外資系企業における開発品目の傾向
～ PhRMA / EFPIA Japan 合同調査結果より ～

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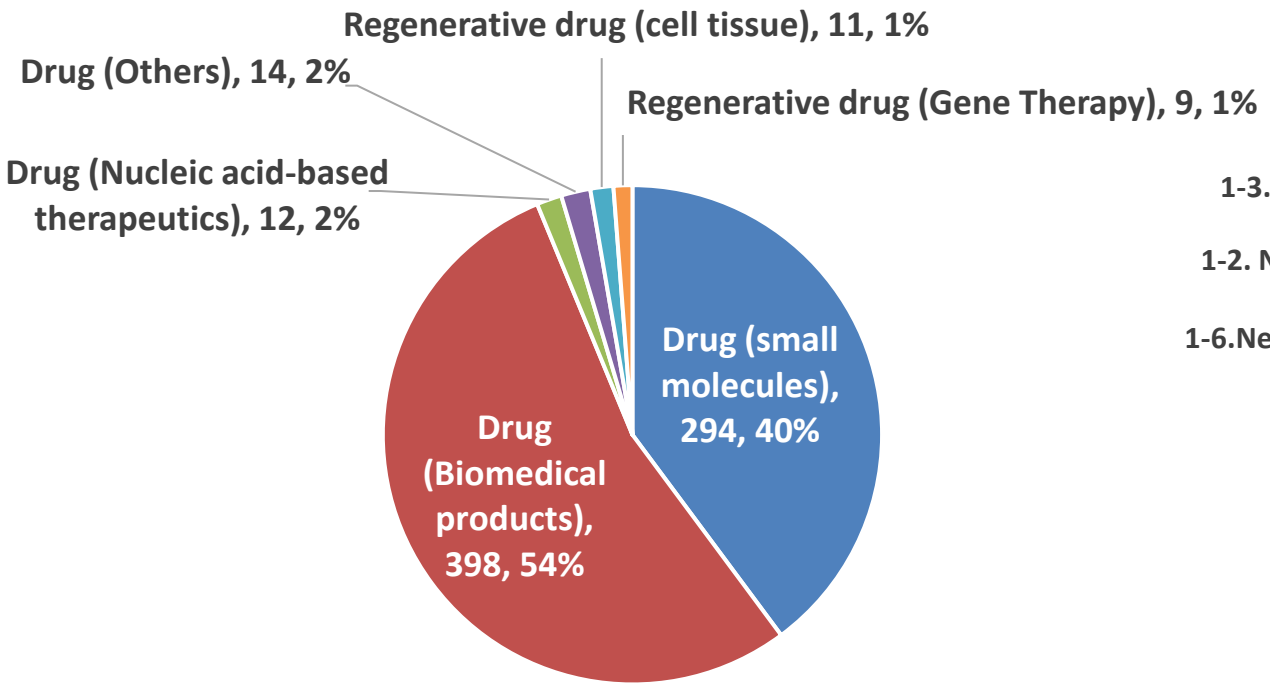
PhRMA/EFPIA Japanで実施した2023年度の合同調査結果は以下のとおりであった。

- 2023年度は24社から738件のプロジェクトの回答が得られた。プロジェクトの申請区分で最も割合が高かったものは、医薬品及び再生医療等製品いずれも新有効性成分／新再生医療等製品であり、それぞれ47%（335件）及び55%（11件）であった。疾患領域では抗悪性腫瘍薬が最も多く、半数を占めていた。
- 先駆的医薬品等指定制度及び条件付き承認制度の利用は検討中も含めて、それぞれ2.7%及び0.8%であり利用割合は低かった。先駆的医薬品の指定基準の変更（令和5年12月22日通知）の影響は限定的であり、事前評価相談制度の改善または廃止を求める意見が多かった。一方、希少疾病用医薬品等の指定制度の利用は29%と他の迅速審査制度よりも利用割合は高い状況であった。
  なお、希少疾病医薬品の指摘基準の変更（令和6年1月16日通知）は、希少疾病医薬品の指定の可否を検討したプロジェクト587件のうち26%に影響があった又は影響を及ぼす可能性があると評価されており、一定の影響があったと考える。
  抗悪性腫瘍薬の迅速審査制度の利用状況では、米国又は欧州で迅速審査制度を利用予定の137件（35.7%）のプロジェクトのうち、日本で迅速審査制度の利用予定があるものは希少疾病用医薬品等の指定制度の48件にとどまっていた。
- 小児開発については、成人のみを対象としたプロジェクト616件のうち72件（12%）は海外で小児開発を計画しており、そのうち35件は日本でも小児の海外臨床試験に参画した又は参画を予定している。
- 開発品目の申請パッケージにリアルワールドデータの活用を検討しているプロジェクトは2%と低い割合であった。
- 日本人第I相試験の実施状況について、新有効成分で第II相及び第III相（II/III相を含む）から国際共同治験に参加した179件のうち、国際共同治験の参加前に別途日本人の第I相試験を実施した割合は76%であった。全プロジェクトの治験実施数は878件であり、そのうち国際共同治験が86.8%と大部分を占めるものの、一定数の国内試験も実施されている状況であった。
- 日本で2025年3月までに申請予定のプロジェクト（104件、14%）で世界最初の申請から3ヵ月以内を予定しているものは52%であり、3ヵ月以内の申請が困難となる最も多い理由は日本特有の規制要件（追加の臨床試験、治験相談による助言）によるものであった。
- ドラッグ・ロスの評価として、2023年度に米国又は欧州のいずれかで承認された新有効成分34品目の日本での開発について調査した結果、日本で開発予定のないドラッグ・ロスとなる可能性のある品目は2品目（5.9%）であった。

Total Projects in FY2023

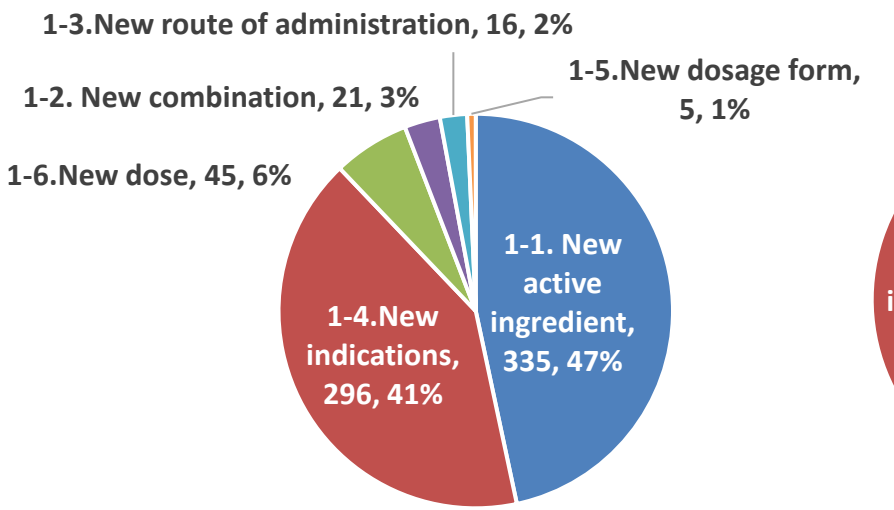
Survey Respondents 738 projects

Projects modality category

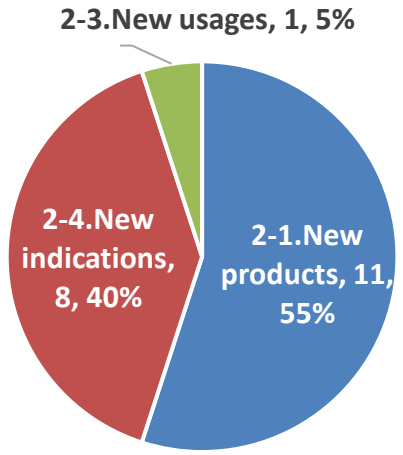


Filing category

Drug



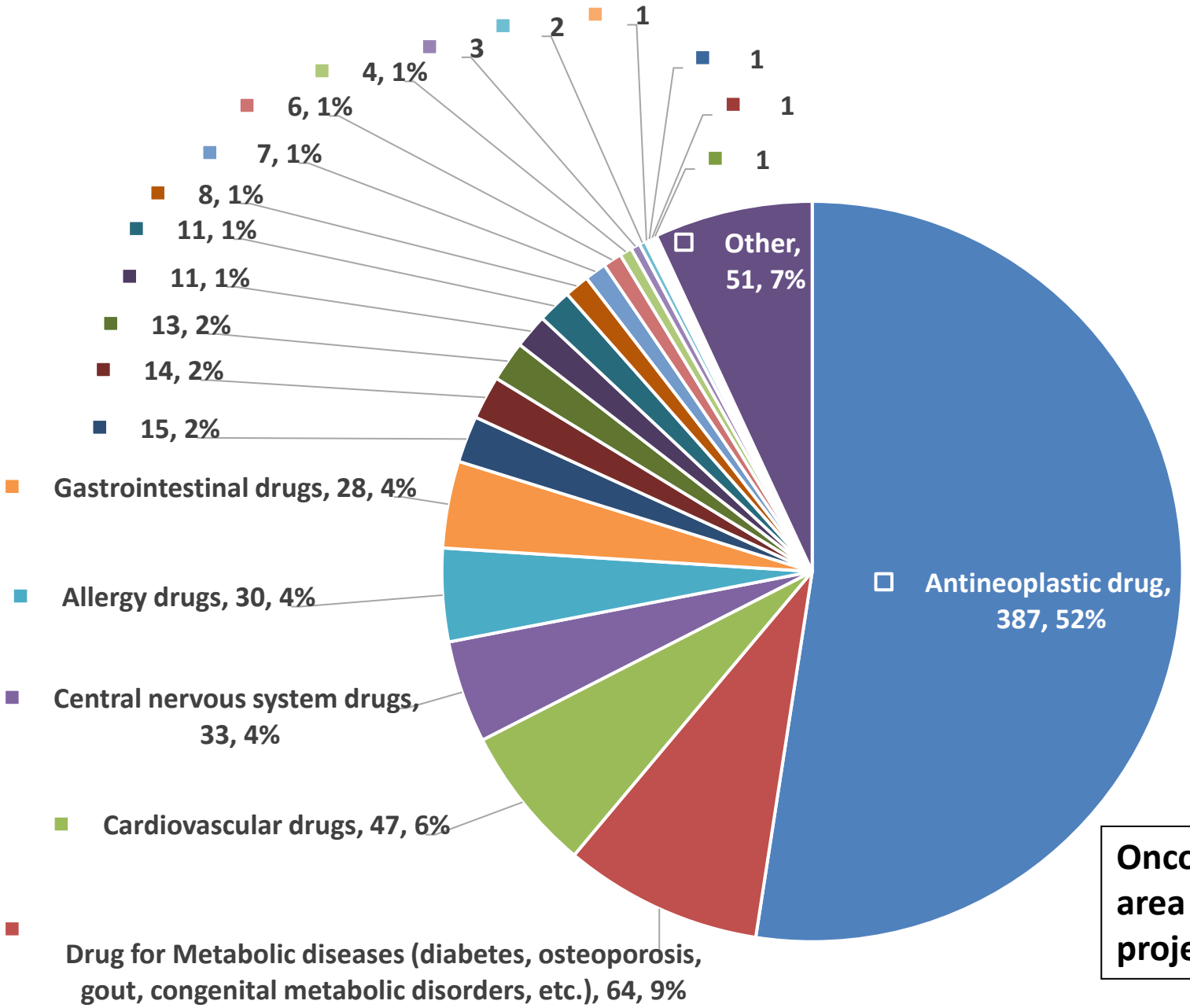
Regenerative medicine



- **In FY2023, the rate of drugs and regenerative medicine products were 97.3% (n=718) and 2.7% (n=20), respectively. The majority were small molecules and Biomedical products of drugs, but there are a certain number of new modality development (nucleic acid drugs and regenerative medicine products); 4% (n=32).**
- **Filling category for both drug and regenerative medicine are mostly new active ingredient/products and new indications.**

Therapeutic Area for Projects in FY2023

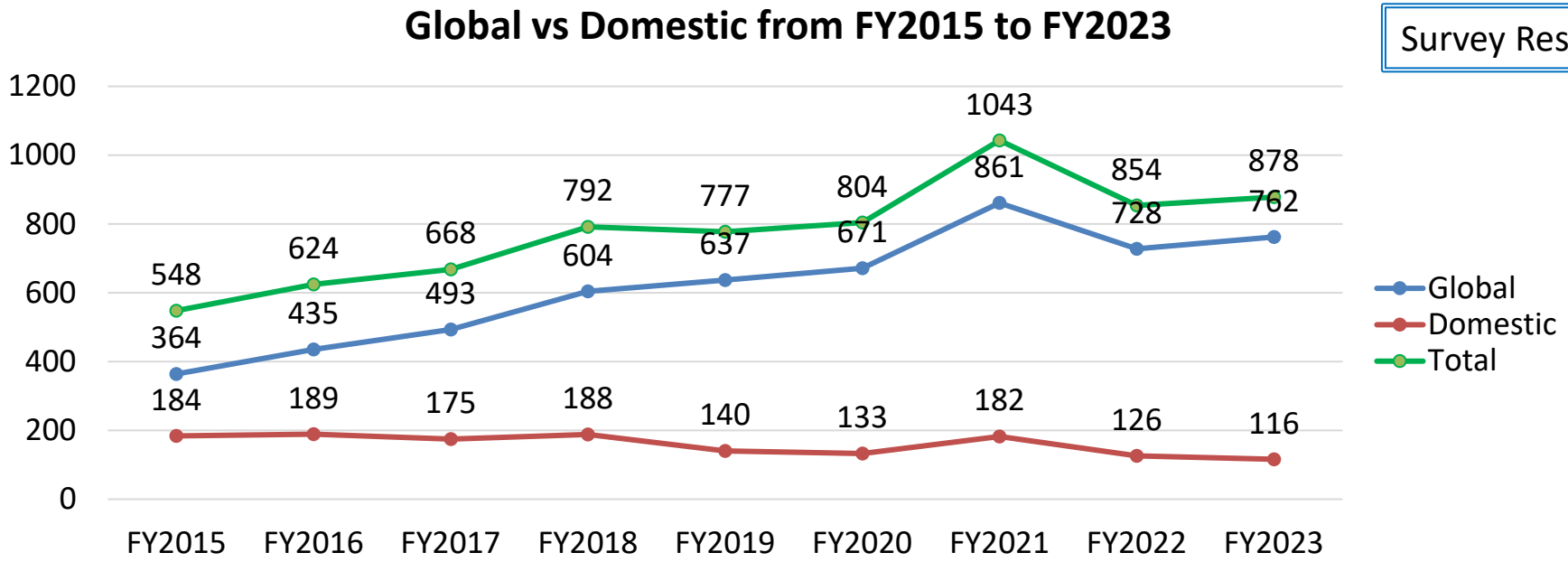
Survey Respondents 738 projects



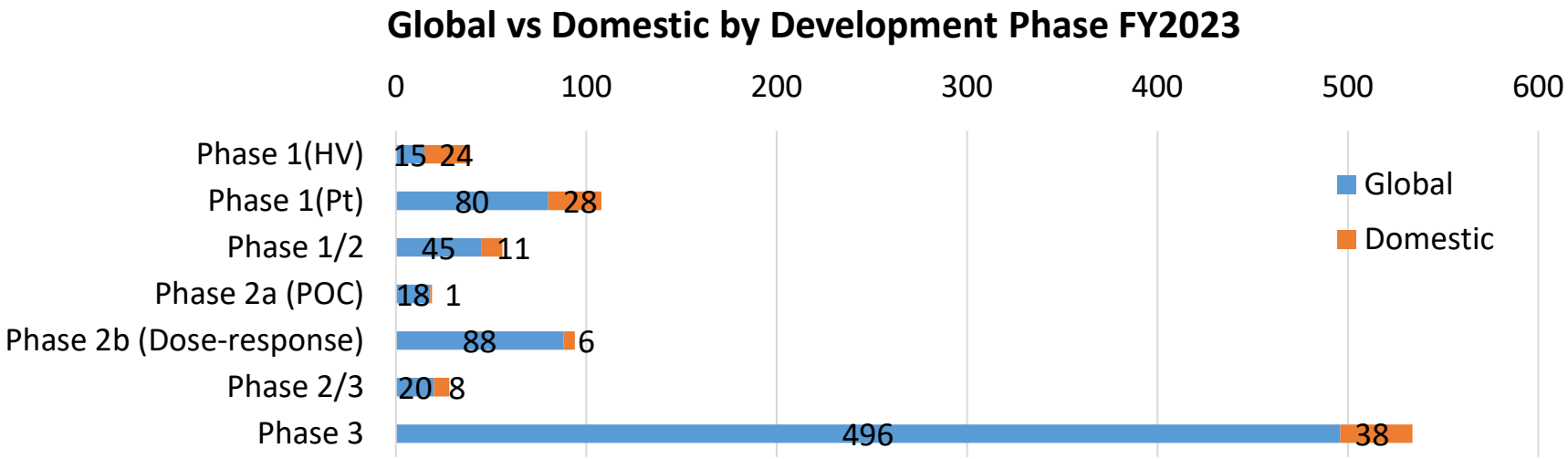
- Respiratory organ drugs 15, 2%
- Alzheimer's disease drugs 14, 2%
- Sensory organ drugs (Excluding those related to inflammatory diseases) 13, 2%
- Antiviral agents 11, 1%
- Blood products 11, 1%
- Peripheral nerve drugs 8, 1%
- Vaccines 7, 1%
- Immunosuppressants 6, 1%
- Medicines for urogenital and anal organs 4, 1%
- Antibacterial agents 3
- Anti-Parkinson drugs 2
- Hormone drugs 1
- HIV infection treatment drugs 1
- Radiopharmaceuticals 1
- Contrast media 1

Oncology (Antineoplastic drug) is a major focus area accounting for 52%(n=387) of the total projects in FY2023.

Number of Clinical Studies (Global / Domestic)



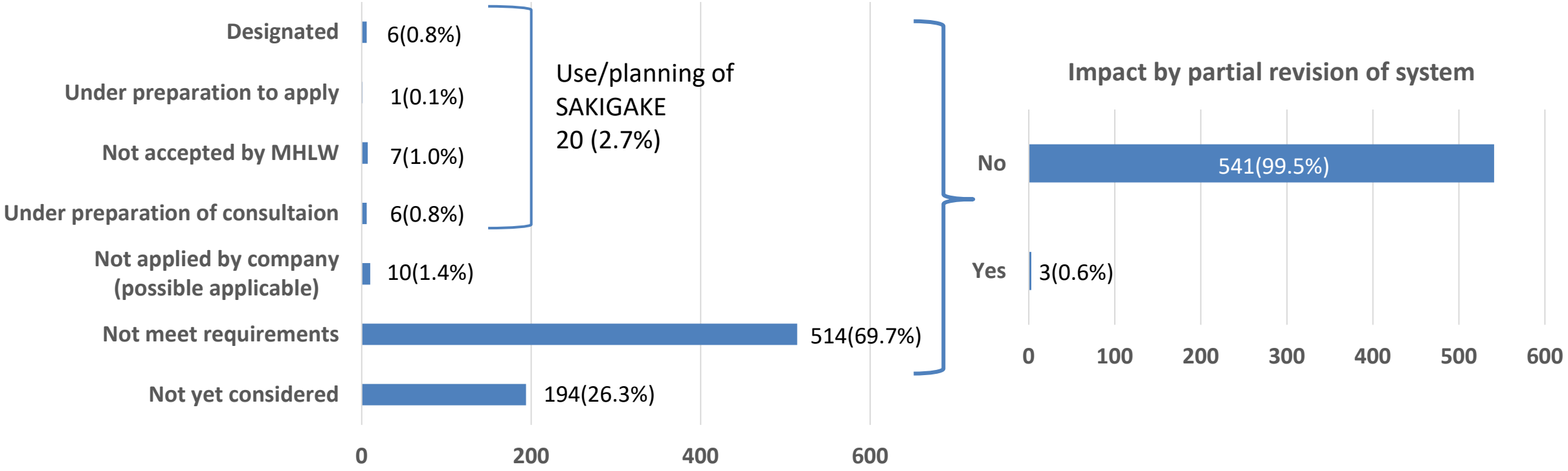
Survey Respondents 878 studies



- **The total number of ongoing clinical studies was 878 and the ratio of Global studies was 86.8% in FY2023.**
- **The most common clinical study was in Phase 3 study, there is a certain number of domestic studies in Phase 1 and 3 studies.**

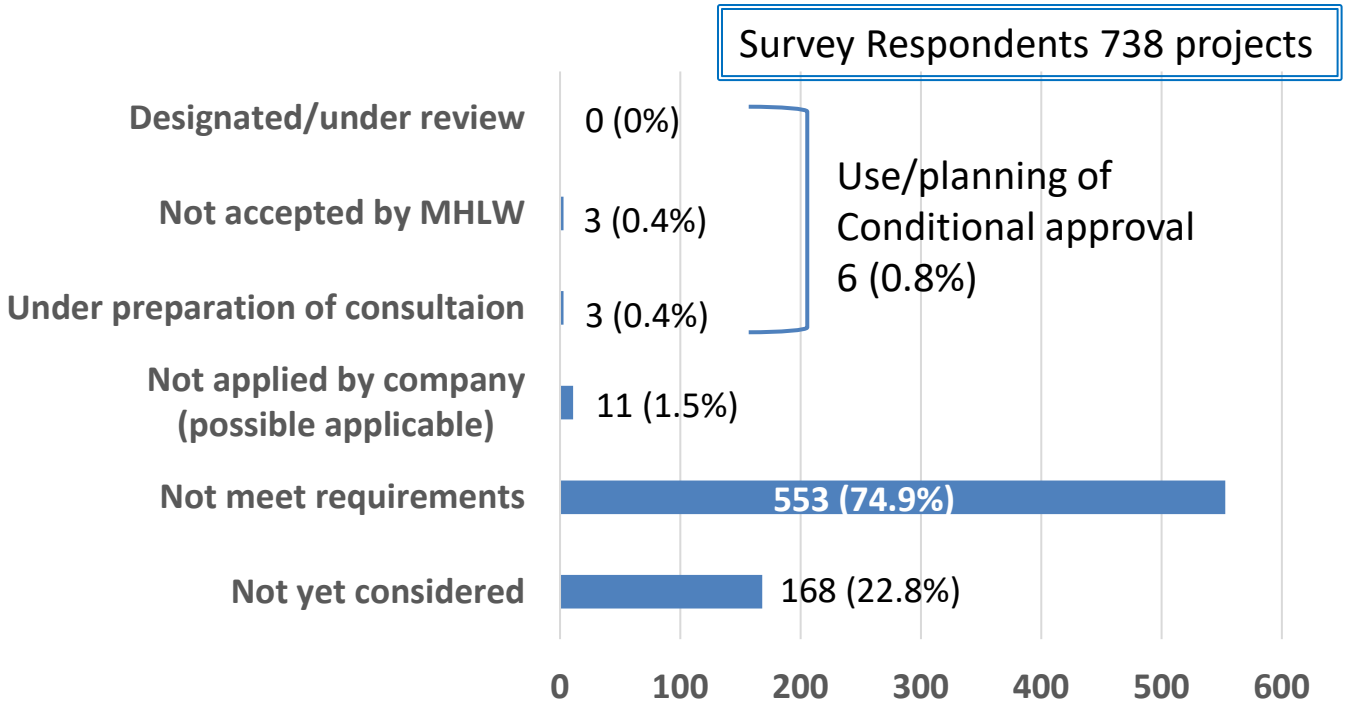
Plan for SAKIGAKE

Survey Respondents 738 projects



The survey respondents only use/planned to use SAKIGAKE for 20 (2.7%) of the total projects including those before consideration. A partial revision to the system in 2023 was made to relax the criteria of simultaneous submission, but this revision only affected 3 (0.6%) of projects that had already been considered.

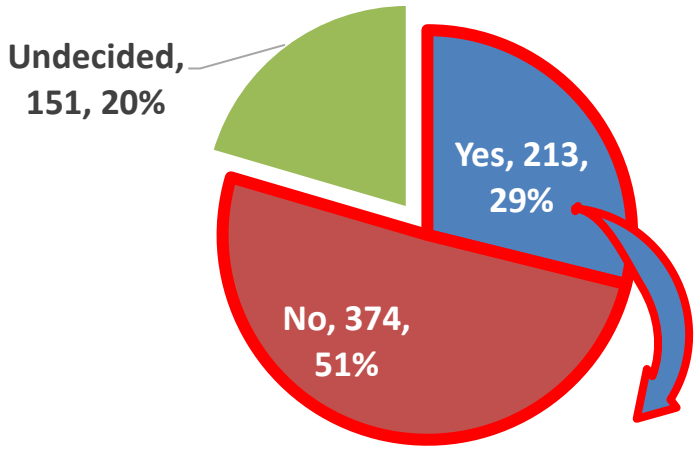
Plan for conditional approval



The survey respondents only use/planned to use conditional approval for 6 (0.8%) of the total projects including those before consideration. Since there are still small number of cases where this system has been applied, it is necessary to consider the scope of the system.

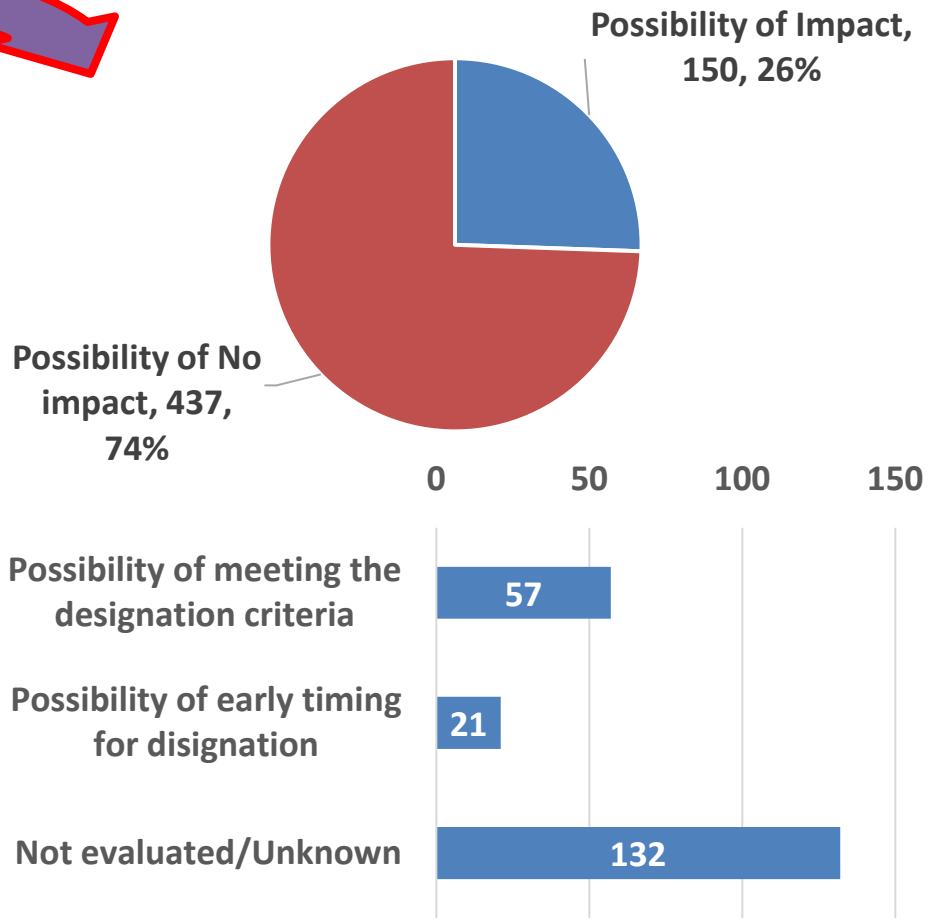
Orphan drug designation

Orphan drug designation plan

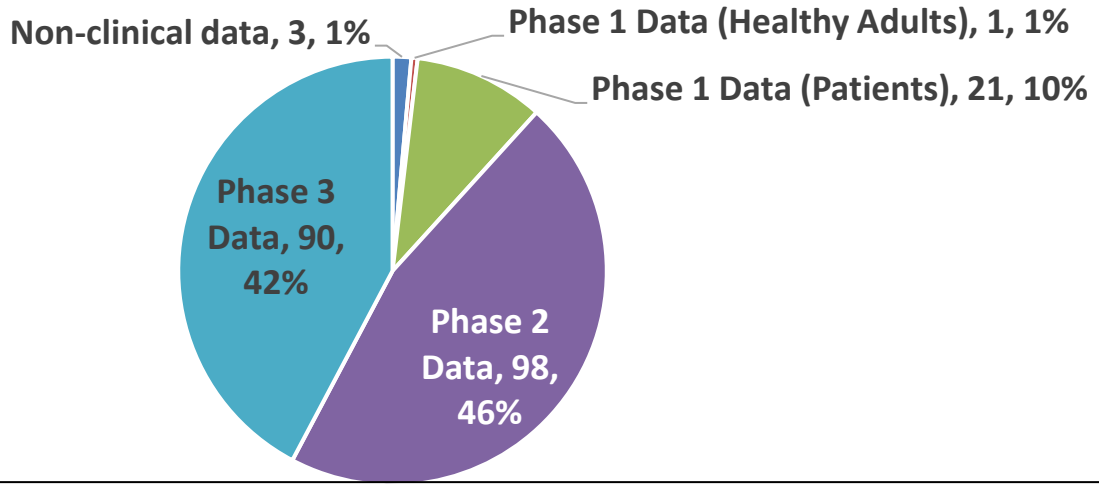


n=587

Impact of the notification for orphan drug designation issued on Jan 16, 2024.



Timing of orphan drug designation application (n=213)

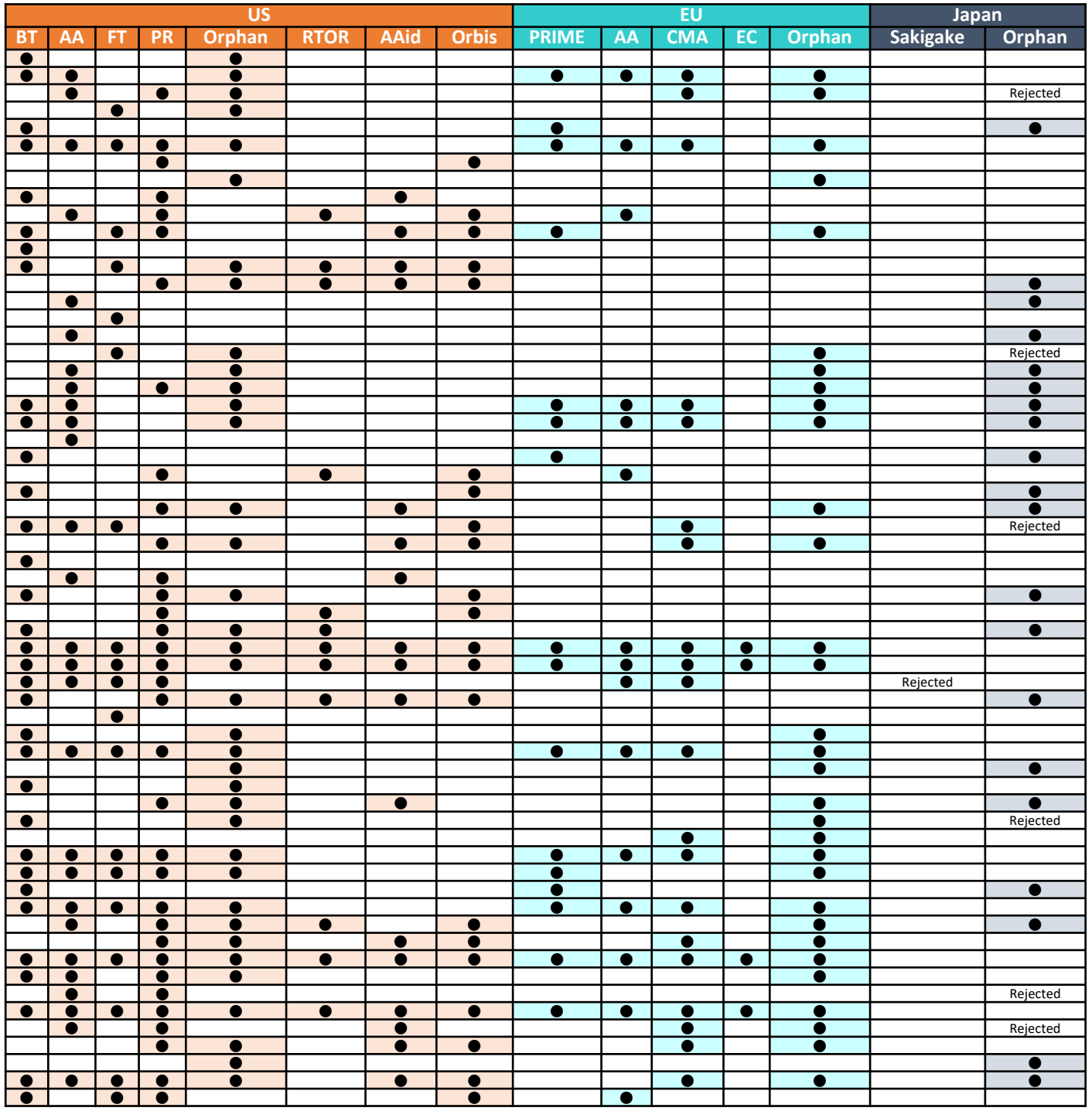


- 29% (n=213) of projects have a designation plan for orphan drugs. Many of them are planned to be applied using data from Phase 2 and 3 studies.
- Of the projects assessed orphan drug designation, 26% projects might be affected by the notification for orphan drug designation issued on Jan 16,2024. The change in designation criteria had a certain impact on the designation.

Utilization of Expedited Programs in Oncology

(NCEs/New biologics/New regenerative medical products)

N=61 out of 387 oncology projects



Note : No projects were consulted or applied for conditional approval in Japan.

US- BT: Breakthrough, AA: Accelerated Approval, FT: Fast Track, PR: Priority Review, RTOR: Real-Time Oncology Review, AAid: Assessment Aid

EU- AA: Accelerated Assessment, CMA: Conditional Marketing Authorization, EC: Exceptional Circumstances

Utilization of Expedited Programs in Oncology

(new indication/ dosage/ combination/ route of administration)

N=76 out of 387 oncology projects

US								EU					Japan	
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US- BT: Breakthrough, AA: Accelerated Approval, FT: Fast Track, PR: Priority Review, RTOR: Real-Time Oncology Review, AAid: Assessment Aid

EU- AA: Accelerated Assessment, CMA: Conditional Marketing Authorization, EC: Exceptional Circumstances

US								EU					Japan	
BT	AA	FT	PR	Orphan	RTOR	AAid	Orbis	PRIME	AA	CMA	EC	Orphan	Sakigake	Orphan
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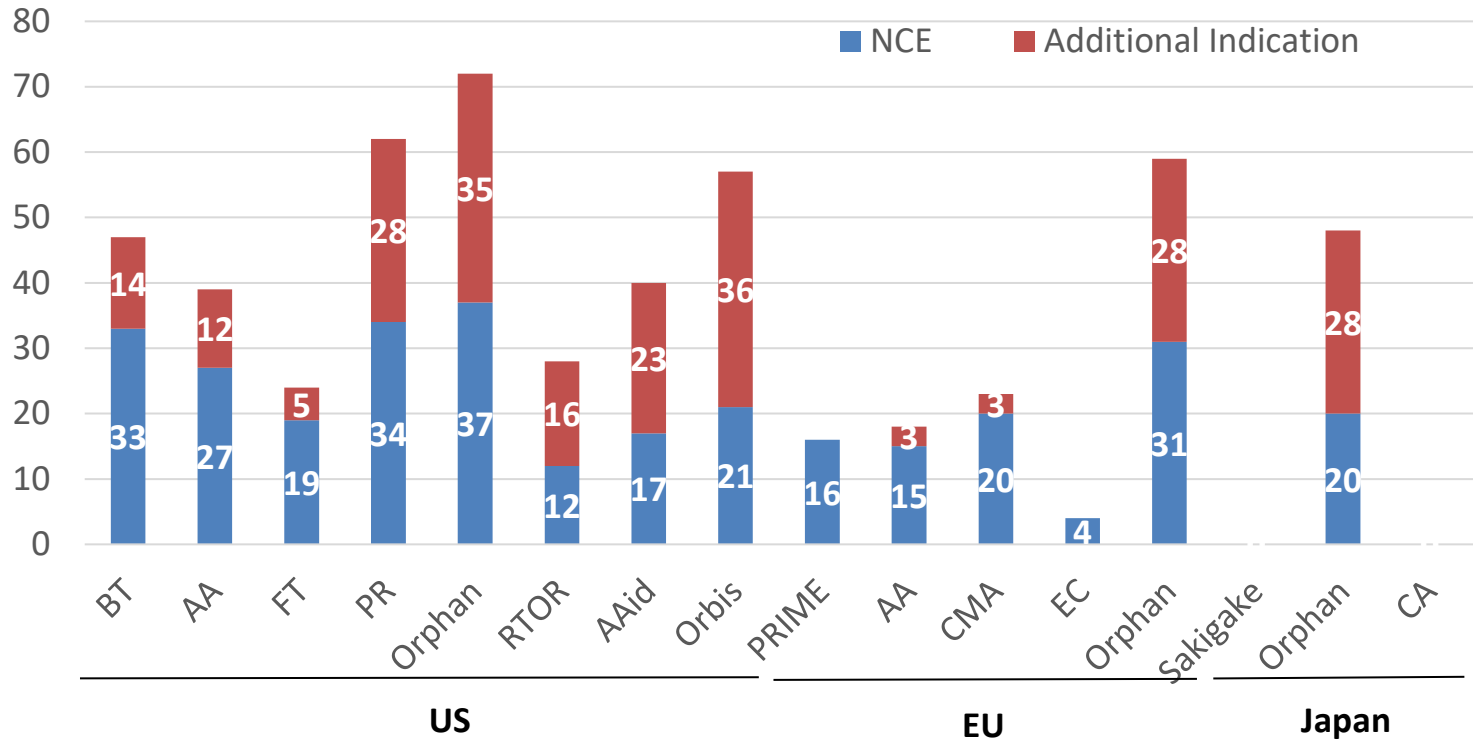
Note：No projects were consulted or applied for conditional approval in Japan.

Utilization of Expedited Programs in Oncology - Summary



US- BT: Breakthrough, AA: Accelerated Approval, FT: Fast Track, PR: Priority Review, RTOR: Real-Time Oncology Review, AAid: Assessment Aid
EU- AA: Accelerated Assessment, CMA: Conditional Marketing Authorization, EC: Exceptional Circumstances
Japan- CA: Conditional Approval

- Number of designated projects using expedited programs in US or EU were 137 over 387 Oncology projects (35.7%). Of these, 61 were NCEs/New biologics/New regenerative medical products and 76 were new indication/ dosage/ combination/ route of administration.
- In the US, 136 of 137 projects used any of 8 expedited programs. Majority of NCE/New biologic/New regenerative medical products using expedited programs were designated by BT, Priority Review or Orphan in US.
- In Japan, usage of expedited programs were limited to 48 of 137 projects, all of which were designated Orphan Drug. No project designated SAKIGAKE or Conditional Approval.

SAKIGAKE and request for further early approval

Company foresee an increase in the use of the Sakigake changed to "within three months" as simultaneous submission (N=24)

Will increase	5
Another improvement needed	19

Requests to make Sakigake more accessible（N=19）

Flexibility or abolition of preliminary evaluation consultation	17
Others Further revision of criteria for simultaneous submission, Flexibility in the scope of conditional approval, broader incentives for NHI price, Patent term, reexamination periods, etc.	4

New expedited system to be made to enable earlier approval

	N
Improve existing pathways, such as conditional approval, orphan designation and SAKIGAKE designation including Preliminary evaluation	11
Introduce rolling Submission	6
Accept CTD in English	6
Improve Japan specific requirement (promotion of global harmonization)	5
Improve pricing system/Reexam period	3
Introduce joint review with FDA/EMA	2
Other	6
None	5

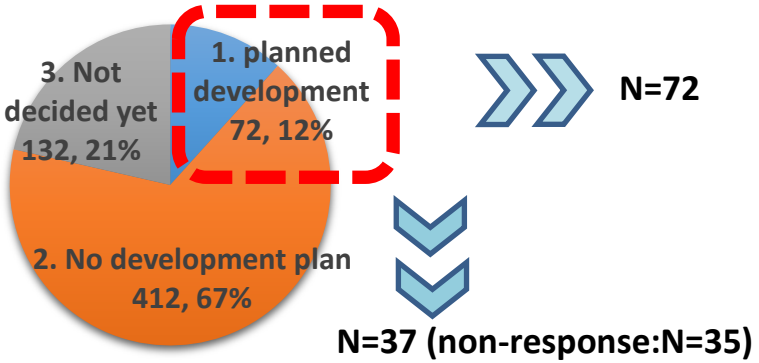
Discussion

Sakigake: While some companies evaluated that the revision of the definition of simultaneous application (simultaneous application within 3 months) was meaningful, many others expressed that the preliminary evaluation consultation should be abolished or relaxed to further promote the use of the system.

Request for further early approval: Many companies expressed the followings are needed to be ; Improved existing systems such as conditional approval, orphan designation, Sakigake, introduced rolling submission, accepted CTD in English, improved Japan specific requirement (promotion of global harmonization).

Pediatric development drug

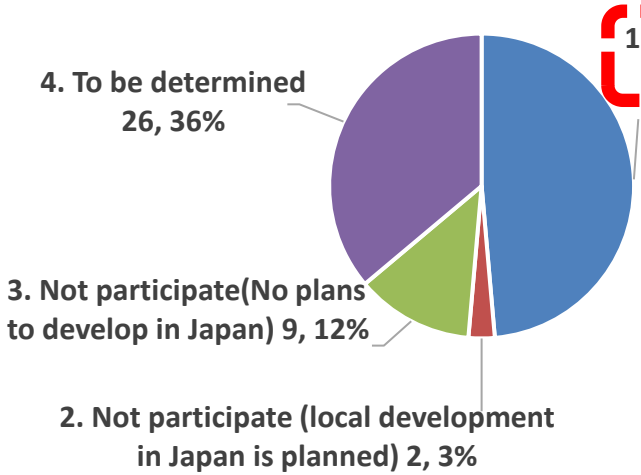
Pediatric development planned globally in projects only for adults N=616



N=72

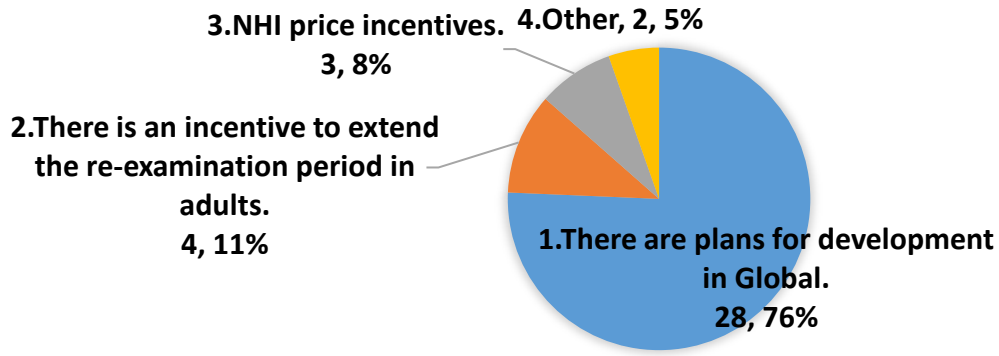
N=37 (non-response:N=35)

Japan joins or will join Global PIP/PSP?

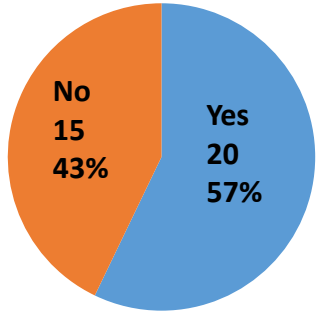


N=35

Most prioritized reason

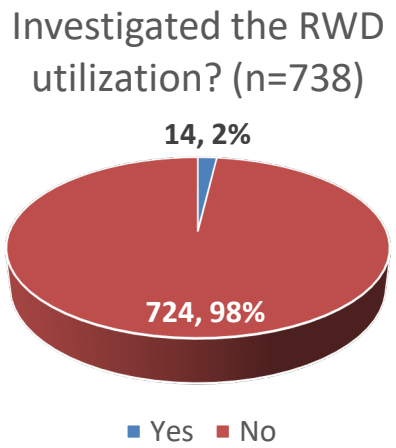


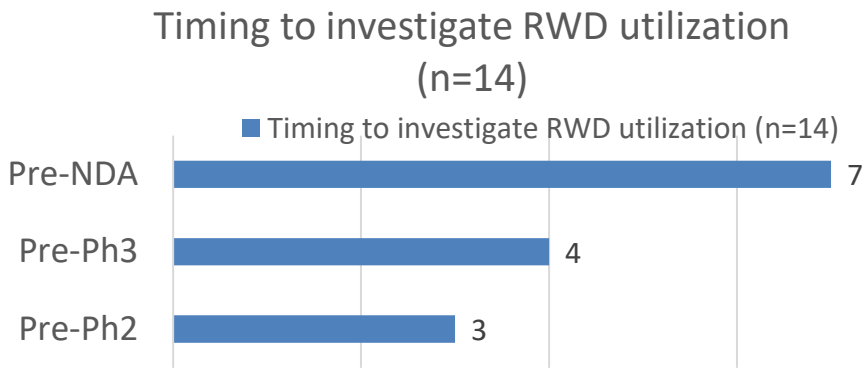
Data package agreement with PMDA?

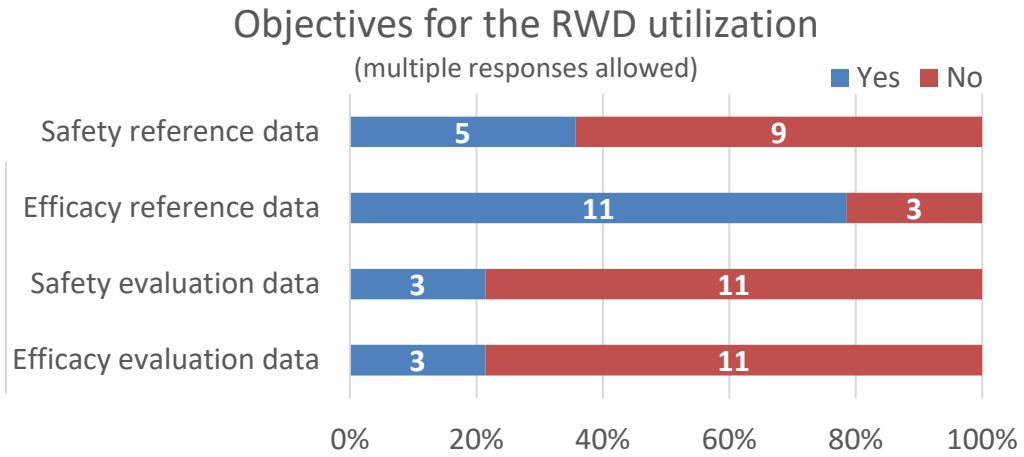


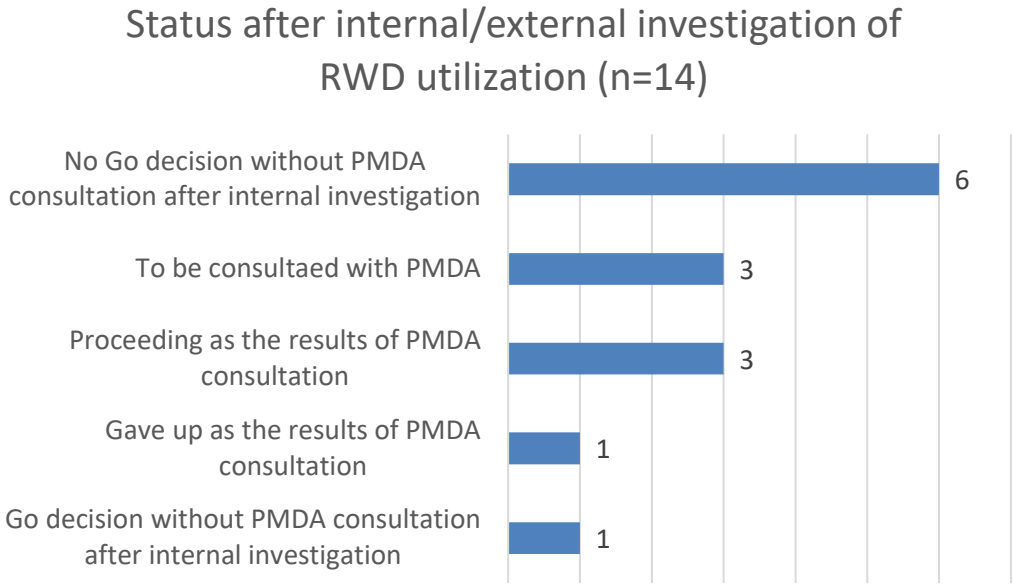
- Respondents had pediatric development plans for 72 of the 616 projects (12%). In most cases, the plan is to develop globally (35 cases, 49%), and more than 50% (20/35 cases,57%) are the data package agreement with PMDA.
- Major reason affected to pediatric development plan in Japan was a global plan, followed by the re-examination period in adults and pricing incentives.
- MHLW has issued a new notification on “The development plan for pediatric drugs to be performed during the development period of a drug intended for adults” on 12 Jan 2024. However, there is limited or no impact on improving pediatric drug loss. The following comments were made to promote pediatric development. System improvement is not sufficient to improve drug loss(50% of 22 companies). Pediatric developing drugs are needed to consider the clinical data package for Japanese pediatric patients, the drug pricing incentives, and an extension of the re-examination period.

Utilization of Real-World Data









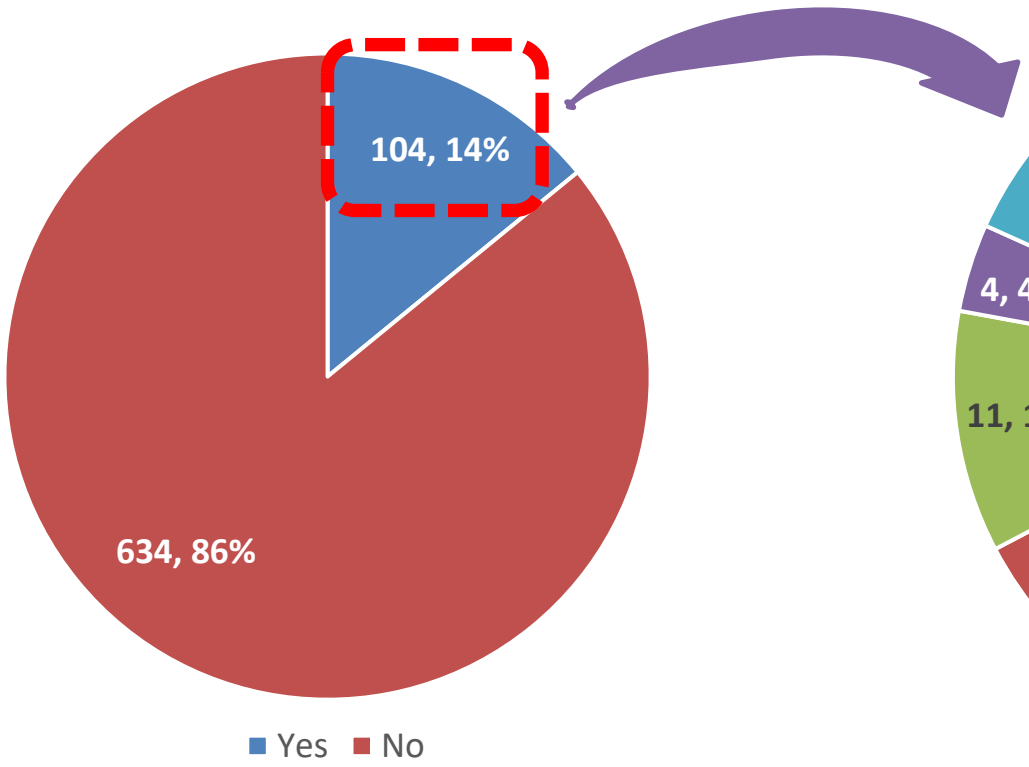
Detail of the reason not to use RWD after internal/external investigation of RWD utilization

- The Global strategy was changed.
- Clinical study data alone were considered sufficient for JNDA as the results of PMDA consultation.
- As the results of PMDA consultation about the acceptability of using RWD in case Japanese data were insufficient in a confirmatory study, the applicant obtained PMDA response that it was difficult to use RWD because the background of the patient population in the PMS data to be used as RWD was different from that in the confirmatory study and PMS was not a randomized controlled trial.

- The number of projects considering the utilization of RWD in the application package of development items was low at 14 (2%) among 738 projects.
- Among 14 projects, the timing to investigate RWD utilization was at Pre-NDA (7 projects), Pre-Ph3 (4 projects) and Pre-Ph2 (3 projects). Most frequent objective for RWD utilization was for efficacy reference data (11 projects).
- Among 14 projects, 3 projects are proceeding with RWD as a result of PMDA consultation, 6 projects decided no-go without PMDA consultation after internal investigation and 3 projects will be consulted with PMDA. 1 project gave up as a result of PMDA consultation and 1 project are proceeding with RWD without PMDA consultation.

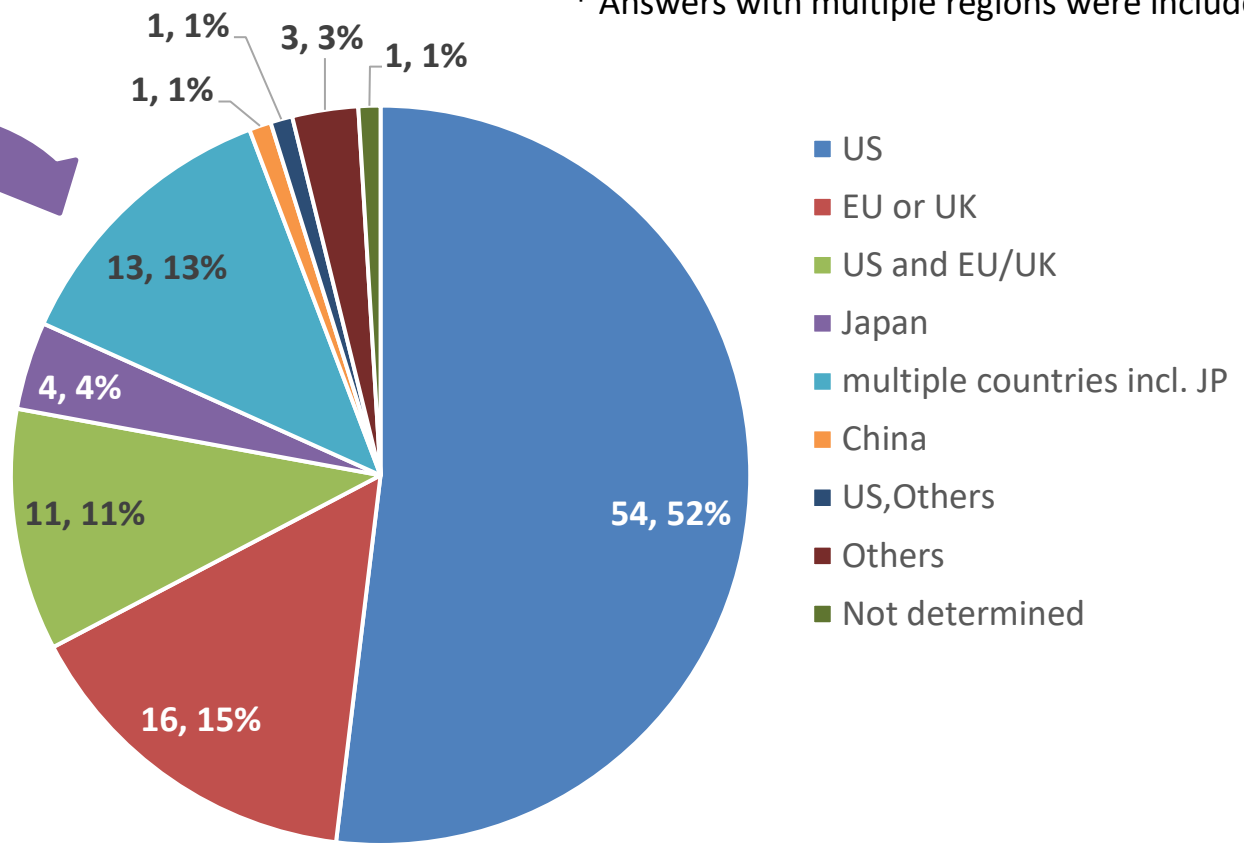
Submission lag (1)

Currently filed or scheduled to be filed to PMDA by end of March 2025 based on the results of global clinical trial(s) (N=738)



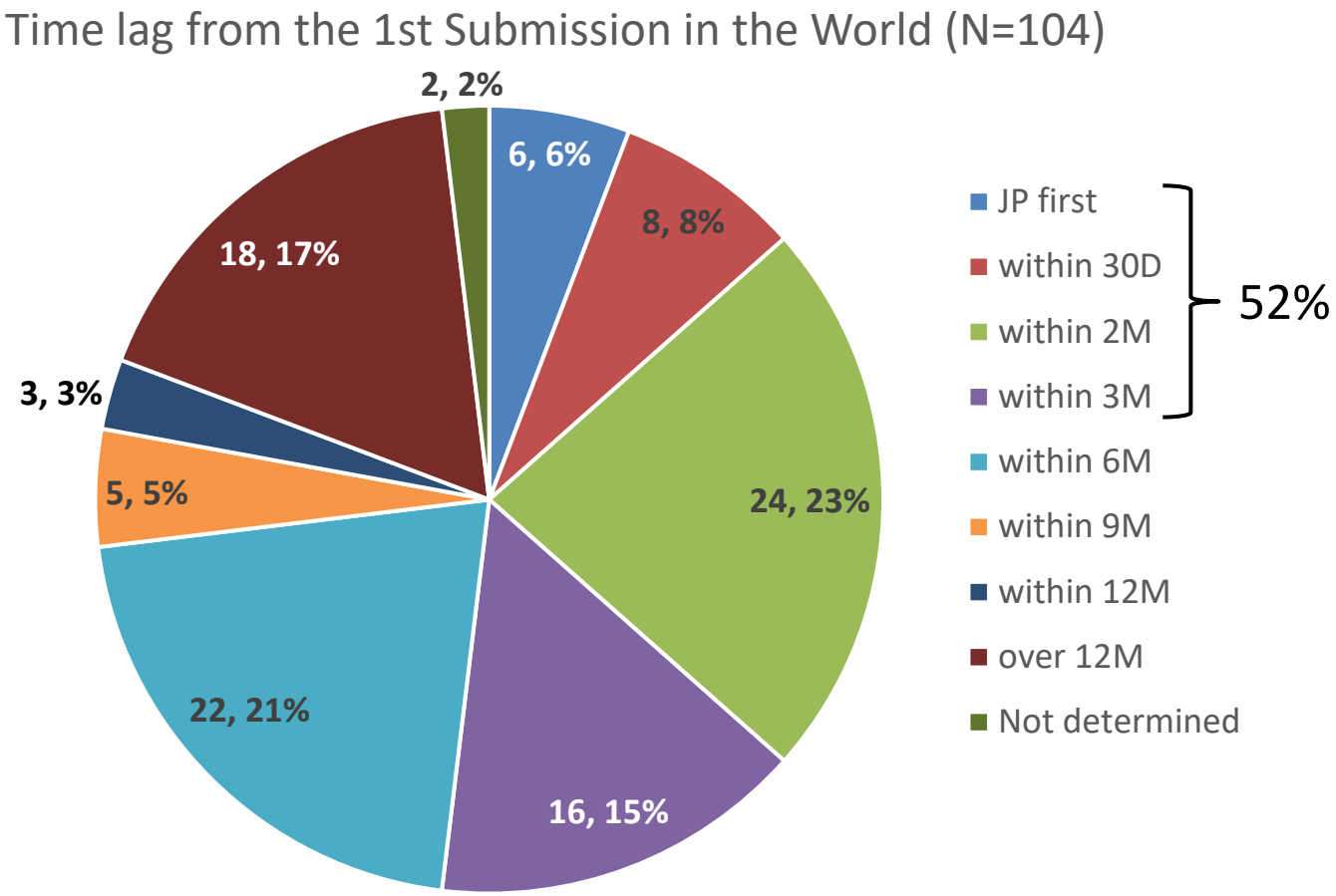
First submission region (N=104)

* Answers with multiple regions were included



Almost all the first submission regions were the US and/or EU･UK (78%). The first submission in multiple countries, including Japan, was 13%, and the first submission in Japan alone was 4%.

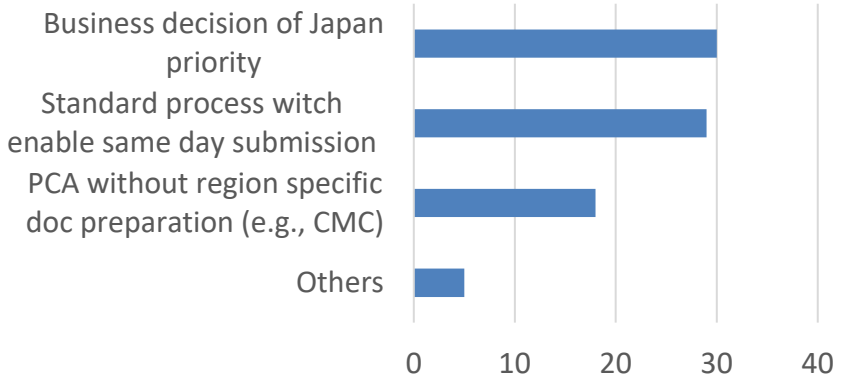
Submission lag (2)



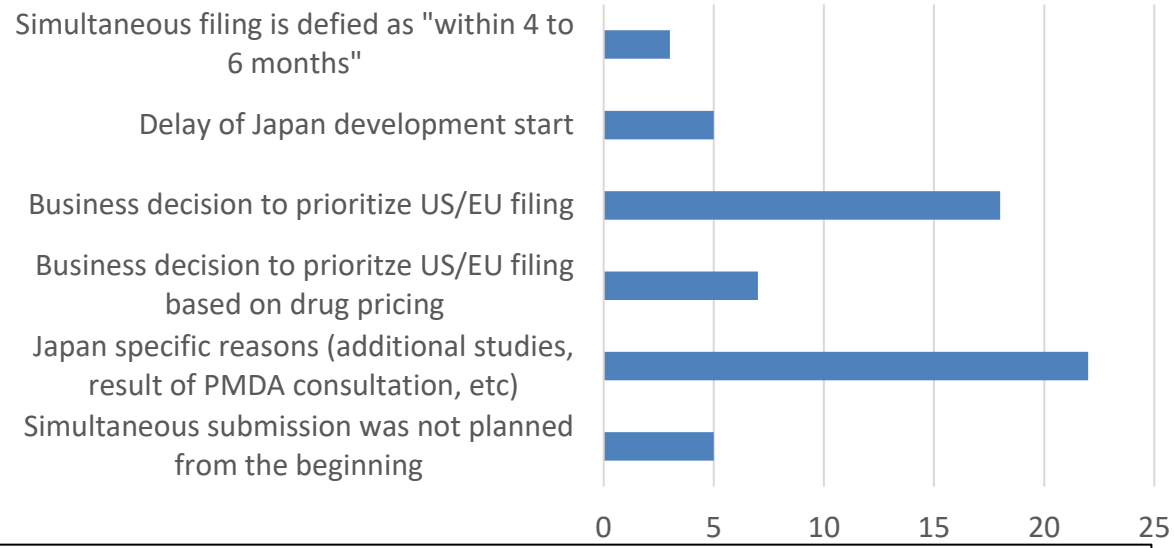
First submission in Japan or same day submission with other regions is 6%, but submission in Japan within 3 months is planned in around 52% projects (increased from 42% in 2023).

Submission lag (3)

Reasons why submission in Japan within 3 months from 1st submission can be done.（n=54, multiple answers）



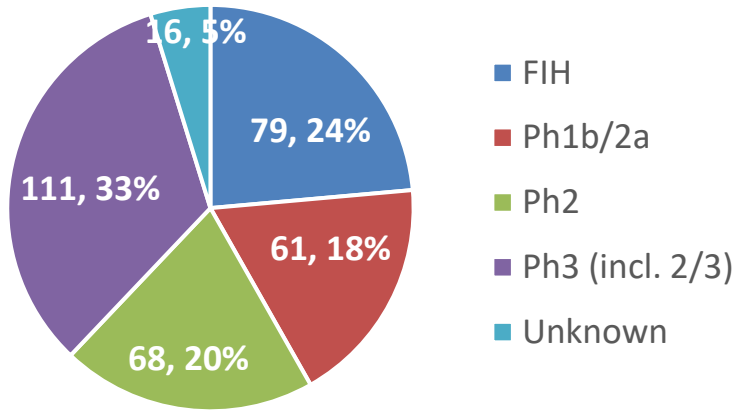
Reasons why submission in Japan within 3 months from 1st submission cannot be done（n=48, multiple answers）



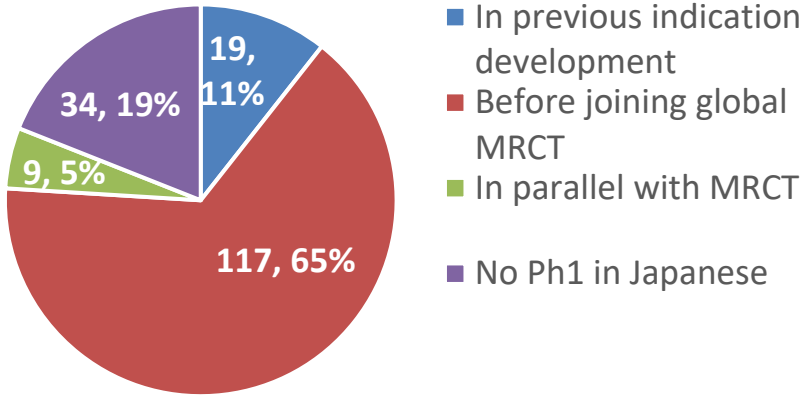
- **Japan first or within 3 months submission with US/EU was achieved by business decision or standard processes that enable same-day submission.**
- **The main reasons for not filing first in Japan was Japan specific regulatory requirements or a business decision.**
- **Major Japan specific reasons which caused delay in Japan submission were:**
  - **PMDA opinion affected submission timing (12/22)**
  - **Preparation of M2.3 or applicant form for Japan (2/22)**
  - **Others (8/22)** →
    - Development of companion diagnostics (2cases)
    - Company decided to conduct pivotal study, but FDA/EMA approved by single arm study.
    - Patient enrollment was delayed in the additional Japanese study.
    - Ph3 study was required at ODD consultation.
    - Japanese study required aside from global study due to difference of clinical practice.
    - The 1st NDA country is quick to apply due to the format of the application.
    - To apply after waiting for initial approval of the active ingredient to be combined.

Phase 1 Study in Japanese Population before joining MRCT (NME)

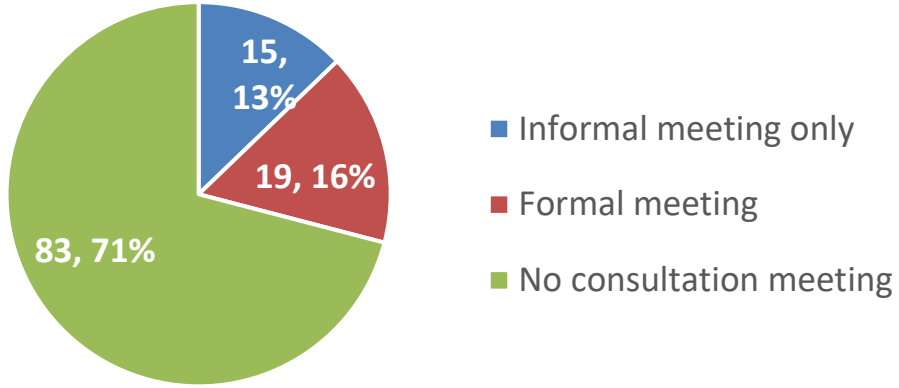
When did Japan join Multi-Regional Clinical Trial? (or planned schedule) (n=335)



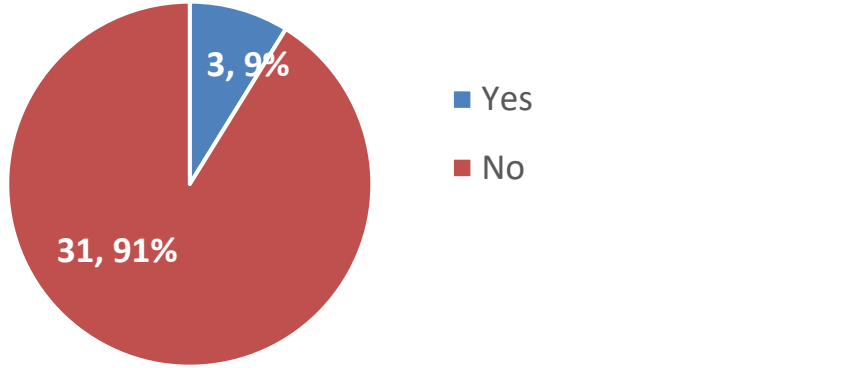
When did you perform Ph1 study in Japanese population? (n=179)



Did you have PMDA consultation before Ph1 in Japanese? (n=117)



Did PMDA show detailed / scientific reasons of necessity of Ph1 in Japanese? (in case, you perform Ph1 in Japanese based on PMDA's instruction) (n=34)



Percentage of joining MRCT until Phase 2 is increased from 49% (2023) to 62% (2024)
76% NME Projects performed Phase 1 in Japanese before joining MRCT (incl. Phase 1 in other indication development)
71% Projects performed Phase 1 in Japanese without PMDA consultation. Even when consulting with PMDA, there were few clear reasons for necessity of Phase 1 study.

Drug Loss

NCEs approved in either the U.S. or Europe at the global headquarters during the year
(from April 2023 to the end of March 2024)

34 products (17 Companies)

Development plan is undecided in Japan branch
1 products

Under development or approved in Japan
30* products
Approved : **15 products**
Under Ph3 study or Under Review : **13 products**
Prior to CTN of Ph3 study : **2 products**

No plan for development in Japan branch
4 products
(All non-Oncology area)

License out
2* products

***: Include one product with duplicate responses (Approved and license out).**

Possibility of drug loss
2/34 products (5.9%)

No license out
2 products

Last year, 34 NCEs were approved in either the US or Europe.
Of these, two products (5.9%) are not planned for development in Japan which may result in drug loss.