establishing the First Edition of Japanese Pharmacopoeia

- Sensai Nagayo, the Head of Health & Medical Bureau of the Ministry of Internal Affairs, asked Dr. A.J.C. Geerts, a Dutchman who instructed the pharmaceutical organization, to create a draft.
- The draft was completed in 1877 using European and American Pharmacopoeia as a reference, mainly the Dutch





Draft for the Japanese Pharmacopoeia (1877): National Institute of Health Sciences Library



Pharmacopoea Japonica

uitgegeven

op last van

het Ministerie van Binnenlandsche Zaken

(Naimusho)

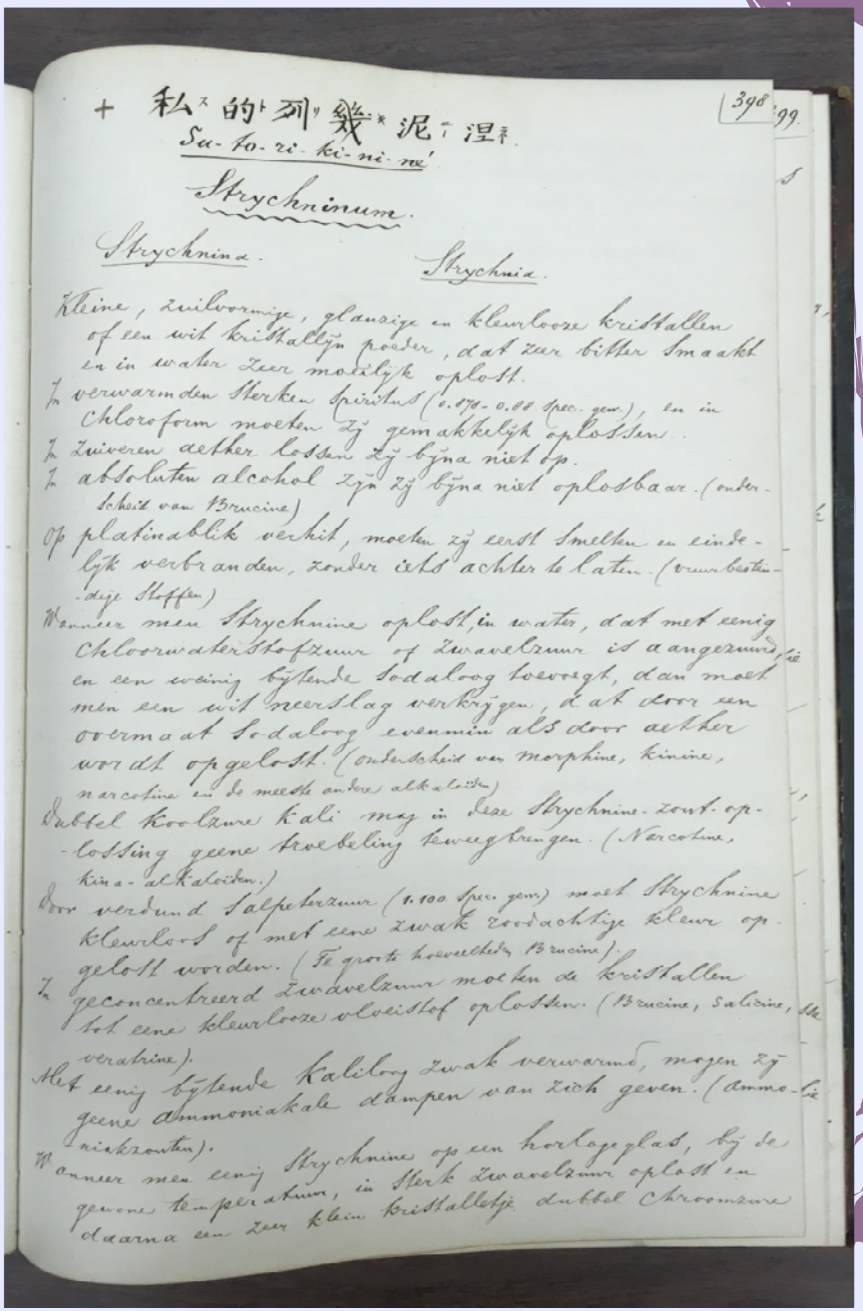
Voorbericht.

Bij het zamenstellen van deze Pharmacopee heeft de Commissie, waaraan door het Ministerie van Binnenlandsche Zaken was opgedragen, gemeend alleen die geneesmiddelen op te nemen, welke in de nieuwere geneeskunde gebruikt worden, terwijl de talrijke andere geneesmiddelen, welke tegenwoordig meer en meer ongebruikt blijven, daaruit niet vermeld zijn.

Volgens de meening der Commissie is het wenschelijk zooveel mogelijk eenvoudigheid te brengen in de geneesmiddelen in allen die zoodanige te blijven aanwenden, waarvan de scheikunde de werkzame bestanddeelen duidelijk heeft aangetoond of de therapie stellig bepaalde werkingen op het menschelijk lichaam heeft verkregen.

Het hoofddoel van deze Pharmacopee is de verschillende stoffen aan te duiden, welke de japansche apotheker of apothekkundige geneeskundige in zijne apotheek moet voorhanden hebben, welke ook eenige geneesmiddelen op te nemen, die wel niet verplicht in de apotheek moeten aanwezig zijn, doch die toch wenschelijk zijn dat bij de vorming daarvan worden in den stoffen de graad van zuiverheid waarmede in te stellen, welke de geneesmiddelen moeten bezitten. Ten einde laatstgenoemd doel voor ieder apotheker duidelijk te maken, is de wijze om de geneesmiddelen op hunne zuiverheid te onderzoeken, zoo uitvoerig mogelijk beschreven.

Deze Pharmacopoea vormt dus een welbeek voor den japanschen apotheker en apothekkundige geneeskundige, waarin hij den aard en den



+ 私的列幾泥涅.

Sa-to-ri-ki-ni-ne'

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Strychninum.

Strychnina. Strychnia.

Kleine, zuilvormige, glanzige en kleurloze kristallen of een wit kristallijn poeder, dat zeer bitter smaakt en in water zeer moeilijk oplost.

In verwarmden sterken spiritus (0.870-0.88 spec. gew.), en in chloroform moeten zij gemakkelijk oplossen.

In zuiveren aether lossen zij bijna niet op.

In absoluten alcohol zijn zij bijna niet oplosbaar. (onderscheid van Brucine)

Op platinablik verkit, moeten zij eerst smelten en eindelijk verbranden, zonder iets achter te laten. (onderscheid van bepaalde stoffen)

Wanneer men Strychnine oplost in water, dat met eenig Chloorwaterstofzuur of Zwavelzuur is aangezuurd, en een weinig bijtende sodaloog toevoegt, dan moet men een wit neerslag verkrijgen, dat door een overmaat sodaloog evenmin als door aether wordt opgelost. (onderscheid van morphine, kinine, narcotine en de meeste andere alkaloïden)

Dubbel koolzure kali mag in deze Strychnine-zout-oplossing geene troebeling teweegbrengen. (Narcotine, kina-alkaloïden.)

Door verdund salpeterzuur (1.100 spec. gew.) moet Strychnine kleurloos of met eene zwak roodachtige kleur opgelost worden. (Te groote hoeveelheden Brucine)

In geconcentreerd Zwavelzuur moeten de kristallen tot eene kleurlooze vloeistof oplossen. (Brucine, Salicine, Veratrine).

Met eenig bijtende kalilog zwak verwarmd, mogen zij geene ammoniakale dampen van zich geven. (ammoniakzouten).

Wanneer men eenig Strychnine op een horlogeglas, bij de gewone temperatuur, in sterk zwavelzuur oplost en daarna een zeer klein kristalletje dubbel chroomzure

Draft for the Japanese Pharmacopoeia (1877): National Institute of Health Sciences Library

Establishing the First Edition of the Japanese Pharmacopoeia

First Edition of the Jaanese Pharmacopoeia/ Official gazette and Latin version

Published as a separate volume to the Ordinance of the Home Ministry, No. 10 (Addendum for the Official Gazette No. 894) in 1886

2 columns, 78 pages of text, 8 pages of index
Each section 468 products, 10 general provisions for pharmaceuticals
Published Latin version in 1888

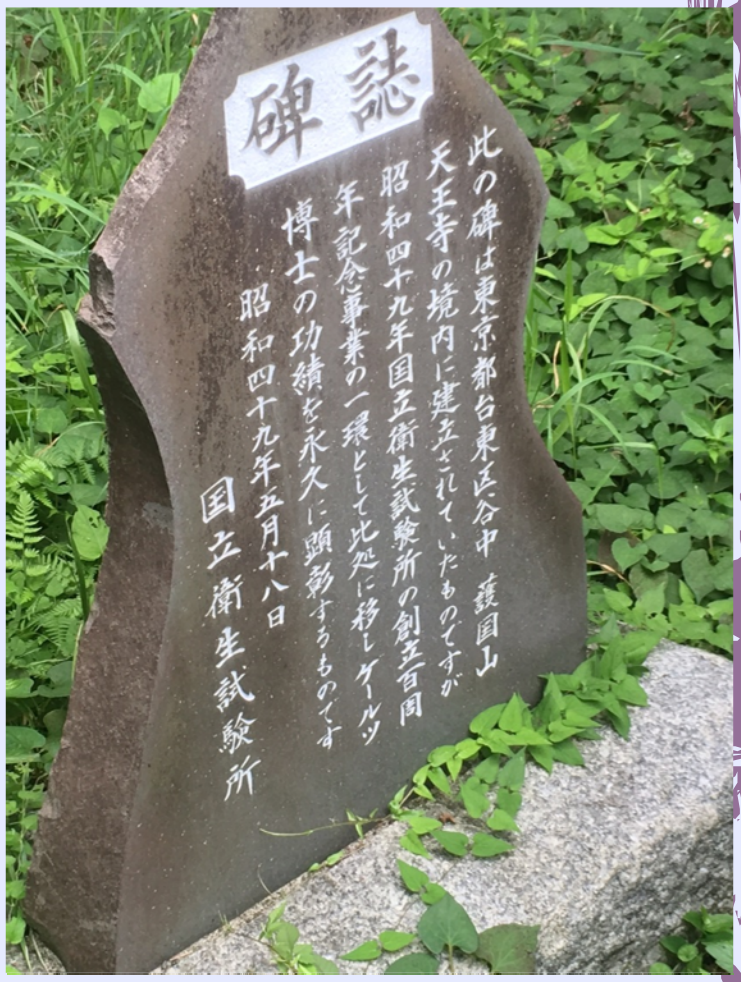
The Health Department of the Home Ministry published “Overview of the Japanese Pharmacopoeia” in 1890

- The first edition was compiled and published in 1886 with cooperation from foreign teachers such as J.F. Eijkmsn, Geerts, and A. Langgard. The Latin version was published in 1888 and the overview was published in 1890.

Crude Drug Specimens that were used as Reference for Listings in the Pharmacopoeia

Monument to Commemorate Dr. Geerts

(Located in the front courtyard of the National Institute of Health Sciences)



2. Revisions of the Japanese Pharmacopoeia and Changes in Pharmaceutical Regulation

Changes in the Revised Pharmacopoeia and Establishment of Pharmaceutical Regulation

- Revisions were made by Japanese alone from the Second Edition (1888~1891).
  - Pharmaceutical Marketing and Handling Regulations published (1889)
  - Establishment of Dainippon Pharma. Manufacturing of domestic pharmaceuticals started (Begin operations in 1885).
  - Official announcement about Institutes of Health Sciences published (1887)
  - Establishment of private pharmacology school (predecessor of Tokyo University of Pharmacy and Life Sciences) (1888)

- From the Third Edition (1906), publishing of the Latin version was abolished and an English version was released.

Changes in the Revised Pharmacopoeia and Establishment of Pharmaceutical Regulation

- In conjunction with the Pharmaceutical Affairs Law (older version) being promulgated, the “National Formulary” (predecessor of the latter Japanese Pharmacopoeia Section 2) was published in 1948.

- In the Pharmaceutical Affairs Law (newer version) enacted in 1961, the Seventh Edition of the Pharmacopoeia was conducted in order to create Pharmacopoeia suitable to our country’s conditions given the rapid advancement of new pharmaceuticals and development of test methods, etc.
  - “National Formulary” was abolished and Pharmacopoeia consisted of two main sections.

History of Japanese Pharmacopoeia Revisions

Edition	Publishing Year	No. of Products Listed
JP1	1886	468
JP2	1891	445
JP3	1906	703
JP4	1920	684
JP5	1932	657
JP6	1951	634
JP7	1961	1227
JP8	1971	1131
JP9	1976	1046
JP10	1981	1016

Edition	Publishing Year	No. of Products Listed
JP11	1986	1066
JP12	1991	1221
JP13	1996	1292
JP14	2001	1328
JP15	2006	1483
JP16	2011	1764
JP17	2016	1962

3. Current Status and Future Prospects of the Japanese Pharmacopoeia

The overview of 17th revision of the Japanese Pharmacopoeia

①General Notices:

"Manufacturing requirement" (control of manufacturing processes), "Residual solvents", "Potential adulteration" and "The definitions of "sterility" etc." were newly added.

②General Tests, Processes and Apparatus:

Glycosylation Analysis of Glycoprotein, Methods of Adhesion Testing, Release Test for Preparations for Cutaneous Application etc. were newly added.

③Official Monographs

76 items were newly added, 472 items were revised and 10 items were deleted. (Total 1,962 items are listed)

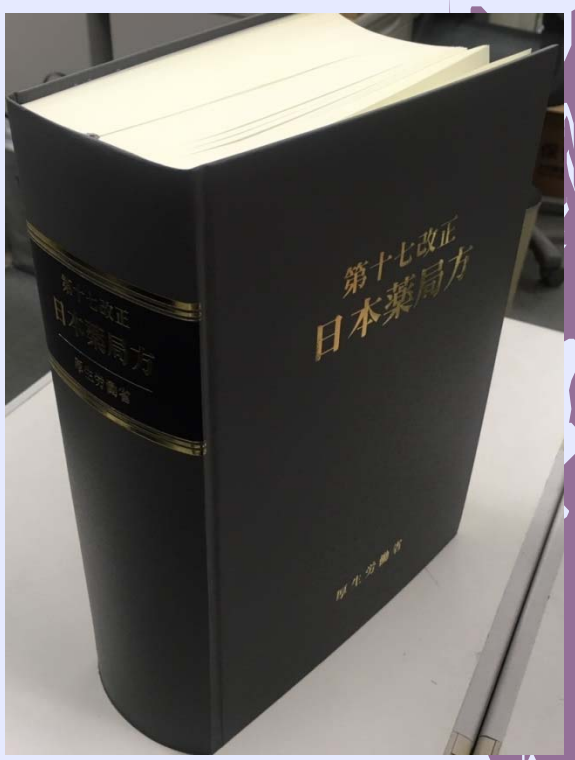
④The Revision of Reference Standards

⑤ The Revision related to Packaging

"General Notices for Packaging of Preparations'' which describe the fundamental requirements were newly added.

⑥Others

Items harmonized in ICH were added (reference information9



For the 18th Edition of the Japanese Pharmacopoeia

To create New Japanese pharmacopeia in accordance with current conditions and necessities, based on the latest scientific knowledge.

- The enhancement of reference standards and management of impurities.
- Making qualitative improvement by introducing the latest science and technology.
- Flexible description in Official Monographs utilizing manufacturing requirement etc.
- Organizing general provisions and monographs for biological products

Background

- Environmental change and innovation surrounding the manufacture of drugs
  - The source of raw material and impurities are diversified by outsourcing of manufacture
  - The progress of Production techniques, such as Continuous Production Technology
  - The advancement of analytical technology
  - The diversification of drugs (Not limited to natural products or synthetic products)

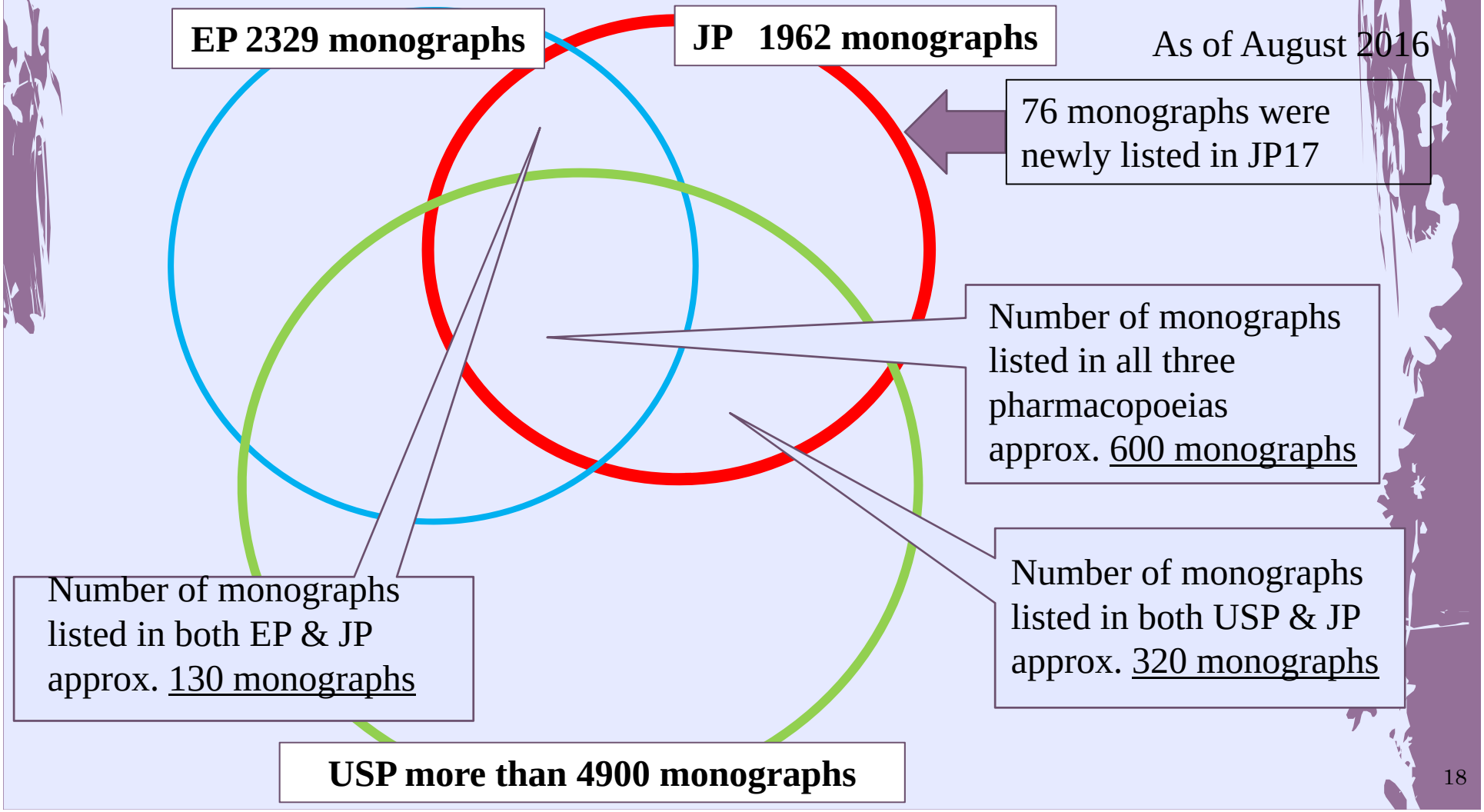
- Evolution to Regulation corresponding to the changes

→Current standards and concepts of Japanese Pharmacopoeia to assure the quality of the drug are also needed to change based on the latest scientific knowledge

Proactive listing of Japanese developed pharmaceuticals

➢ Abundant listing of products in each pharmaceutical section

Comparing the Number of Listed monographs in JP, USP and EP



Aiming to Create an Appealing Japanese Pharmacopoeia

- Promoting globalization through addition of Japanese Pharmacopoeia as a reference Pharmacopoeia overseas
- Early release of the English version of the Japanese Pharmacopoeia

Strategy for Harmonization of International Pharmaceutical Affairs

~Regulatory Science Initiative~

June 26, 2015

Ministry of Health, Labour and Welfare

3 Strategic Efforts for Each Field with a Clarified Priority
~Aiming for a More Effective Response~

Promote the Japanese Pharmacopoeia as a reference Pharmacopoeia in each Asian country.

Conclusion

- Along with the changes surrounding drugs, the weight and roles of Japanese Pharmacopoeia are changing.
- The Japanese Pharmacopeia also should catch up with current requirement.

→We should further enhance the Japanese Pharmacopeia based on Regulatory Science.