Provisional Translation (as of April 2025) *

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March 21, 2025

To (Noted elsewhere)

Pharmaceuticals and Medical Devices Agency
Director of Center for Product Evaluation
Director of Center for Regulatory Science
(Official seal omitted)

# Initiatives to Promote Pediatric Drug Development

There have been growing concerns about the expansion of "drug loss" in Japan, where pharmaceuticals approved in the Europe Union and the United States are not being developed for Japanese patients. This issue is particularly challenging for pediatric drugs and orphan drugs. The Pharmaceuticals and Medical Devices Agency (PMDA) established the Consultation Center for Pediatric and Orphan Drugs Development in July 2024 and started receiving applications of Consultation on Confirmation of Pediatric Drug Development Programs. Furthermore, as part of its cross-sectoral efforts in regulatory science, PMDA has consistently identified issues related to pediatric drug development and explored measures to facilitate pediatric drug development from the early stages of drug development for adults.

As part of its initiatives to promote pediatric drug development, PMDA has decided to provide essential advice and guidance based on a comprehensive understanding of the overall drug development plan, including the pediatric drug development plan, during its clinical trial consultations and other services. This decision follows discussions led by the Project Team for Addressing Inquiries Related to Pediatric Development Status, a cross-sectoral project team focused on regulatory science. We have summarized the basic principles and important considerations regarding the development of pediatric drugs in the attached document. We ask for your cooperation in disseminating this information to relevant businesses and organizations within your jurisdiction.

The Summary of Discussions on Revision of the Pharmaceutical and Medical Device

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* This English version of the Japanese Notification is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

Act and Related Regulations (issued by the Pharmaceutical and Medical Device Regulatory Subcommittee of the Health Sciences Council, Ministry of Health, Labour and Welfare, on January 10, 2025) outlined a policy to address the need for further promotion of pediatric drug development and resolution of drug loss. This policy stipulates that applicants for marketing authorization of drugs with new active ingredients or new indications for adult use should be obligated to make efforts for planning of pediatric drug development program. In the future, if there are revisions to the regulatory framework and operational practices for promoting pediatric drug development, resulting in changes to the basic principles regarding pediatric drug development, the basic principles and important considerations outlined in the attached document may also be subject to revision.

Attachment

# Initiatives to Promote Pediatric Drug Development

## 1. Background and Purpose

There have been growing concerns about the expansion of "drug loss" in Japan, where pharmaceuticals approved in the Europe Union (EU) and the United States (U.S.) are not being developed for Japanese patients. This issue is challenging for pediatric drugs.

In the U.S. and the EU, pediatric drug development is mandatory. Pharmaceutical companies and other developers are required to submit a pediatric drug development plan to regulatory authorities at an early stage of development for drugs with new active ingredients or new indications for adults (after completion of Phase II studies in the U.S. and after completion of Phase I studies in the EU). Furthermore, when submitting a marketing authorization application for an adult drug, the applicant must include the pediatric drug development plan that has been agreed upon with the regulatory authorities in the dossier. In contrast to the U.S. and the EU, pediatric drug development is not currently a regulatory requirement in Japan. Consequently, there are few instances where a pediatric drug development plan with the same indications as an adult drug has been agreed upon with the Pharmaceuticals and Medical Devices Agency (PMDA) by the time of the submission of a marketing authorization application for the adult drug. Moreover, it is not uncommon for clinical trials in pediatric populations to have already been completed or to be ongoing overseas by the time a development plan for the pediatric drug in Japan is presented to PMDA.

To advance pediatric drug development in Japan without lagging behind other countries, PMDA considers it crucial to understand the comprehensive drug development plan, including pediatric drug development, from the early stages of adult drug development. When necessary, PMDA should encourage pharmaceutical companies and other developers to pursue pediatric drug development in Japan. Therefore, as part of its initiatives to promote pediatric drug development, PMDA will implement the following approach during clinical trial consultations for adult drugs: When the drug under development is expected to be used in children for the diseases and conditions targeted in adult drug development, PMDA will actively verify the status of pediatric drug development both domestically and internationally. This aims to encourage the initiation of pediatric drug development in Japan without lagging behind other countries. Furthermore, during clinical trial consultations for adult drug development, if requested by the applicant, PMDA will confirm the pediatric drug development plan based on Planning of Pediatric Drug Development Programs during Development of Drugs for Adults (PSB/PED Notification No. 0112-3 issued by the Director of the Pharmaceutical

Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare, dated January 12, 2024, partially revised on March 29, 2024; hereinafter referred to as the "2024 Notification").

This document outlines PMDA's basic principles on pediatric drug development and important considerations to be taken into account during clinical trial consultations for adult drug development.

## 2. Basic Principles

To advance pediatric drug development without lagging behind adult drug development and considering the status of pediatric drug development both in Japan and overseas, it is crucial in Japan to formulate comprehensive development plans that include pediatric drug development and to proceed with consideration of pediatric drug development plans from the early stages of adult drug development. Considering the approach in the U.S. and the EU, where pediatric drug development plans are formulated during adult drug development, it is desirable to plan pediatric drug development programs that assume Japan's participation in Multi-regional clinical trials from the stage when pediatric clinical trials are planned in the U.S. and the EU, unless clear differences in intrinsic or extrinsic ethnic factors are confirmed or anticipated. When the development of a pediatric dosage form is necessary, it is appropriate to advance this development in time for the marketing authorization application for the addition of pediatric dosage and administration.

Based on these principles, PMDA will, during clinical trial consultations for adult drug development, actively verify the status of pediatric drug development and provide advice or guidance as necessary to ensure that pediatric drug development in Japan is initiated without lagging behind adult drug development. Through these efforts, PMDA will encourage applicants to pursue pediatric drug development in Japan.

## 3. Considerations during Clinical Trial Consultations for Adult Drug Development

In accordance with the basic principles outlined in Section 2 above, applicants for clinical trial consultations regarding Phase II (Proof of Concept studies) or later stages of adult drug development should take note of the following points:

- In the consultation briefing document, applicants should indicate whether pediatric drug development programs exist in Japan and overseas at the time of consultation. It is desirable to include, as much as possible, the information specified in the Implementation Guidelines for the Consultation on Confirmation

of Pediatric Drug Development Programs. In cases where the drug development program includes pediatric subjects who can be evaluated alongside adults, applicants should describe the overall pediatric drug development plan. This description should include whether there are development plans for pediatric age groups for which drug development is deemed necessary, in addition to the development program for the specific pediatric population being evaluated with adults. If the consultation briefing document does not include information on the existence of pediatric drug development plans in Japan and overseas, PMDA may, as necessary, inquire about these plans through additional questions.

- If an applicant for clinical trial consultation regarding adult drug development wishes to have their pediatric drug development plan confirmed based on the 2024 Notification, they should include "Confirmation of Pediatric Drug Development Plan" as a consultation item, and in the consultation briefing document, provide the necessary information as specified in the Implementation Guidelines for the Consultation on Confirmation of Pediatric Drug Development Programs, such as the specific pediatric drug development plan for Japan, along with a statement requesting confirmation of the pediatric drug development plan based on the 2024 Notification. In this case, the scope of the development plan confirmation based on the 2024 Notification, conducted during the clinical trial consultation, will be limited to what is covered under the Consultation on Confirmation of Pediatric Drug Development Programs service. Only when the aforementioned steps are taken, PMDA will confirm their pediatric drug development plan based on the 2024 Notification during the ongoing clinical trial consultation regarding adult drug development.

## 4. Other

If an applicant wishes to consult PMDA regarding the appropriateness of study designs for pediatric drug development or the adequacy of the clinical data package for pediatric populations, they should separately utilize other clinical trial consultation services, such as the consultation after completion of Phase II studies for drugs.

## 5. References

1) Planning of Pediatric Drug Development Programs during Development of Drugs for Adults (PSB/PED Notification No. 0112-3 by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare, dated January 12, 2024)

2) Partial revision of Planning of Pediatric Drug Development Programs during Development of Drugs for Adults (PSB/PED Notification No. 0329-1 by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare, dated March 29, 2024)
3) Q & A for Planning of Pediatric Drug Development Programs during Development of Drugs for Adults (Administrative Notice of the Pharmaceutical Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare, dated March 29, 2024)