10 Drug Development—Japan

By Monique Carter, MS, RAC

Introduction

The Ministry of Health, Labour and Welfare (MHLW), commonly known as Kōrō-shō in Japanese, is the cabinet-level governmental branch that oversees pharmaceutical drug development policy and makes the final decision on product marketing in Japan.[1] In conjunction with the MHLW, the Pharmaceutical and Medical Device Agency (PMDA) conducts scientific reviews of pharmaceutical marketing authorization applications, including benefit-risk assessments of the quality, efficacy, and safety of products across the development continuum, from preclinical to risk mitigation in the post-marketing setting. PMDA also is responsible for good clinical practice (GCP) inspections, good manufacturing practice (GMP) inspections, clinical trial consultation, and relief services for health damage caused by risk factors.[2]

The MHLW and PMDA requirements for approval based on the quality, efficacy, and safety of pharmaceuticals, quasi-pharmaceutical products, cosmetics, medical devices, and regenerative medicine products is regulated under Article 1 of the *Pharmaceutical and Medical Devices* (*PMD*) *Act*.[3] This is the region-specific legislation that mandates plans for the development of adult pharmaceuticals in Japan. Conversely, there are no laws or regulations established for pediatric drug development in Japan.[4] **Table 10-1** provides a comparison of Japan, US, and EU pediatric development regulations.

History

There is currently no planned date for issuance of Japan-specific pediatric legislation. Per PMDA, the lack of pediatric study feasibility is a priority that must be considered prior to implementation of any regulation.[5] Appropriately sized pediatric domestic studies leading to the needed level of evidence is often difficult to perform in Japan due to the number of children in the region ranging from ages 0–14 years.[6] However, there are a number of ongoing key initiatives supporting pediatric development in Japan. **Table 10-2** provides a timeline of key initiatives supporting pediatric development in Japan. As a founding member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), since December 2000, Japan has recognized ICH E11 *Guideline on Clinical Investigation of Medicinal Products in the Pediatric Population*.[7] The original guidance was published and issued in Japan as Notification No. 1334 of the Evaluation and Licensing Division. This guidance provides an outline of critical issues in pediatric drug development and approaches to the safe, efficient, and ethical study of medicinal products in the pediatric population.[8] It was later amended (ICH E11 (R1)) in 2017 to complement and provide clarification and current regulatory perspective on scientific advancements relevant to pediatric populations and drug development.[9]

In February 2010, the Unapproved Drugs/Indications Scheme and study group were established. The scheme objective is to improve

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Table 10-1. Comparison of Japan, US, and EU Pediatric Development Regulations

	Japan	US	EU
Regulations	None	• PREA[a] • RACE[b] • BPCA[c]	Mandatory • Pediatric Regulation (2007) • Regulation EC (1901/2006)
Regulatory Obligations	None	• PSP must be submitted by the end of a Phase II study for adults (*PREA*) • WR by FDA conducting a clinical trial for drug development (optional)	• Pediatric investigation by the end of a Phase I study in adults • PIP submitted prior to completion of human adult PK studies

Notes: Pediatric investigation plan (PIP), pharmacokinetic (PK), pediatric study plan (PSP), written request (WR)

a. *Pediatric Research Equity Act (PREA)* of 2003 amended the *Federal Food, Drug, and Cosmetic Act* to require license applications for new drugs and biological products to assess such drug's or product's safety and effectiveness for relevant pediatric subpopulations, including dosage.
b. *Research to Accelerate Cures and Equity for Children Act (RACE)* of 2017 amended the *Federal Food, Drug, and Cosmetic Act* to require sponsors of certain drugs and biological products for adult cancer to assess the use of their medications in pediatric populations.
c. *Best Pharmaceuticals for Children Act (BPCA)* of 2002 provides an incentive of additional marketing exclusivity to sponsors who voluntarily complete pediatric clinical studies outlined in a written request issued by FDA.

access through expedited development of highly needed drugs or drugs with new indications/dosages, including pediatric use, not yet approved in Japan but already approved and widely used in at least one of six western countries. These countries include Australia, Canada, France, Germany, the UK, and the US.[10]

Under this scheme, pharmaceutical sponsors receive requests to develop or submit a Japan new drug application (JNDA) for designated drugs and/or indications. Once submitted, PMDA conducts an accelerated fast track JNDA review. The agency can waive the requirement for additional region-specific studies, if deemed acceptable. **Figure 10-1** provides Japan's unapproved drug scheme workflow. Public knowledge can serve as the basis for approval. The following are examples of public knowledge that can be considered:

- Clinical data submitted to support drug approval in one of the six aforementioned countries and (off-label) clinical use.
- Literature (major medical textbooks or guidance documents) to support usage of the drug.[11]

In November 2011, PMDA established the Pediatric Drugs Working Group.[12] As of 2014, it was composed of 18 PMDA members, including pediatricians, physicians, and pharmacists from the Office of New Drugs and Office of Safety. The objective of the group is to promote efforts to encourage the pharmaceutical industry and clinical investigators to develop medicinal products for children. PMDA collaborates with foreign regulatory agencies, including US FDA, EU EMA, Health Canada (HC), and Australia's Therapeutics Goods Administration (TGA), to discuss issues raised in precedented drug data package reviews to establish more appropriate strategies. Views and positions are then shared internally within PMDA and exchanged externally with domestic stakeholders (e.g., medical institutions, industry groups).[13] **Figure 10-2** outlines Japan's pediatric drugs working group stakeholder and process overview.

In July 2011, PMDA launched the Pharmaceutical Affairs Consultation on Research and Development (R&D) Strategy.[14] It is focused on promising "seed-stage" research or technologies to achieve realization of innovative drugs, medical devices, and cellular and tissue-based products being developed by universities, research institutions, and start-up companies. Advice is provided on quality, nonclinical, and clinical challenges that arise in earlier stages of development.[15] Although the initiative is not solely focused on pediatrics, one of its key goals is to help stakeholders understand and appreciate pediatric-specific issues

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Table 10-2. Timeline of Key Initiatives Supporting Pediatric Development in Japan

Initiative/Guidance	Year
ICH E11 Pediatric Guidance adopted	2000
Council for Unapproved Drugs/ Indications Scheme	2010
PMDA Pediatric Drugs Working Group	2011
Pharmaceutical Affairs Consultation on R&D Strategy	2011

and approaches to potentially support increased pediatric development opportunities.

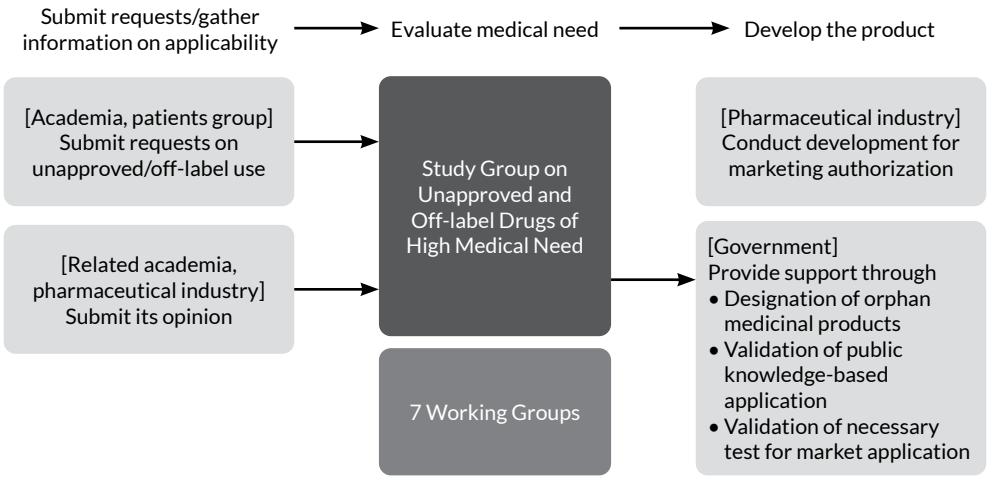
Benefits

Unlike other major region regulatory bodies, Japan has implemented sponsor incentives to improve pediatric drug development. **Table 10-3** provides a timeline of key Japan pediatric development incentives. Two key incentives include extending the re-examination period and providing premium reimbursement pricing associated with approved pediatric indications.

In Japan, the re-examination period is a unique market exclusivity and data protection system that serves as an incentive for drug development sponsors. The system applies to new chemical entities and drugs previously approved for new clinical indications. Japanese regulators re-examine the safety and efficacy of drugs following approval in view of the data collected during the re-examination period.[16,17] The re-examination period can range from four to 10 years after drug approval. The data submitted during the period is not available to generic drug manufacturers. The re-examination period mandate for pediatric drug development is outlined in the Pharmaceutical and Medical Safety Bureau (PMSB) Notification No. 1324 "Concerning Enforcement of the Partial Revision of the Ministerial Ordinance relating to Good Post-Marketing Surveillance Practice and Review of Post-Marketing Surveillance for Drug Review" dated 27 December 2000. The re-examination period can be extended to 10 years if a clinical trial is planned to study pediatric dosage during or after marketing authorization application of a drug.[18]

An additional incentive for pediatric drug development in Japan is that a premium rate is added to the reimbursement drug price for approved products with pediatric dosage indications that describe use in the entire pediatric patient population or specific age subsets.[19] This

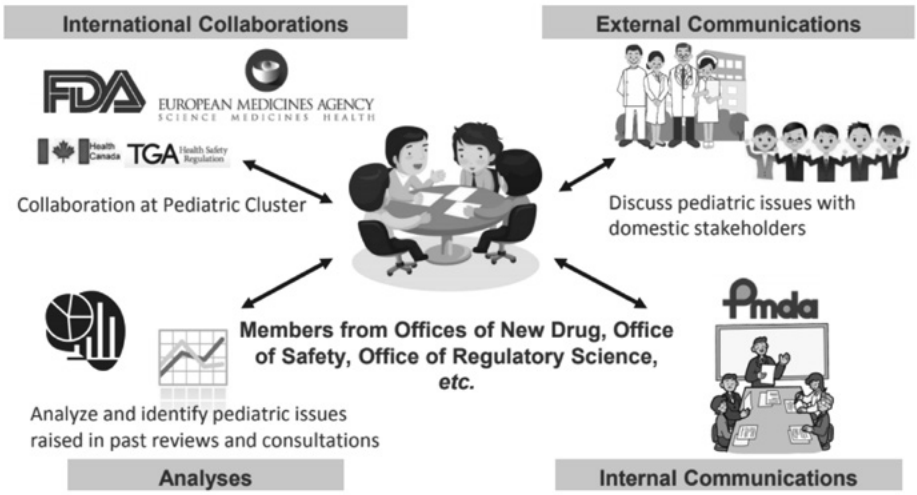
Figure 10-1. Japan Unapproved Drug Scheme Workflow



Source: Hirata M. Pediatric Drug Development in Japan and International Regulatory Collaboration. 14th DIA Japan Annual Meeting 2017.

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Figure 10-2. Pediatric Drugs Working Group Stakeholder and Process Overview



Source: Hirata M. Pediatric Drug Development in Japan and International Regulatory Collaboration. 14th DIA Japan Annual Meeting 2017.

premium can range from 5% to 20%.[20] The rate is decided by Chuikyo, Japan's Central Social Insurance Medical Council, which is an MHLW advisory body.[21]

Clinical Trial Application/Marketing Authorization Application

In Japan, the same regulatory standards (quality, safety, and efficacy) for adult products apply to clinical trial and marketing authorization applications for pediatric products.

Conclusion

There are no region-specific pediatric regulations or legislation in Japan. MHLW and PMDA have established many different initiatives and sponsor incentives to improve conditions for pediatric drug development. Japan regulators continue to actively collaborate with their counterparts in other major regions to further understand how to address pediatric clinical study feasibility concerns, implementation of innovative clinical trial tool use, and regulatory reform framework intricacies.

Table 10-3. Timeline of Key Japan Pediatric Development Incentives

Incentive	Year
Notification for extension of re-examination period for pediatric development	2000
Premium price for approved products with additional pediatric indications	2006

References

1. Sato D. PMDA ACTO Satellite symposium. Japanese regulation of regenerative medicine. PMDA website. https://www.pmda.go.jp/files/000199507.pdf. Accessed 25 August 2021.
2. Ibid.
3. Regulatory Information Task Force. Japan Pharmaceutical Manufacturers Association. Information of Japanese Regulatory Affairs. 2020. JPMA website. http://www.jpma.or.jp/english/parj/pdf/2020.pdf. Accessed 25 August 2021.
4. Ibid.
5. Ishikawa M. PMDA's Experiences and Challenges in Pediatric Drug Development. PMDA website. https://www.pmda.go.jp/files/000205910.pdf. Accessed 25 August 2021.
6. Ibid.

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7. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. Addendum to ICH E11: *Clinical Investigation of Medicinal Products in the Pediatric Population E11 (R1)*. ICH website. https://database.ich.oarg/sites/default/files/E11_R1_Addendum.pdf. Accessed 25 August 2021.
8. Medicinal product. EMA website. https://www.ema.europa.eu/en/glossary/medicinal-product. Accessed 25 August 2021.
9. Op cit 7.
10. Hirata M. Pediatric Drug Development in Japan and International Regulatory Collaboration. 14th DIA Japan Annual Meeting 2017. PMDA website. https://www.pmda.go.jp/files/000224497.pdf#:~:text=Re-examination%20Period%20%28market%20exclusivity%20and%20data%20protection%29%20of,per%20the%20necessary%20time%20to%20conduct%20appropriate%20study. Accessed 25 August 2021.
11. Ibid.
12. Op cit 5.
13. Ibid.
14. Baum V, Bax R, Heon D, et al. Pediatric Drug Regulation: International Perspectives. *Pediatric Anesthesia*. 1039;29:572-582.
15. Ibid.
16. Op cit 5.
17. Op cit 10.
18. Op cit 14.
19. Op cit 14.
20. Ibid.
21. Pacific Bridge Medical. Japan to increase drug price rates for innovative products. Pacific Bridge Medical website. https://www.pacificbridgemedical.com/news-brief/japan-to-increase-drug-price-rates-for-innovative-products/. Accessed 25 August 2021.

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11 Regulations—Australia and New Zealand

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Introduction

This chapter provides an overview on the regulation of pediatric medicines and medical devices in Australia and New Zealand. In addition to describing the legal framework governing medicines and medical devices for children, the chapter also summarizes pediatric labeling and market access issues.

Background

In spite of many pediatric medicine initiatives through professional and government advisory bodies, formal legislative and regulatory reforms addressing pediatric medicines are still missing in Australia and New Zealand.

Providing children with better access to safe and effective medicines to address their therapeutic needs has been widely recognized, yet a true regulatory framework has not been established. However, regulators in both countries have found efficient ways of addressing unmet pediatric development needs within the existing regulatory framework, which will be further discussed in the following sections.

Regulation of Pediatric Medicines in Australia

Legal Framework

Pediatric medicines in Australia are regulated within the general framework of the *Therapeutic Goods Act 1989*, as amended, and the *Therapeutic Goods Regulations 1990*, as amended.

In contrast to the EU and the US, there is no statutory requirement for a sponsor of a marketing authorization application to gain agreement with the Australian Therapeutic Goods Administration (TGA) on a dedicated pediatric investigation plan as a prerequisite for marketing authorization.

However, in line with International Conference of Harmonisation (ICH) Harmonised Guideline M4E(R2) Efficacy adopted by TGA,[1] efficacy and safety in the pediatric population should be routinely analyzed in applications for a proposed adult indication that also occurs in children. Thus, TGA will by default assess whether a new medicine is likely to be used in children and whether the dosage form(s) proposed are age-appropriate for the pediatric population.

Information related to pediatrics should be provided in all Category 1 comparable overseas regulators (CORs)-based applications to register:[2]

- New chemical entities
- New combinations
- Extensions of indications
- Major variations

TGA may deny or delay approval if pediatric data is not included in a marketing authorization application for a new medicine where it is deemed appropriate. Thus, it is recommended

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