17th DIA Japan Annual Meeting 2020

- Beyond Innovation -

November 8-10, 2020 | ※ Virtual Event

Review of Pharmaceutical Products for Children

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Agenda

- Regulations for pediatric drug development
- Present situation of pediatric drug development in Japan
- Challenges to promote pediatric drug development in Japan
- Current topics

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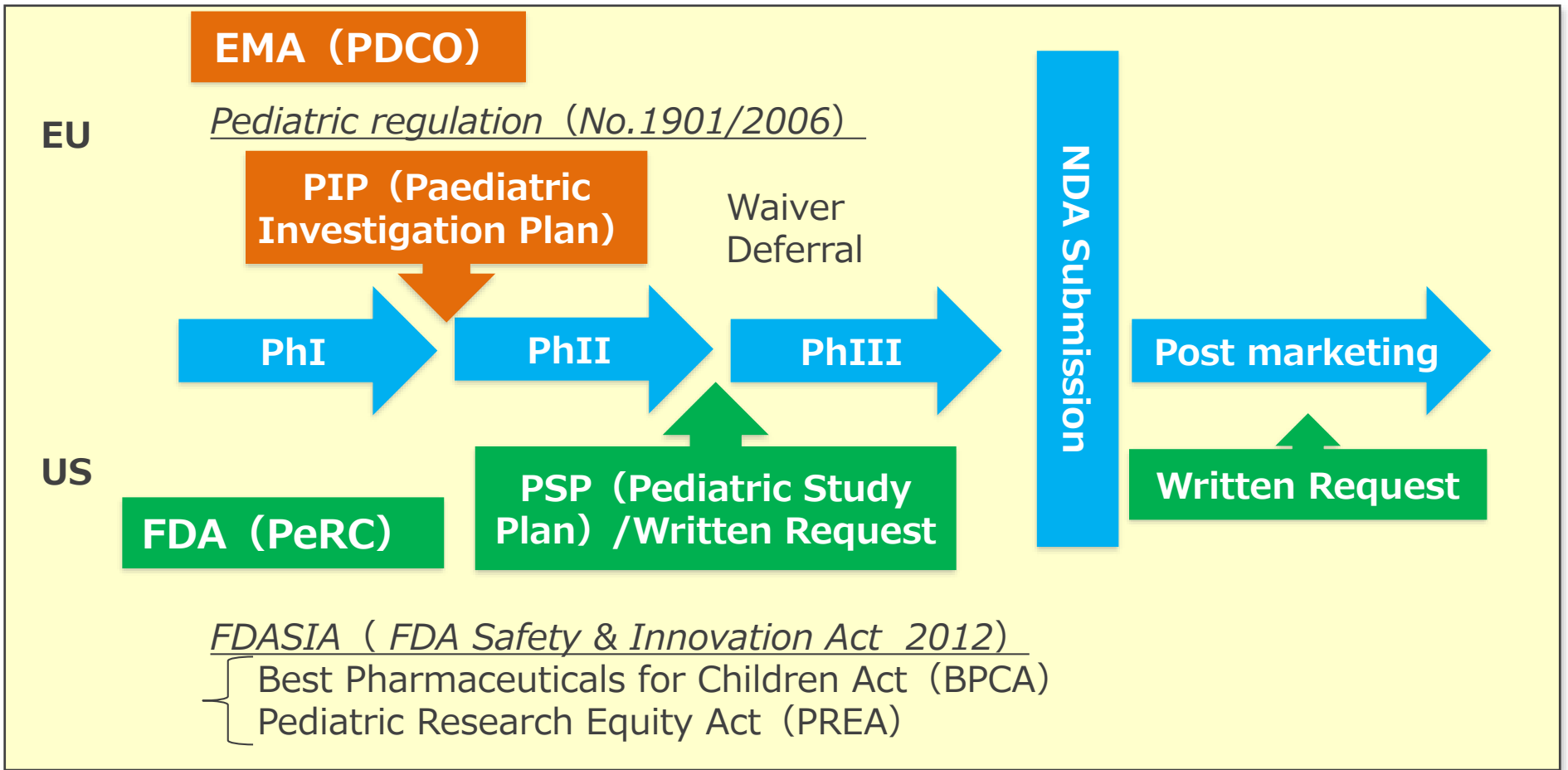
Pediatric regulation in EU and the US

- Pediatric drug development is required by law and is considered in the process of adult drug development.



In Japan…

- There are no laws or regulations that require pediatric drug development.

Incentives and initiatives to promote pediatric drug development in Japan

- Extension of re-examination period
- Drug reimbursement premium
- Evaluation Committee on Unapproved or Off-labelled Drugs with High Medical Needs
- Pediatric Clinical Trials Network

etc.

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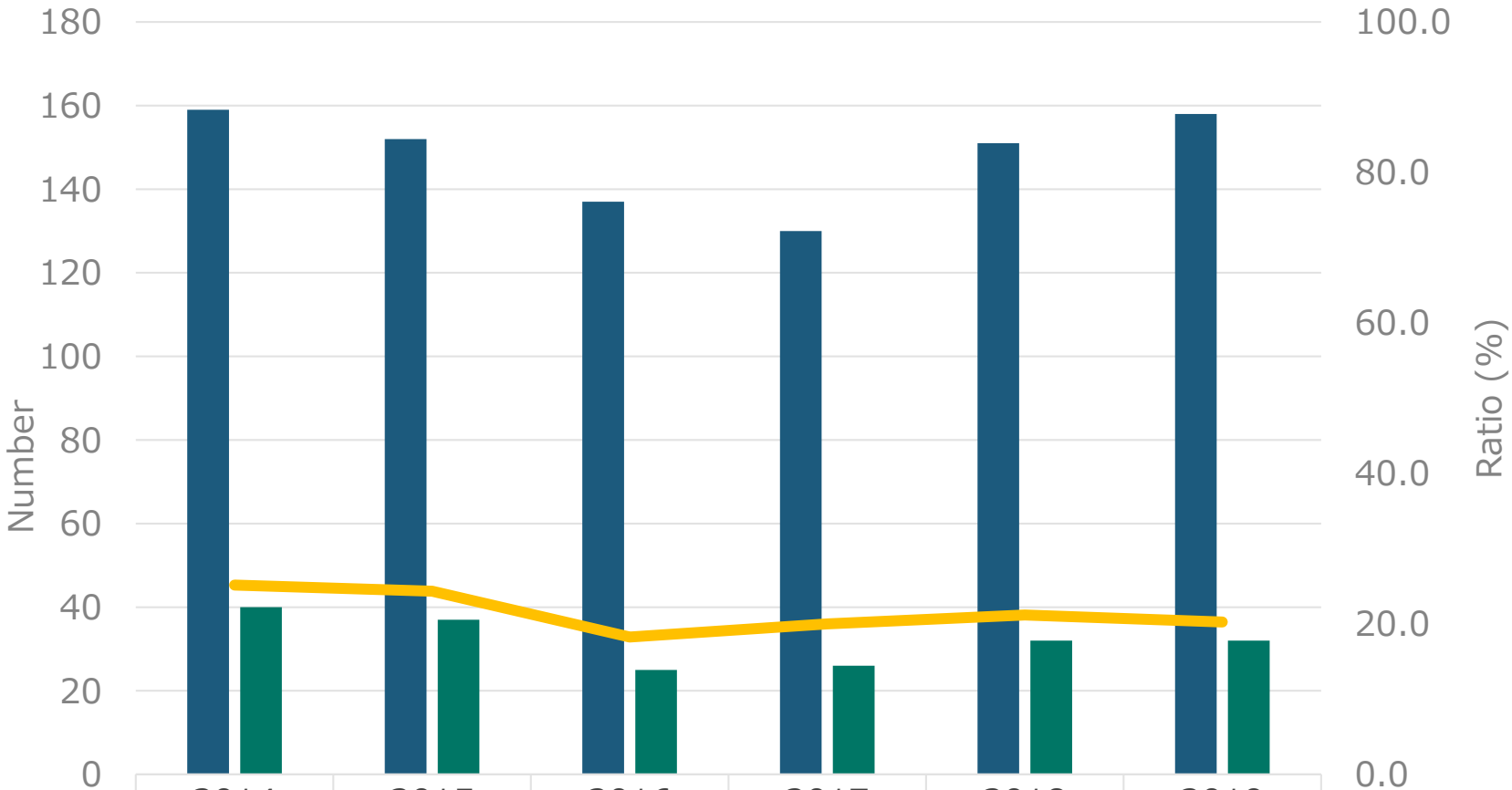
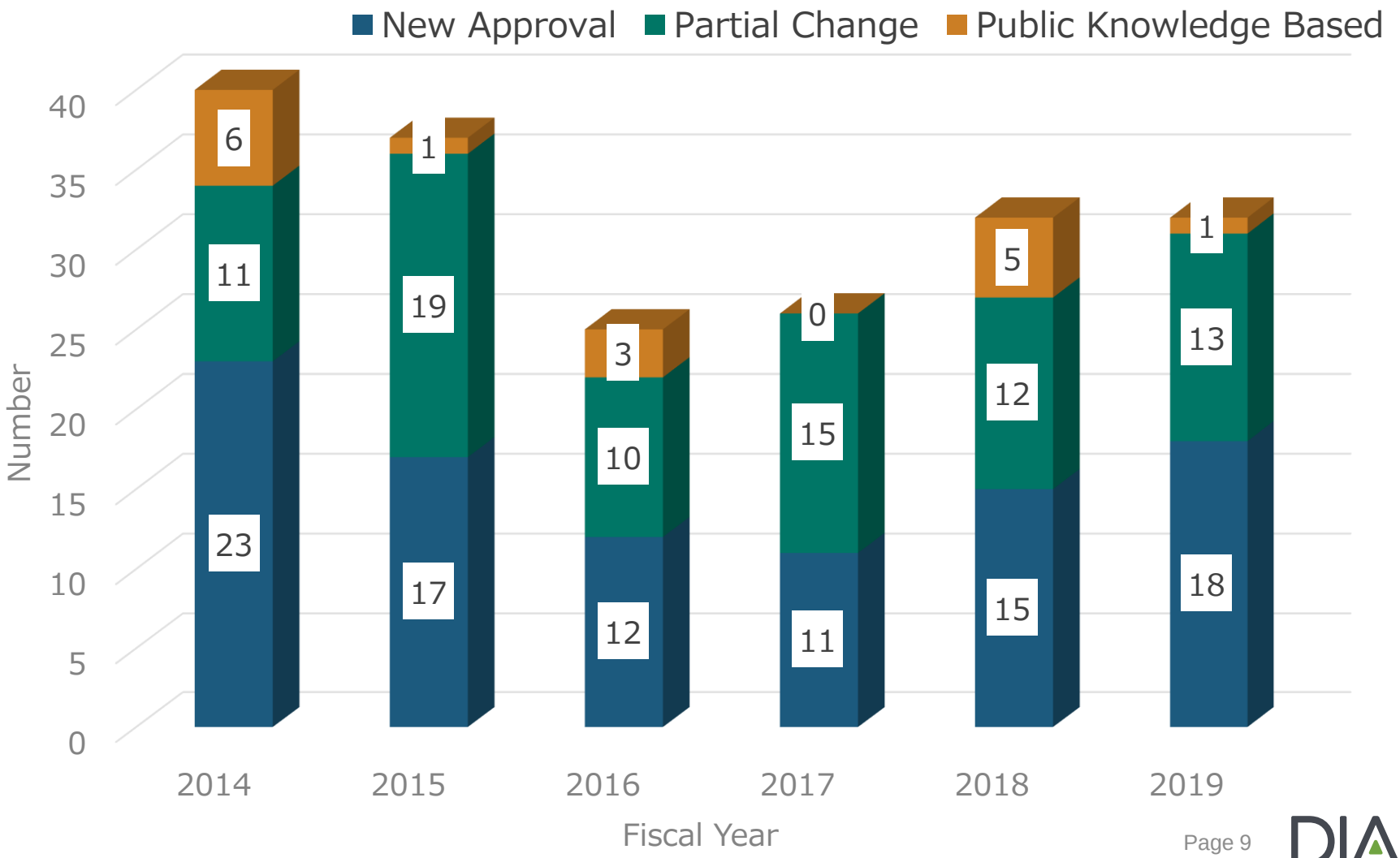
Recent new drug approvals for pediatrics in Japan (2014-2019)



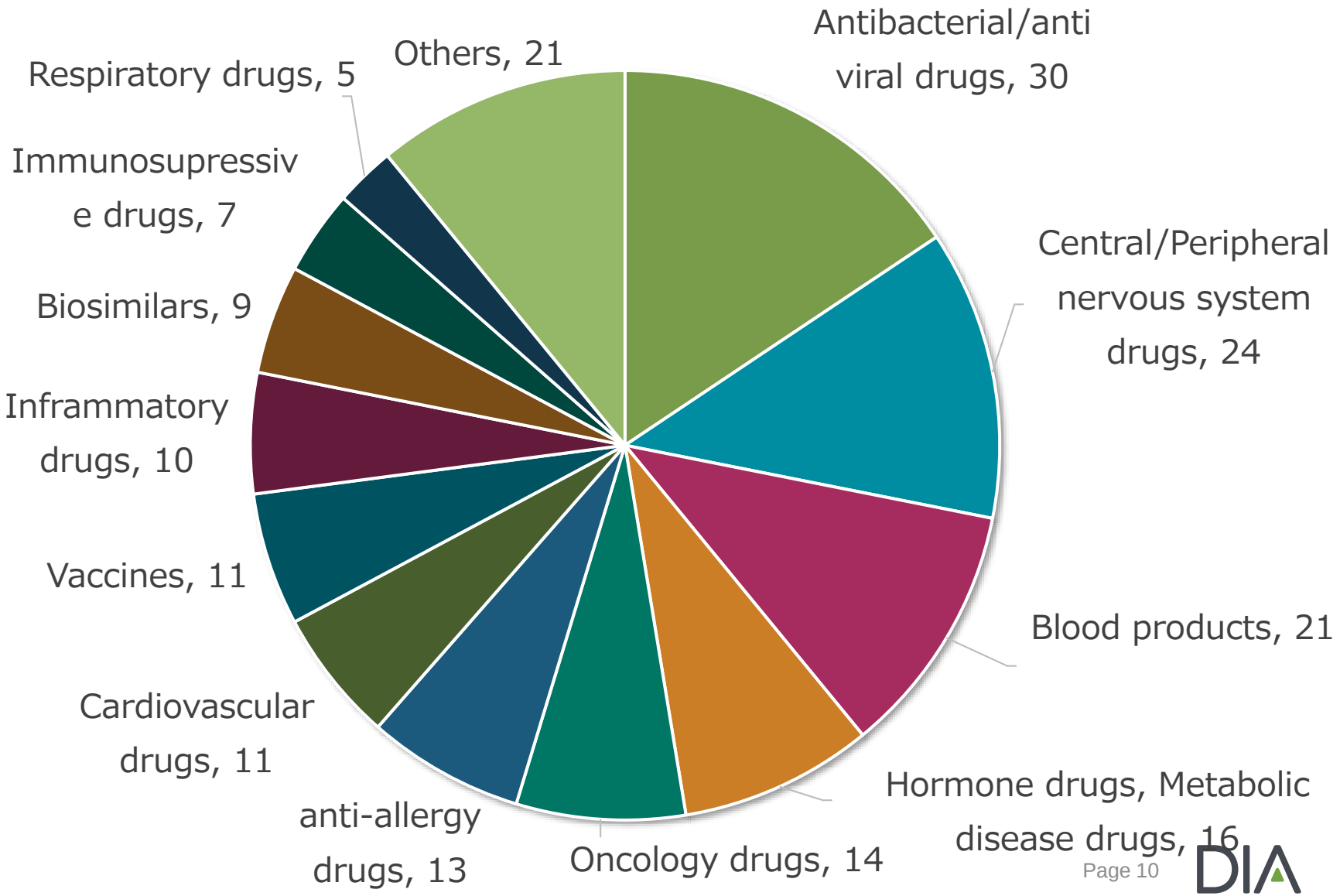
Fiscal year	2014	2015	2016	2017	2018	2019
Total	159	152	137	130	151	158
Padiatric	40	37	25	26	32	32
Ratio (%)	25.2	24.3	18.2	20.0	21.2	20.3

https://www.pmda.go.jp/review-services/drug-reviews/review-information/p-drugs/0010.html

Basis of pediatric approvals (2014-2019)



Pediatric approvals by indication (2014-2019)



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Pediatric Drugs WG in PMDA

International Collaborations

FDA, EMA, Health Canada and TGA

Collaboration at Pediatric Cluster

External Communications

Discuss pediatric issues with domestic stakeholders

Members from Offices of New Drug, Office of Safety, Office of Regulatory Science.

Analyze and identify pediatric issues raised in past reviews and consultations

Analyses

Internal Communications

PMDA initiatives to enhance pediatric drug development

- Regulatory Science research
  - Examination of utilization of PK-PD and M&S for pediatric dosage setting (FY2012-2015)
  - Research on the preparation of guideline related to the utiliz
    drugs an
    intractab
  - Researc
    the deve
    medica
    FY2017-

- Guideline on Population Pharmacokinetic and Pharmacodynamic Analysis, May 15, 2019
- Guideline for Exposure-Response Analysis of Drugs, June 8, 2020
- Guidelines for Analysis Reports Involving Physiologically based Pharmacokinetic Models(draft), Sep 18, 2019

- Considerations for Clinical Evaluation of Drugs in Pediatric Patients (10 or 12 years of age and older) Who can be Evaluated Together with Adults (→described later)

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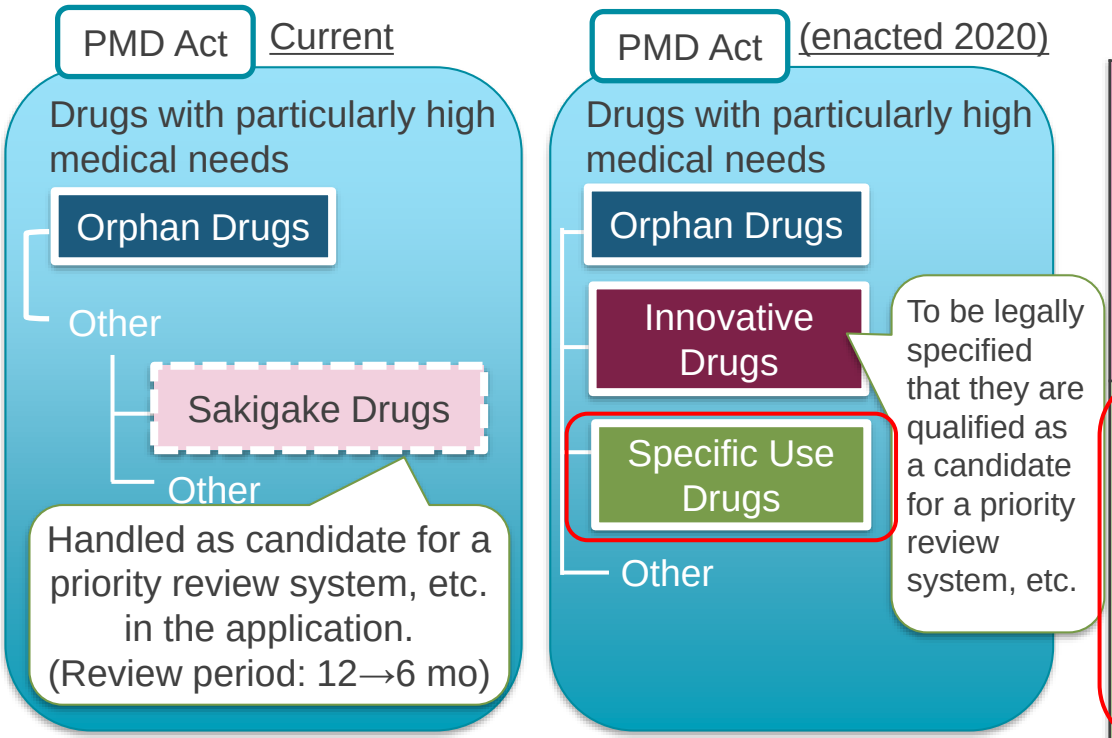
Legislation of "Sakigake Designation System" and "Specific Use Drug Designation system"

○ A system to designate drugs/medical devices/regenerative medical products whose action mechanisms are clearly different form those approved in Japan/other countries as "**innovative drugs**" shall be defined by law, and the designated products shall be clearly qualified by law to be a candidate for a priority review system, etc.

○ A system to designate drugs addressing significant unmet medical needs such as drugs with no indication for pediatric patients as "**specific use drugs**" shall be defined by law, and the designated products shall be clearly qualified by law to be a candidate for a priority review system, etc.

○ It shall be legally stipulated that specific use drugs (limited to those for the small number of patients) are eligible for tax benefits and subsidies to promote development as well as existing orphan drugs.

(*) Tax benefits have already been included in the 2019 tax reform plan.



Designation requirements

Innovative drugs	1. Having clearly different action mechanisms from products approved in Japan/other countries. 2. Markedly useful in that particular use. ➢ Assuming the same drugs for the current "Sakigake designation system".
Specific use drugs	1. Being used for the treatment of specific diseases (*). * • Being used to treat pediatric diseases but dosage and administration for children not stipulated. • Infectious diseases caused by drug-resistant bacteria, etc. 2. The need for specific use drugs is significantly unmet. 3. Markedly useful in that specific use.

Specific Use Drugs

薬生薬審発 0831 第５号
令 和 ２ 年 ８ 月 31 日

各都道府県衛生主管部（局）長　殿

厚生労働省医薬・生活衛生局医薬品審査管理課長
（　公　印　省　略　）

特定用途医薬品の指定に関する取扱いについて

医薬品、医療機器等の品質、有効性及び安全性の確保等に関する法律の一部を改正する法律（令和元年法律第 63 号。以下「改正法」という。）が令和元年 12 月４日に公布され、小児に対する用法又は用量が設定されていないなど、医療上のニーズが著しく充足されていない医薬品の研究開発の促進に寄与することを目的として、特定用途医薬品の指定制度が創設されました。改正法による改正後の医薬品、医療機器等の品質、有効性及び安全性の確保等に関する法律（昭和 35 年法律第 145 号。以下「法」という。）第 77 条の２第３項に規定する特定用途医薬品の指定について下記のとおり取り扱うこととしましたので、御了知の上、貴管内関係団体、関係機関等に周知いただきますよう御配慮願います。

Drugs which are intended for use in the diagnosis, treatment or prevention of disease in children and satisfying all of the following requirements.

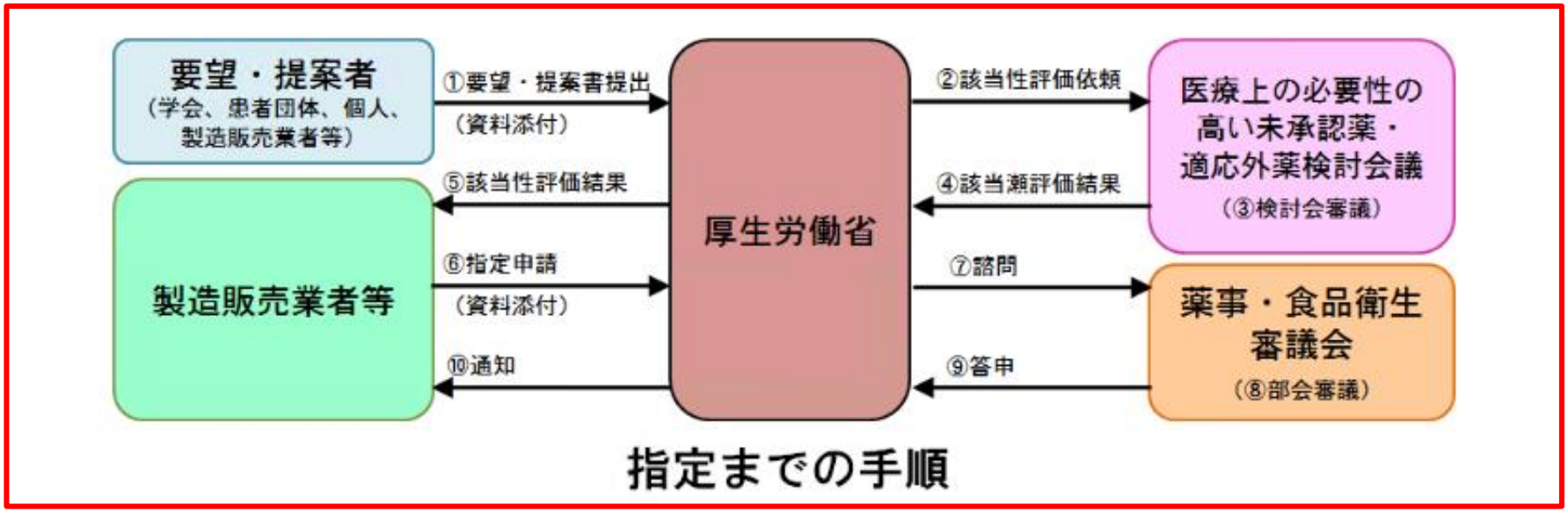
A To develop either (i) Change of dosage and administration or (ii) Additional dosage form.

B Significantly unmet medical needs ((i) No standard treatment or (ii) More medically useful than existing treatments)

C Particularly excellent utility value ((i) target disease is serious and (ii)established as standard therapy in guideline etc. or high evidence based on RCTs).

Process of Specific Use Drug Designation

- Applicability to Specific Use Drug will be evaluated at the Evaluation Committee on Unapproved or Off-labelled Drugs with High Medical Needs.
- Designation of Specific Use Drug will be deliberated at Pharmaceutical Affairs and Food Sanitation.



https://www.mhlw.go.jp/stf/newpage_12717.html

Extension of re-examination period (revision)

薬生薬審発 0831 第 16 号
令 和 2 年 8 月 31 日

各都道府県衛生主管部（局）長 殿

厚生労働省医薬・生活衛生局医薬品審査管理課長
（ 公 印 省 略 ）

再審査期間の取扱いについて

医療用医薬品の再審査期間の取扱いについては、「薬事法及び医薬品副作用被害救済・研究振興基金法の一部を改正する法律の施行について」（平成５年８月25日付け薬発第725号厚生省薬務局長通知。以下「平成５年局長通知」という。）、「薬事法及び医薬品副作用被害救済・研究振興基金法の一部を改正する法律の施行について」（平成５年10月１日付け薬新薬第92号厚生省薬務局新医薬品課長、医療機器開発課長、安全課長通知。以下「連名課長通知」という。）、「医薬品の市販後調査の基準に関する省令の一部を改正する省令の施行及び医薬品の再審査に係る市販後調査の見直しについて」（平成 12 年 12 月 27 日付け医薬発第 1324 号厚生省医薬安全局長通知。以下「平成 12 年局長通知」という。）、「医薬品の再審査期間の取り扱いについて」（平成 12 年 12 月 27 日付け医薬審第 1813 号厚生省医薬安全局審査管理課長通知。以下「課長通知」という。）及び「新有効成分含有医薬品の再審査期間について」（平成 19 年４月１日付け薬食発第 0401001 号厚生労働省医薬食品局長通知）で示してきたところである。

今般、医薬品、医療機器等の品質、有効性及び安全性の確保等に関する法律等の一部を改正する法律（令和元年法律第 63 号。以下「改正法」という。）により、特定用途医薬品指定制度が明文化されたこと等に伴い、「医療用医薬品の再審査期間について」（令和２年８月 31 日付け薬生発 0831 第 11 号厚生労働省医薬・生活衛生局長通知）が発出されたところですが、再審査期間の取扱いの詳細については下記によることとしましたので、貴管下関係事業者に対し指導方御配慮願います。

なお、本通知は令和２年９月１日から施行します。

For drugs that were recognized to require clinical trials regarding the setting of dosage for pediatric patients at the time of approval, a development plan for pediatric dosage setting was submitted and planned by the end of the approval review, and the planned clinical trials were started without delay. In that case, the re-examination period can be extended to a range not exceeding 10 years.

Considerations for Clinical Evaluation of Drugs in Pediatric Patients (10 or 12 years of age and older) Who can be Evaluated Together with Adults

事　務　連　絡
令和２年６月30日

各都道府県衛生主管部（局）　御中

厚生労働省医薬・生活衛生局医薬品審査管理課

成人と合わせて評価可能な小児（10歳又は12歳以上の小児）
の臨床評価の留意点について

今般、小児を対象とした医薬品の臨床開発の一層の効率化、適正化を図ることを目的として、成人と合わせて評価可能な小児の年齢層及び疾患について、臨床評価の留意点を別添のとおり取りまとめましたので、貴管下関係事業者に対し周知願います。

なお、本留意点は、現時点での原則的な考え方をまとめたものであり、個別事例によっては、必ずしもここに示された考え方が当てはまらない場合もあり得ることを申し添えます。

Considerations for Clinical Evaluation of Drugs in Pediatric Patients (10 or 12 years of age and older) Who can be Evaluated Together with Adults

Background

- Among the pedi ugs established on the basis o es, there exist cases where the u , e.g., 12 years of age and older ha been approved with <u>the same regimen as that of adults</u>.
- FDA issued a draft guidance on oncology clinical trials last year that states that adolescents should be included in adult clinical trials when the target malignancy has similar pathological and biological characteristics among adults and adolescents with respect to the clinical evaluation of antineoplastics.

Allergy, Asthma,
Blood coagulation
factor deficiency etc.

Considerations for Clinical Evaluation of Drugs in Pediatric Patients (10 or 12 years of age and older) Who can be Evaluated Together with Adults

- Objectives

To further streamline and optimize the clinical development of drugs for the pediatric population, the present considerations have been compiled to outline the age groups and diseases in pediatric patients who can be evaluated together with adults.

- Applicable Disease or Condition

Type 2 diabetes mellitus, familial hypercholesterolemia, Allergic diseases, Antimicrobials/Antivirals, Hematopoietic Malignancy

*Other diseases will also be discussed in the future as necessary

- Applicable Trials

In principle, clinical trials after the efficacy and safety of the drug in adults have been evaluated in exploratory studies to establish a dosing regimen.

Summary and future perspectives

- Although there is no law or regulation that mandate pediatric drug development in Japan, the environment for pediatric drug development is improving through various efforts.
- It is expected that pediatric drug development will gain momentum further with latest revision of the PMD Act (Specific Use Drugs Designation) and other new initiatives in Japan.