Regulatory Updates regarding Pediatric Drug Development in Japan

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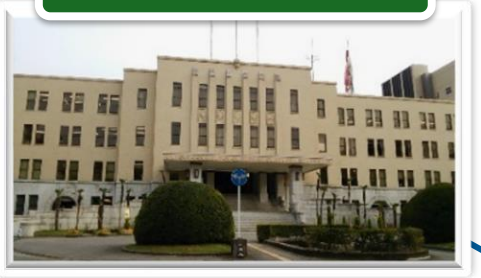
Pediatric Drugs Working Group

Pharmaceuticals and Medical Devices Agency

PMDA
Pharmaceuticals and Medical Devices Agency

Date of Establishment : April 2004

Hokuriku Branch



Kansai Branch

Major Responsibilities

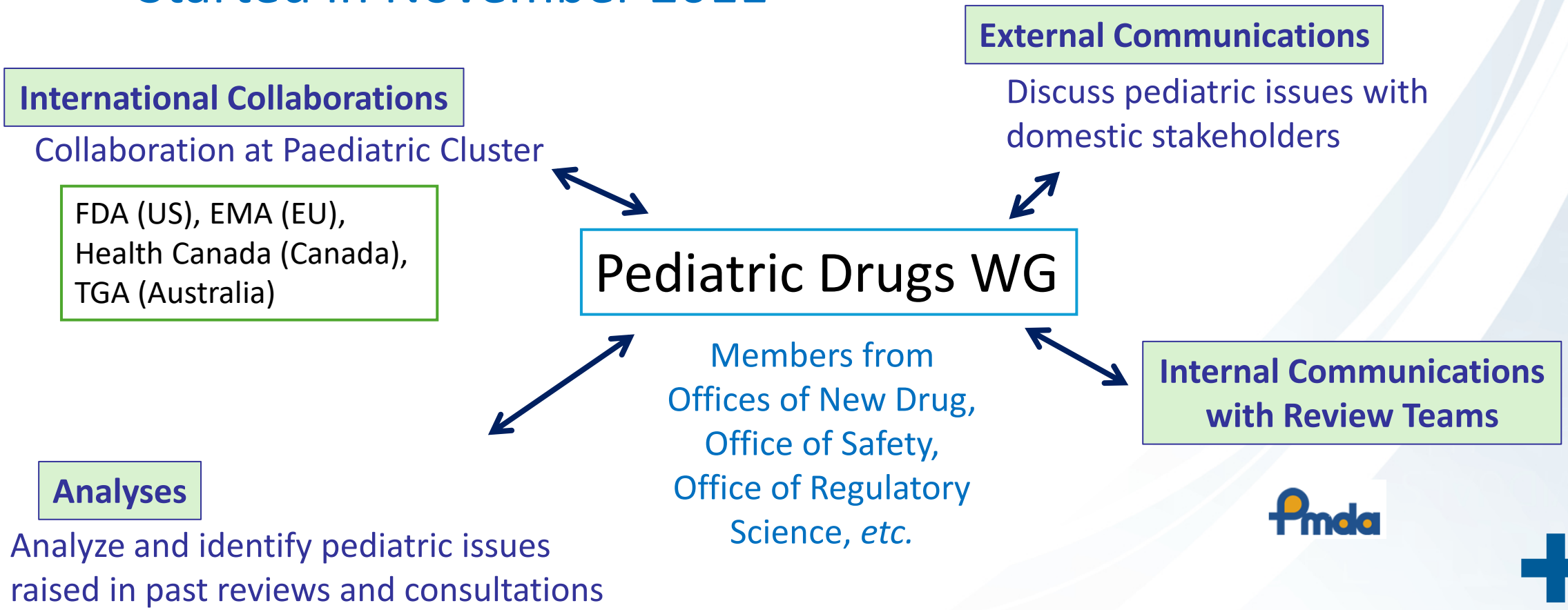
- Scientific Review for Drugs, Medical Devices and Regenerative Medical Products
- GCP, GMP Inspection
- Consultation on Clinical Trials
- Safety Measures
- Relief Services

Working in close relationship with Ministry of Health, Labor and Welfare (MHLW)

MHLW

PMDA Pediatric Drugs WG

- An across-office project team in the PMDA
- Started in November 2011



Regulatory-academic interaction

- **Expert Discussion:** Discussion with external experts on drug approval
  - During the review process, the PMDA reviewers exchange opinions with external experts to ensure that more effective reviews are conducted by making use of their advanced expertise.

- **Health and Labor Sciences Research:** Research to propose new review criteria for early commercialization of drugs for childhood cancer and rare diseases in children (2023-)
  - The MHLW and the PMDA cooperate with the Research Group

Pediatric Regulations In Japan

- There is no regulation mandating pediatric drug development.
- ICH-E11, ICH-E11(R1) and ICH-E11A
- Several frameworks to enhance pediatric drug development have been implemented so far.

Legislation

- Specific Use Drug Designation System

Incentives for companies

- Drug Price Premium for Pediatric Use (5~20%) (updated in 2024)
- Extension of re-examination period (revised in 2020)

Development facilitation

- Council for unapproved and off-label drugs with high medical needs
- Considerations for clinical evaluation of drugs in pediatric patients (10 or 12 years of age and older) who can be evaluated together with adults

Development support

- Pediatric clinical trial network, etc.

Regulatory Updates in Japan

- **New Approach to Enhance Pediatric Drug Development**
  - Planning of the Pediatric Drug Development Program during Development of Drugs for Adults

- **PMDA Regulatory Affairs Consultation Center dedicated to Pediatric and Orphan Drugs**
  - Consultation on Confirmation of the Pediatric Drug Development Program

Planning of the Pediatric Drug Development Program during Development of Drugs for Adults

Applied from April 1, 2024

PSB/PED Notification No.0112-3. dated January 12,2024, partially revised in March 29, 2024

https://www.pmda.go.jp/files/000268523.pdf (English translation by the PMDA)

- Encourage pharmaceutical companies to
  - prepare a pediatric drug development plan
  - confirm with the PMDA before submitting new drug application for adult use
  - proceed with the development without delay based on the prepared development plan
- Not only the implementation of clinical trials in Japanese children, but also using clinical data from adults and non-Japanese pediatrics, real-world data, and modeling & simulation, etc. should be considered and confirmed by the PMDA.

When pharmaceutical companies develop pediatric drugs in accordance with this new approach

Incentives related to the drug price

Consultation on Confirmation of the Pediatric Drug Development Program

Starts from July 1, 2024

- Dedicated to confirmation of the Pediatric Drug Development Program based on the new approach
- Consultation prerequisites
  - The pharmaceutical company is planning to conduct a pediatric clinical trial and has already conducted scientific consultation for adult indication with the PMDA regarding clinical trial design, etc..

    AND
  - The adult use is before filing an application for approval.
- Exceptions
  - Regarding the validity of the clinical trial design and the sufficiency of the application data package
  - Regarding pediatric drug development plan for drugs with different indications between adults and children
  - Regarding the utilization of real-world data, modeling & simulation, etc., without conducting pediatric clinical trials

Existing scientific consultation

Incentives related to the drug price

- **Enhanced evaluation of pediatric drugs**
  - The premium rate for drugs for pediatric use at the time of new listing, at the time of drug price revision, and at the time of application of repricing for market expansion shall be determined as follows: The premium rate shall be determined flexibly within the range currently specified, taking into account the recent development status of drugs, difficulty in conducting clinical trials due to the number of cases, etc. [Operational measures]

  - Products that have clear efficacy/effectiveness and dosage/administration for children and may be subject to evaluation with the pediatric premium shall be added to the product requirements for the price maintenance premium. [Revision of Standards]

Incentives related to the drug price

- **Evaluation on simultaneous development for adults and children** [Revision of standards]
  - If a development is conducted based on the development plan that has been confirmed by the PMDA and the pediatric indication is approved, the premium rate for pediatric use at the time of drug price listing, drug price revision and repricing for market expansion is highly evaluated.
- **Evaluation of companies working on pediatric development** [Revision of standards]
  - When repricing for market expansion is applied to the products under simultaneous development for adults and children, the same evaluation as the corrective premium for repricing for market expansion will be performed and the reduction rate will be reduced, even at the stage of development.

Summary and Future Perspectives

- The environment for pediatric drug development in Japan is improving through various efforts.
- It is expected that pediatric drug development will gain further momentum with the latest new approach and new initiatives in Japan.

Better medicines for children!