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

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1：米国研究製薬工業協会（PhRMA Japan）　2：欧州製薬団体連合会（EFPIA Japan）

COI開示：演題発表内容に関連し、発表者らに開示すべき利益相反はありません。

RS学会：冒頭(青色枠)：調査結果概要メッセージ

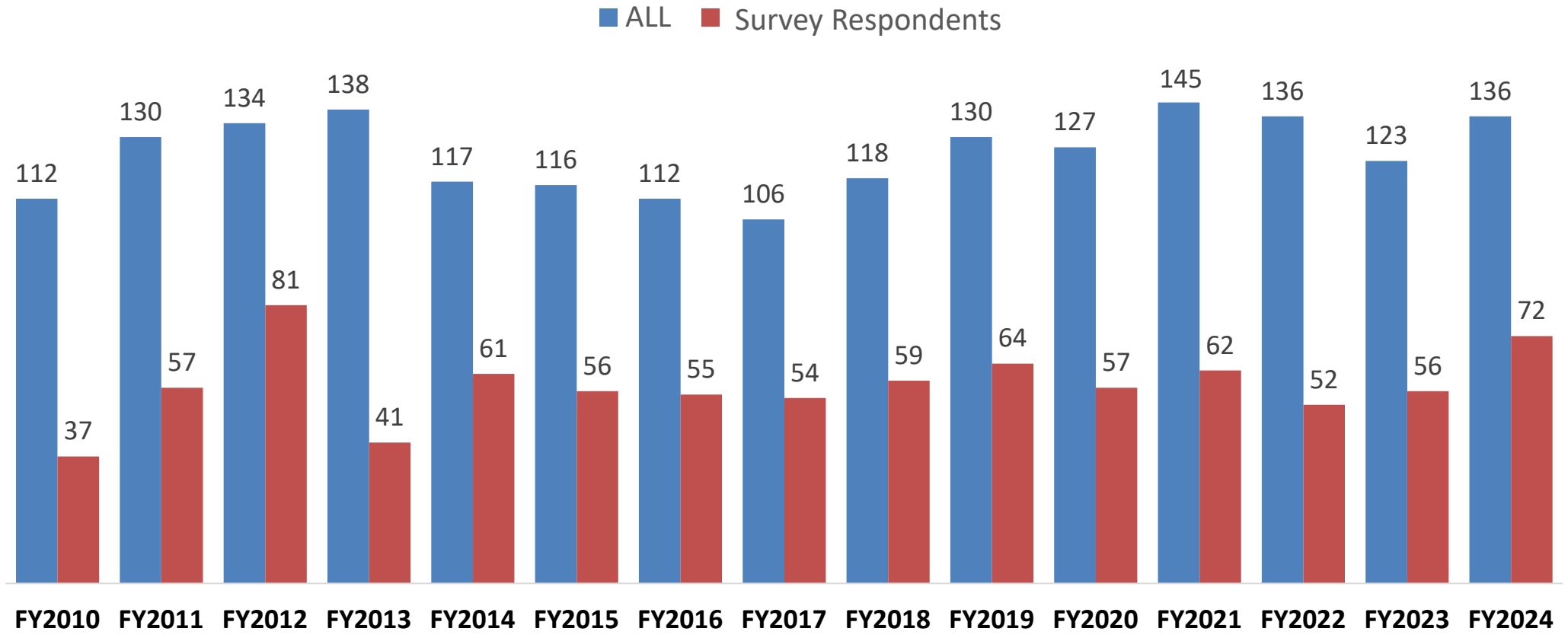
- PhRMA又はEFPIA Japan加盟会社24社を対象に、2024年度（2024年4月～2025年3月）の承認品目（新医薬品）についてアンケート調査を実施し、回答が得られた72品目について分析した。
- 審査期間（80パーセンタイル）は、通常審査品目が11.8カ月（総合機構の審査期間目標値は12カ月）、優先審査品目が8.4カ月（同9カ月）であった。
- 優先審査品目、希少疾病用医薬品指定品目の割合はいずれも17品目（24%）であり、先駆的医薬品指定品目及び条件付き承認制度利用品目はいずれもなかった。
- 臨床データパッケージにおけるピボタル試験は、国際共同第3 相試験が51%、国際共同第2 相試験が11%であった。
- 68品目（事前評価済公知申請の4品目を除く）のうち、海外で承認申請した又は申請予定である品目は64品目（94%）であり、そのうち20品目（31%；20/64品目）において日本が最初に申請又は同時申請（最初の国の申請から3ヵ月以内）を達成した。
- 承認適応が小児を含んでいない51品目のうち、小児開発を別途行う予定があるのは9品目であり、そのうち6品目が小児開発について成人の審査終了までにPMDAの確認を受けた。

PhRMA/EFPIA Joint Survey 2025

1. ***Review Time***
   - The Number of New Drug Approvals in Japan
   - Review Time for Standard Review and Priority Review
2. ***Category of Approved New Drugs***
   - Category of Approved Drugs
   - Utilization of Expedited Program
3. ***Orphan Drug Designation***
   - Timing of Orphan Drug Designation
   - Impact of the Revised Notification
4. ***Clinical Data Package***
5. ***Submission/Review/Approval Lag***
6. ***Evaluation of Submission Lag***
7. ***Utilization of Expedited Program***
8. ***Pediatric Development***

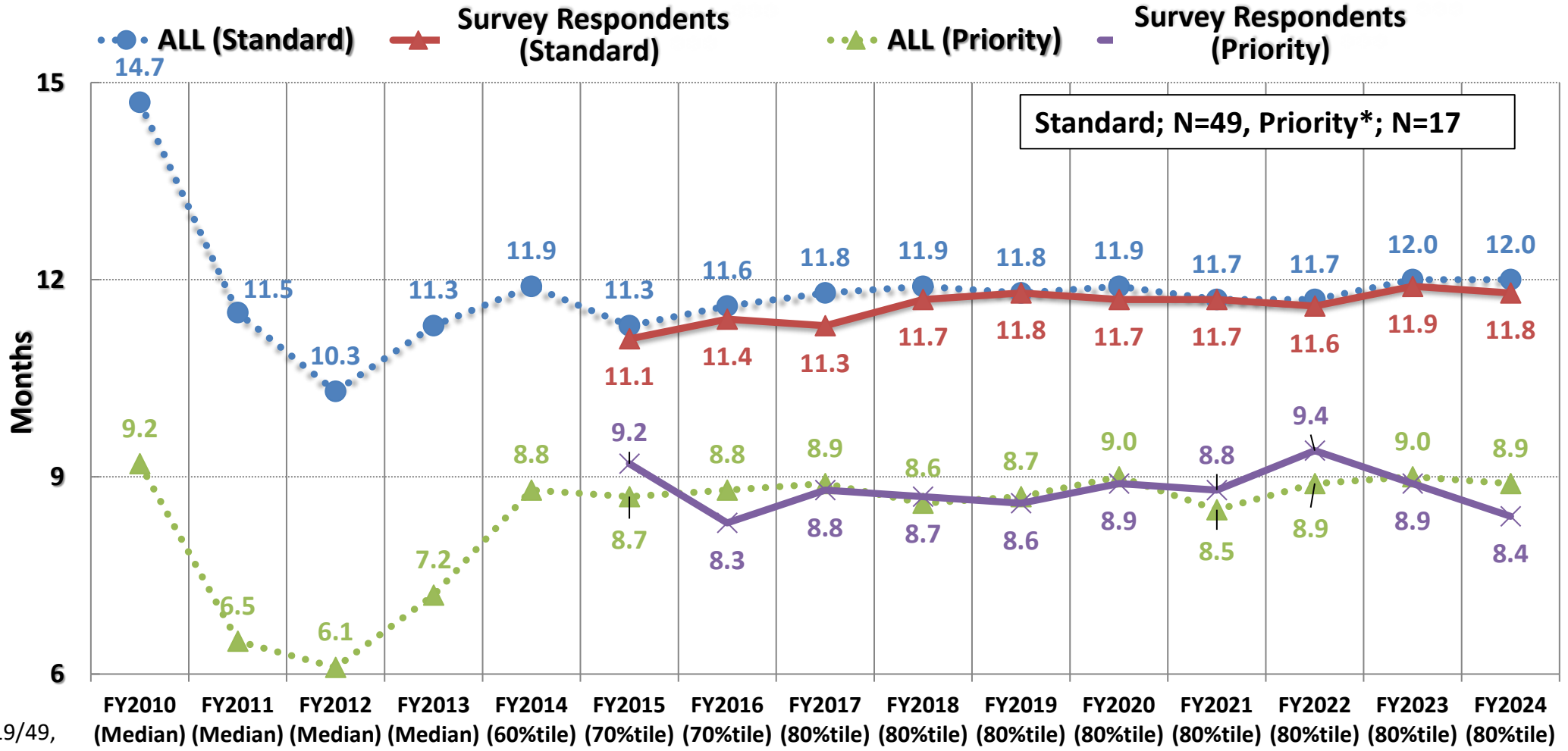
Drug Approvals and Review Times

The Number of New Drug Approvals in Japan



The survey respondents accounted for 53% (72/136) of the total new drug approvals in Japan in FY2024.

Review Time for Standard Review and Priority Review



Note:

Standard
- Oncology: 19/49,
- Non-oncology: 30/49

Priority
- Oncology: 11/17,
- Non-oncology: 6/17

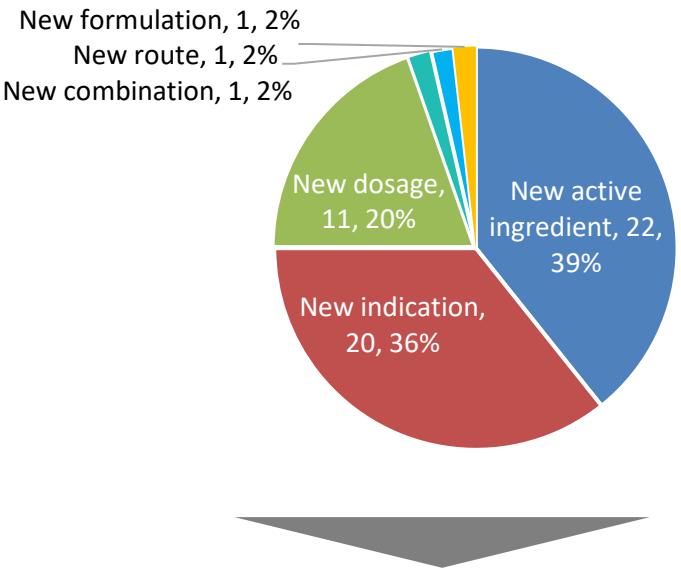
- Duration of JNDA Review for "Standard Review" in FY2024 was 11.8 months (80th percentile).
- Duration of JNDA Review for "Priority Review" in FY2024 was 8.4 months (80th percentile).

**New drugs designated under the Sakigake pathway were excluded.*

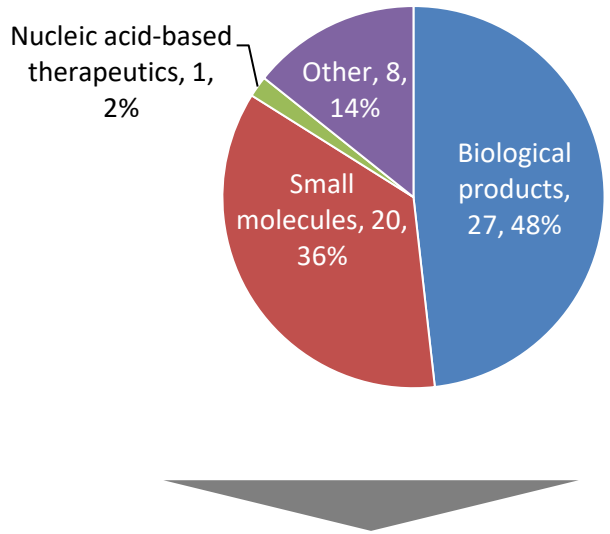
Category of Approved New Drugs

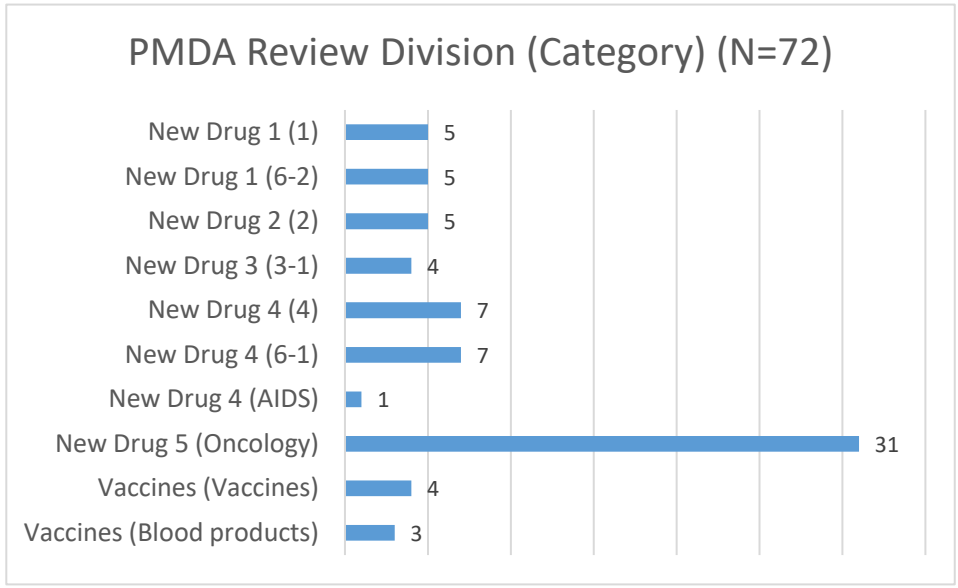
Category of Approved Drugs

Category of NDA in FY2023 (N=56)

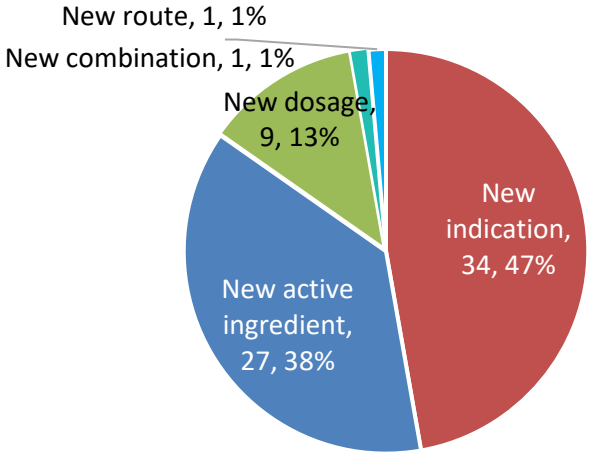


Drug Modalities in FY2023 (N=56)

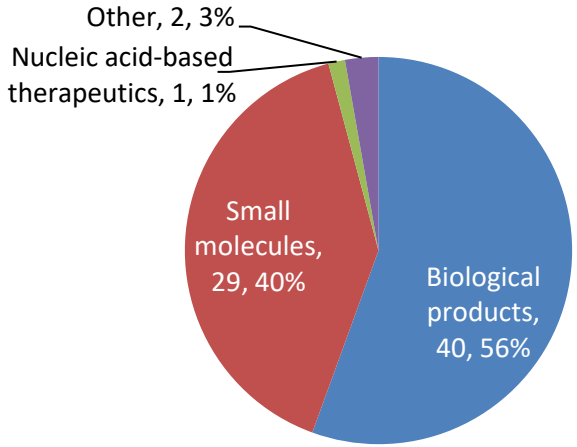




Category of NDA in FY2024 (N=72)



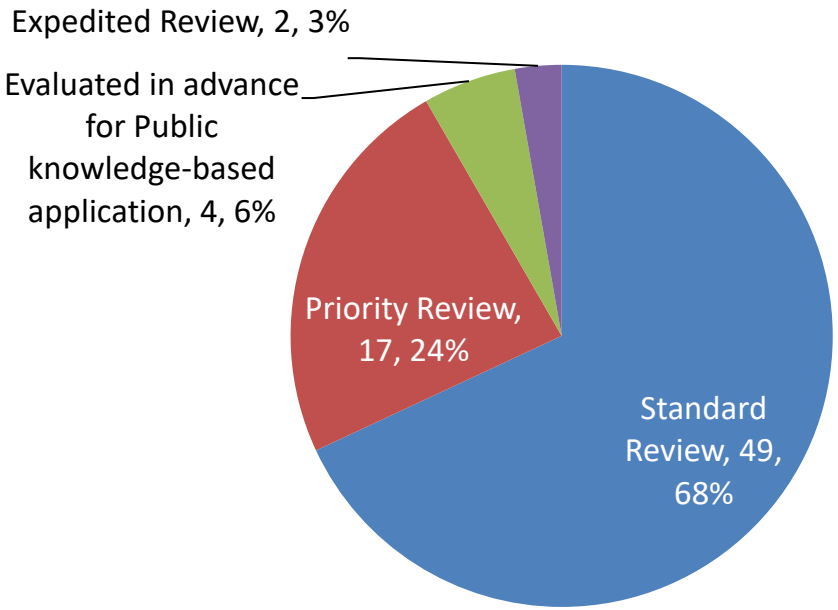
Drug Modalities in FY2024 (N=72)



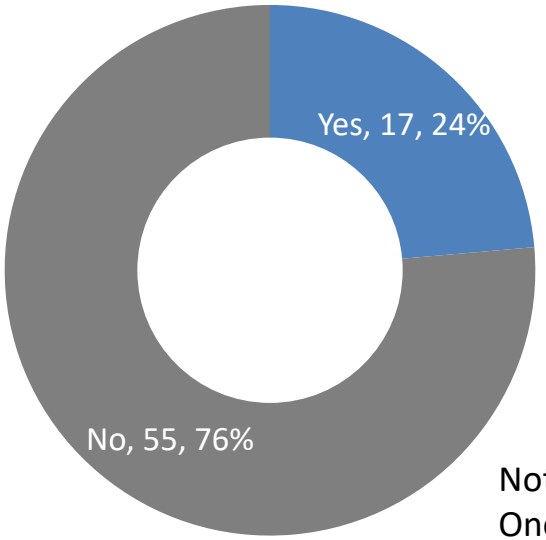
- "New indication" (34/72; 47%) accounted for the largest proportion in FY2024.
- The number of biological products (40/72; 56%) further increased in FY2024.
- 31 of the 72 approved products (43%) were for oncology (the largest divisional category, as it was last year).

Utilization of Expedited Program

Review Category (N=72)

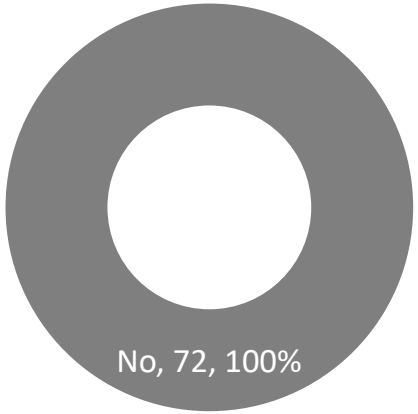


Orphan (N=72)

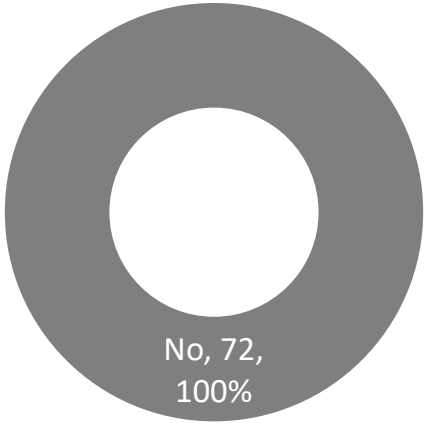


Note:
Oncology: 9/17
Non-oncology: 8/17

Sakigake (N=72)



Conditional Early Approval (N=72)

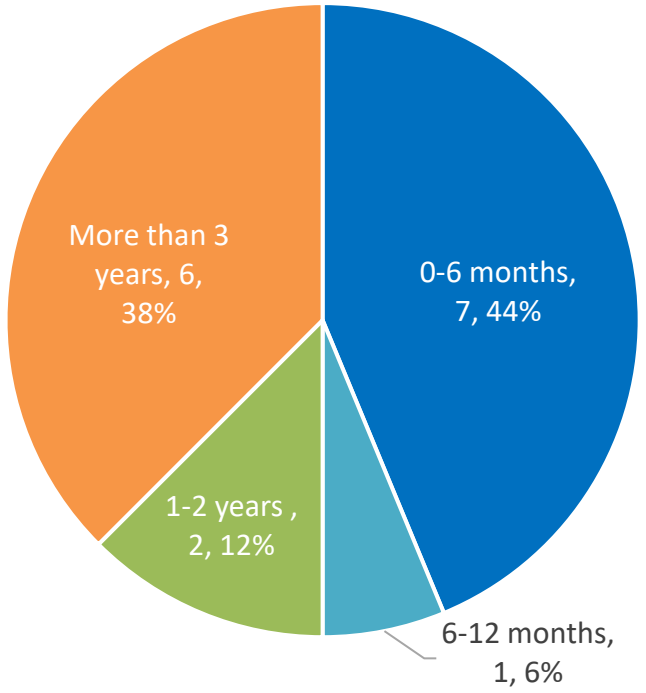


- In FY2024, 17 products (24%) were approved through the Priority Review through the Orphan Drug Review.
- There was no product approved under the Sakigake pathway; none were approved through Conditional Approval.

Orphan Drug Designation

Timing of Orphan Drug Designation (N=17)

From orhan designation to JNDA



- New active ingredient: 2
- New indication: 5

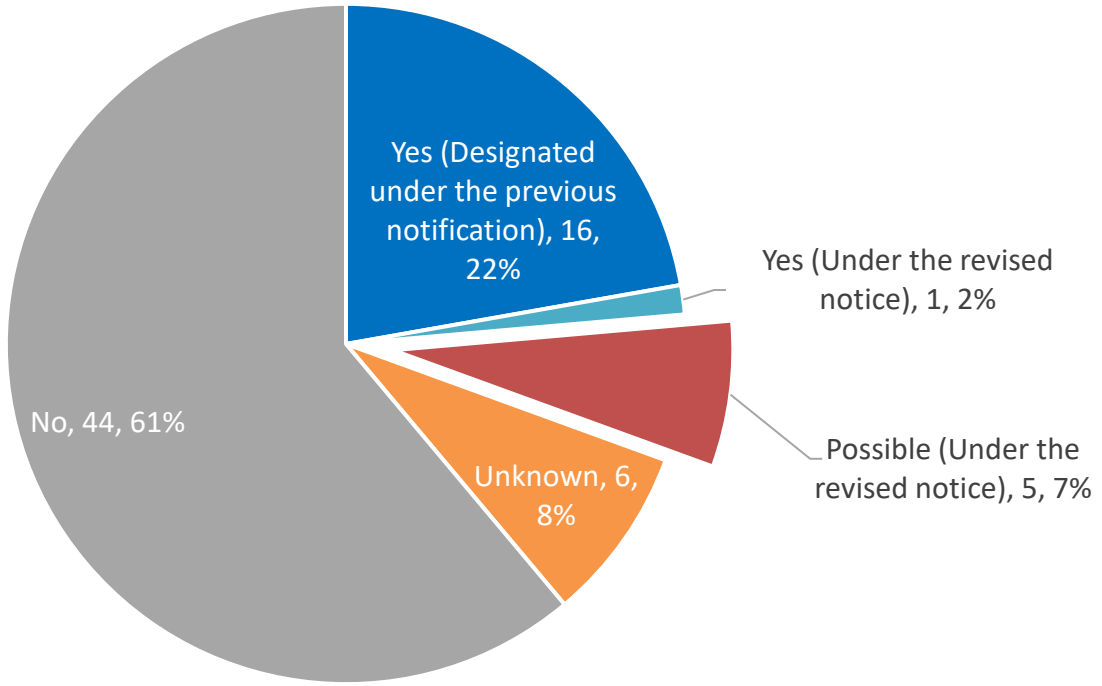
- New active ingredient: 1

Note: JNDA category (N=17)
- New active ingredient: 5
- New indication: 10
- New dosage: 2

- In FY2024, approximately half of the approved products received Orphan Drug designation within one year of their approval application.

Impact of the Revised Notice on Orphan Designation (N=72)

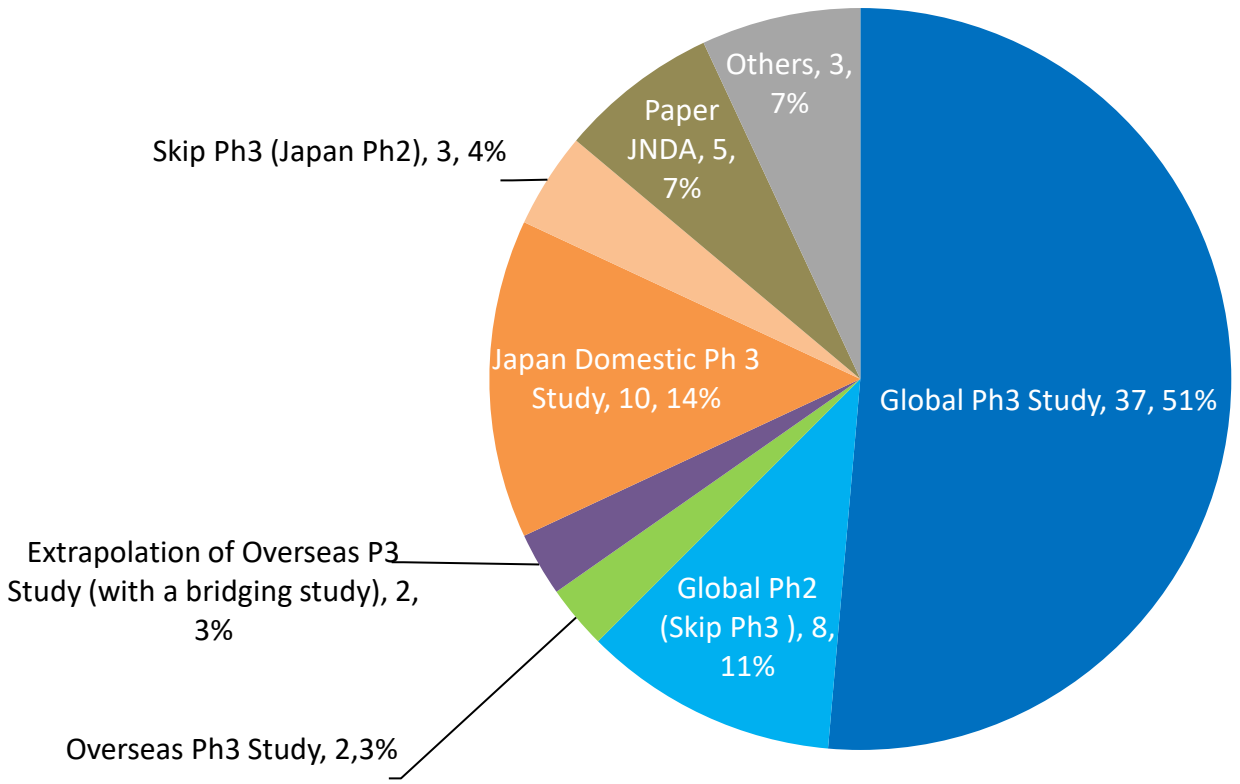
According to the revised notice on the designation of orphan drugs on January 16, 2024, could it be considered an orphan drugs?



- Under the revised notice, 1 product was additionally approved with orphan drug designation.
- 5 additional approved products (7%) would have the potential to meet the criteria of the orphan drug designation under the revised notice.
- The revised notice on the designation of orphan drugs (issued on Jan 16 ,2024) may lead to an increase in the earlier designation of orphan drugs in the future.

Clinical Data Package

Pivotal Study in Clinical Data Packages (N=72)



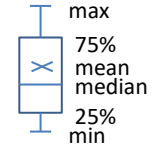
Pivotal study in Clinical Data Package were:

1) mainly “Global study (Ph3 or Ph2 study)”: 45 cases; 62% (FY2023: 69%)
2) “Japan Domestic Study”: 10 cases; 14% (FY2023: 16%)
3) “Extrapolation of Overseas Study with a bridging study”: 2 cases; 3% (FY2023: 7%)

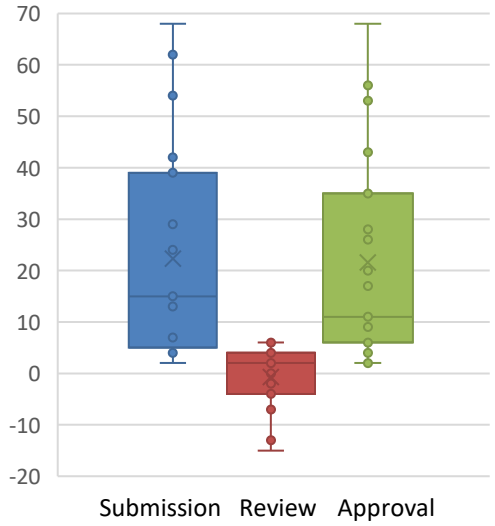
Submission/Review/Approval Lag

Submission / Review / Approval Lag (vs. US** & vs. EU***)

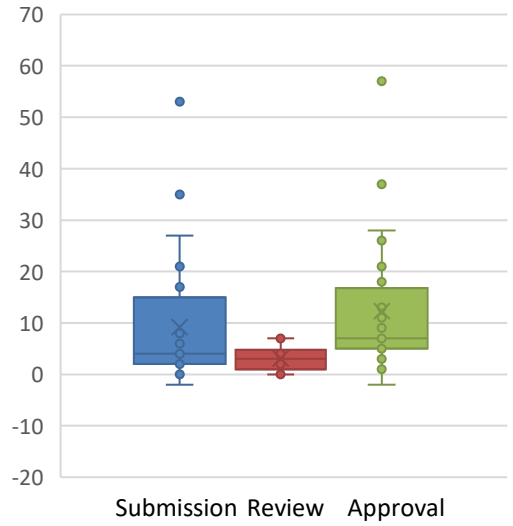
** approved in US *** approved in EU incl. UK



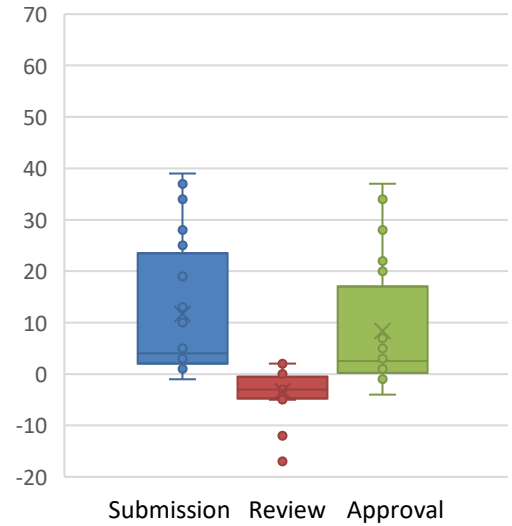
(Months) NMEs (vs. US) *1*2*3*4
N=19



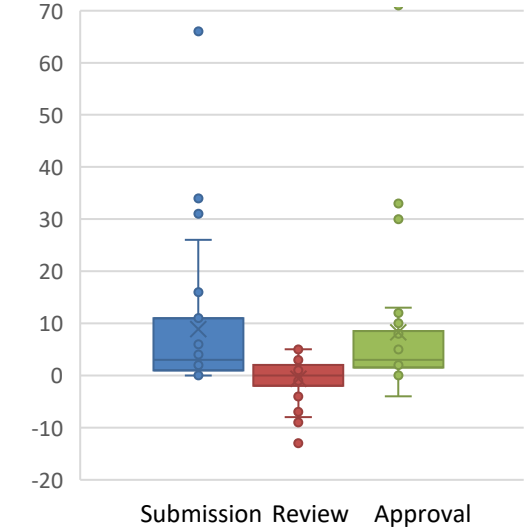
(Months) LCMs (vs. US) *1*2*4
N=32



(Months) NMEs (vs. EU) *3*5
N=20



(Months) LCMs (vs. EU) *4*6
N=29



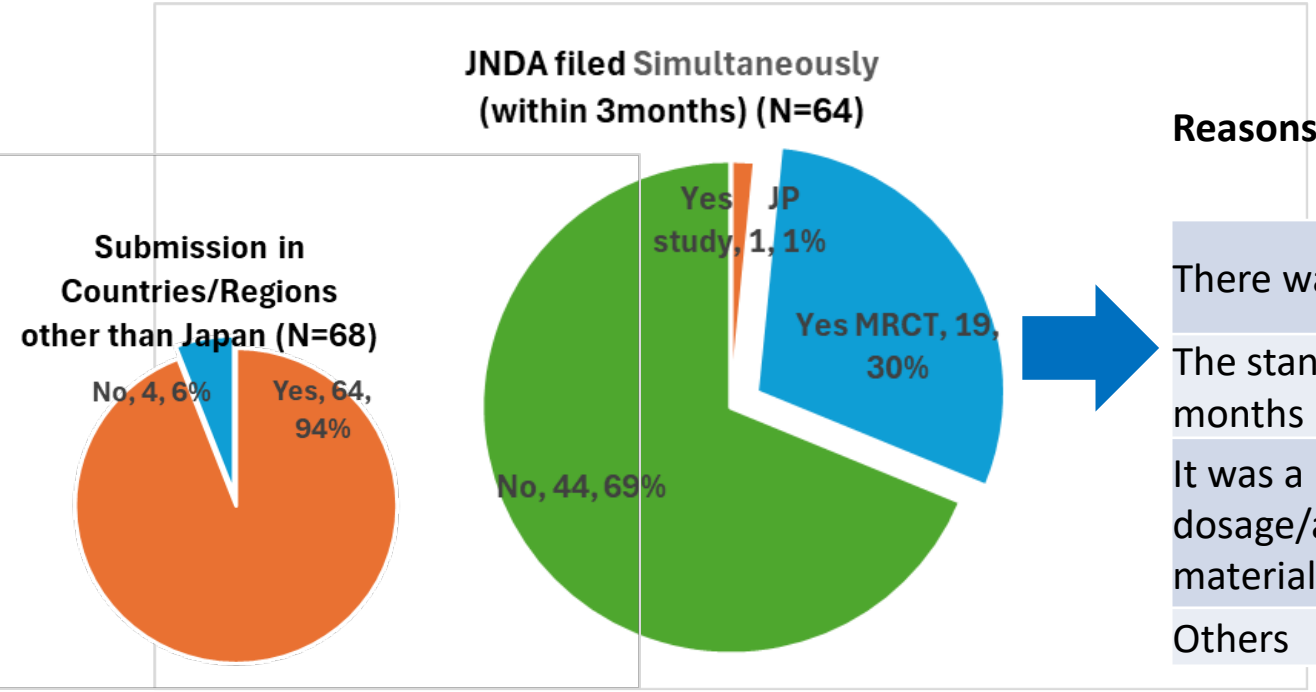
*1 NME is defined as “new active ingredient” in category of J-NDA and LCM (Life Cycle Management) is defined as other categories.
*2 Exclude 2 cases under review in US
*3 Exclude 3 cases of submission/approval date unknown
*4 Exclude 2 cases of ＞100 months of submission/approval lag

*5 Exclude 2 cases of ＞100 months and around 100 months of submission/approval lag
*6 Exclude 3 cases under review in EU
Note: Calculated with 30 days per month

- The following trends were observed, which were similar to those in FY2023.
  - Review duration lag tends to be limited.
  - Overall, submission lag is presumed to be the main reason for approval lag.
- For NMEs (vs. US), submission/approval lag (median and mean) was greater than that for FY2023, which is because the number of products with a large lag increased.

Evaluation of Submission Lag

Simultaneous J-NDA Filing within 3 Months

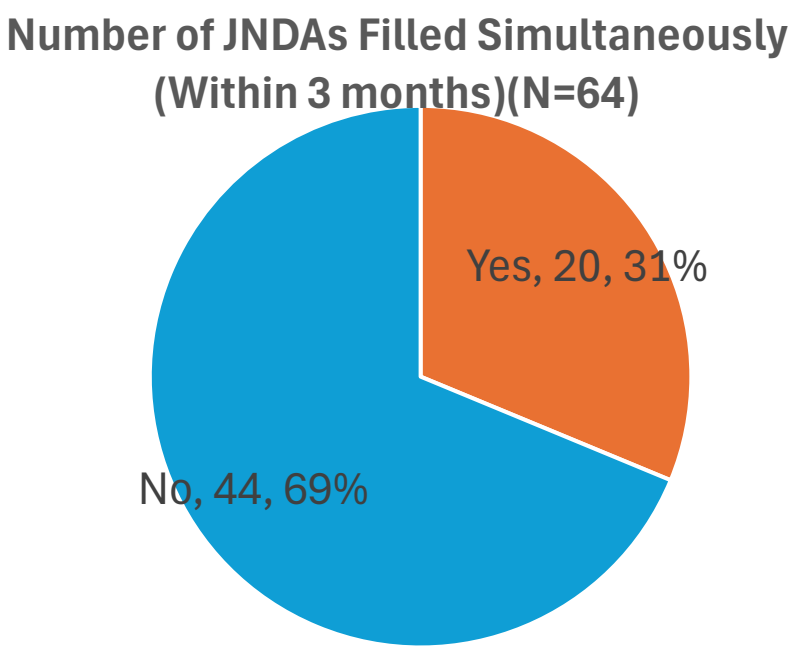


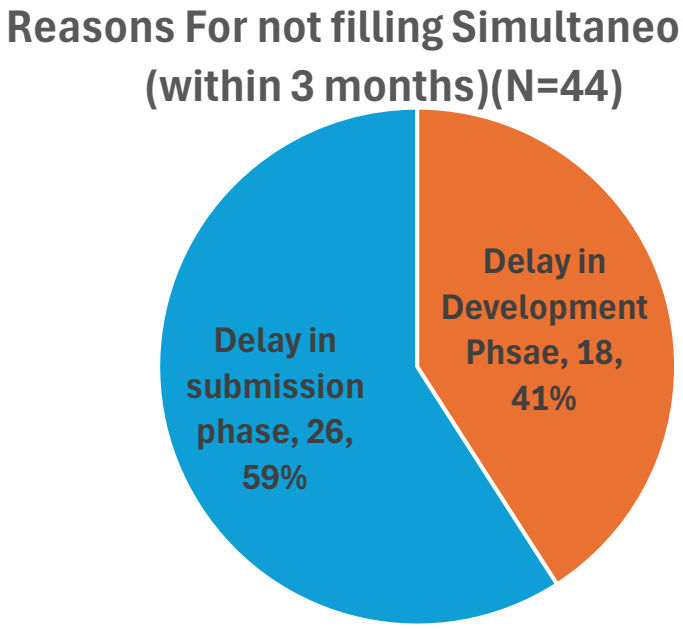
Reasons for Simultaneous J-NDA Filing (within 3 months) based on MRCTs (N=19; multiple answers allowed)

There was a business decision to prioritize Japan	16 (84%)
The standard process that allows the application within 3 months has been established	17 (89%)
It was a partial change application for the indication and dosage/administration, and there was no need to prepare materials for Japan such as CMC	7 (37%)
Others	1 (5%)

- Of the 64 products that achieved or planned submission globally, 20 J-NDAs (31%) were filed first in JP or simultaneously.
- Primary reasons for these simultaneous applications tend to be the same as last year; “there was a business decision to prioritize Japan” (16 cases, 84%) and “the standard process that allows the application within 3 months has been established” (17 cases, 89% of the applications).
- Seven cases (37%) were partial change applications which need no preparation of materials for Japan such as CMC.

Simultaneous J-NDA Filing: Submission Lag More than 3 Months





- Of the 64 products that achieved or planned submission/approval globally, 44 J-NDAs (69%) were **NOT** filed simultaneously.
- Reasons for not filing simultaneously (i.e., within three months) consist of “delays in the submission phase” in 26 cases (59%), which decreased from 21 (70%), and “delays in the development phase” in 18 cases (41%), which increased from 9 (30%), compared to the previous year.

Simultaneous J-NDA Filing: Submission Lag More than 3 months

Reasons for the Delay in Development Phase (N=18: multiple answers allowed)

Japan was unable to join the MRCT (verification study) as it had been already started	6 (33%)
Already approved overseas	5 (28%)
Did not consider Japan development due to license-in product	5 (28%)
Japanese phase 1 study became necessary before joining MRCT	2 (11%)
Japanese dose-finding study became necessary before joining MRCT	1 (11%)
Others	6 (33%)

Reasons for the Delay in Submission Phase (N=26: multiple answers allowed)

Business strategy	11 (42%)
Preparation of Japanese Module 2.3 or approval application	7 (27%)
Interim results were not accepted	2 (8%)
Expedited review in overseas	2 (8%)
Conducted additional analysis for consideration of consistency between Japanese and entire population	1 (4%)
Preparation of tables for CTD	1 (4%)
Preparation time for e-data submission	1 (4%)
Waited for stability test results	1 (4%)
Waited for long-term safety data	0 (0%)
Others	8 (31%)

Main reasons for the delays were:

- Development phase: “unable to join MRCT” in 6 cases (33%), “already approved overseas” and “licensed-in product” in 5 cases (28%)
- Submission phase: not limited to technical/regulatory ones. Submission lags could derive from business/strategic decisions in certain cases.

Simplification of internal processes such as development planning, CTD preparation and review contributed to minimization of the submission lag. Reduction/elimination of Japan-specific requirements related to expansion of scope/acceptance of CTD written in English, CMC, and CDx were suggested as one of the possible measures to promote simultaneous submissions.

Utilization of Expedited Approval Pathways/Novel Regulatory Programs

Utilization of Expedited Approval Pathways/Novel Regulatory Programs (Oncology)

NME (N=12)	Japan		US								EU					Review Period (Mo)		
	PR	ODD	BTD	AA	FT	PR	ODD	RTOR	AAid	Orbis	PRIME	AA	CMA	EC	ODD	Japan	US	EU
1																11	8	11
2	✓			✓						✓		✓				8	23	8
3				✓									✓			11	5	15
4				✓		✓	✓						✓			12	8	17
5	✓	✓	✓			✓	✓		✓	✓	✓		✓		✓	7	10	7
6							✓									13	10	16
7				✓		✓	✓						✓		✓	9	NA	NA
8			✓	✓												13	7	11
9	✓	✓	✓	✓			✓	✓	✓	✓						7	7	NA
10								✓	✓							11	8	14
11					✓		✓								✓	9	15	14
12				✓				✓		✓						10	6	8

PR: Priority Review, ODD: Orphan Drug Designation, BTD: Breakthrough Therapy Designation, AA: Accelerated Approval (US); Accelerated Assessment (EU), FT: Fast Track, RTOR: Real-Time Oncology Review, AAid: .Assessment Aid, PRIME: Priority Medicines, CMA: Conditional Marketing Authorisation, EC: Exceptional Circumstances , NA: Not Applied

Utilization of Expedited Approval Pathways/Novel Regulatory Programs (Oncology)

LCM (N=19)	Japan		US								EU					Review Period (Mo)		
	PR	ODD	BTD	AA	FT	PR	ODD	RTOR	AAid	Orbis	PRIME	AA	CMA	EC	ODD	Japan	US	EU
1																12	Under Review	10
2	✓		✓			✓		✓	✓	✓						8	1	7
3																8	NA	NA
4	✓	✓	✓			✓			✓	✓					✓	8	7	16
5	✓	✓				✓										9	6	12
6										✓						12	9	8
7								✓		✓						11	10	12
8								✓		✓						11	7	6
9	✓	✓	✓			✓			✓	✓					✓	8	7	14
10																11	8	10
11	✓	✓	✓			✓	✓		✓	✓						8	6	8
12																9	NA	NA
13			✓			✓			✓							11	6	NA
14	✓	✓		✓			✓								✓	8	4	17
15																12	8	10
16	✓	✓				✓	✓	✓		✓						8	5	7
17	✓	✓				✓				✓						8	6	7
18			✓	✓					✓				✓		✓	11	6	9
19						✓	✓								✓	9	6	10

PR: Priority Review, ODD: Orphan Drug Designation, BTD: Breakthrough Therapy Designation, AA: Accelerated Approval (US); Accelerated Assessment (EU), FT: Fast Track, RTOR: Real-Time Oncology Review, AAid: .Assessment Aid, PRIME: Priority Medicines, CMA: Conditional Marketing Authorisation, EC: Exceptional Circumstances , NA: Not Applied

Utilization of Expedited Approval Pathways/Novel Regulatory Programs (Non-Oncology)

NME (N=15)	Japan		US					EU					Review Period (Mo)		
	PR	ODD	BTD	AA	FT	PR	ODD	PRIME	AA	CMA	EC	ODD	Japan	US	EU
1	✓	✓					✓						8	15	25
2													12	NA	NA
3	✓	✓	✓		✓	✓	✓						8	6	NA
4													11	13	12
5							✓						10	12	13
6													10	6	12
7			✓		✓	✓	✓		✓	✓		✓	14	8	15
8									✓				5	NA	7
9			✓			✓	✓	✓				✓	10	8	13
10													12	NA	NA
11												✓	11	12	13
12			✓		✓								13	26	15
13													10	Under Review	13
14							✓					✓	12	Under Review	17
15	✓	✓		✓		✓	✓				✓	✓	7	11	19

PR: Priority Review, ODD: Orphan Drug Designation, BTD: Breakthrough Therapy Designation, AA: Accelerated Approval (US); Accelerated Assessment (EU), FT: Fast Track, PRIME: Priority Medicines, CMA: Conditional Marketing Authorisation, EC: Exceptional Circumstances, NA: Not Applied

Utilization of Expedited Approval Pathways/Novel Regulatory Programs (Non-Oncology)

LCM (N=26)	Japan		US					EU					Review Period (Mo)		
	PR	ODD	BTD	AA	FT	PR	ODD	PRIME	AA	CMA	EC	ODD	Japan	US	EU
1													13	6	NA
2						✓	✓					✓	13	6	8
3													10	NA	NA
4						✓							11	9	8
5	✓	✓				✓	✓					✓	9	5	Under Review
6	✓	✓				✓							7	6	20
7						✓							11	6	Under Review
8													12	NA	NA
9	✓	✓											7	NA	14
10			✓	✓		✓							11	8	12
11		✓					✓						10	6	8
12													4	NA	NA
13													10	NA	NA
14													10	10	10
15													11	10	11
16													11	Under Review	Under Review
17													15	12	14
18													10	10	10
19													11	10	15
20					✓								10	5	9
21													6	NA	NA
22				✓		✓							11	6	8
23													11	10	NA
24													12	10	13
25		✓											6	NA	NA
26							✓						11	12	6

PR: Priority Review, ODD: Orphan Drug Designation, BTD: Breakthrough Therapy Designation, AA: Accelerated Approval (US); Accelerated Assessment (EU), FT: Fast Track, PRIME: Priority Medicines, CMA: Conditional Marketing Authorisation, EC: Exceptional Circumstances, NA: Not Applied

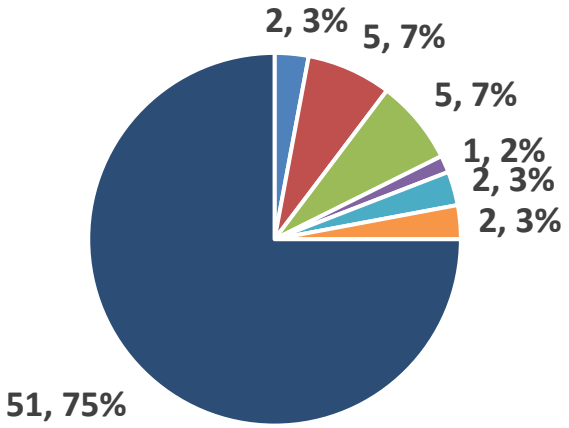
Findings

- Almost all products which received priority reviews in Japan were designated as orphan drugs
- Expedited program is widely granted to oncology projects by FDA resulting in a review lag between Japan and the U.S.
- EU's expedited review system was not widely utilized compared to the U.S. and Japan
- Review gap with more than a 4-month b/w US and Japan is
  - Oncology: 16%(5/31) {This is an improvement compared to last year.（last year 38% (5/13)）}
  - Non-oncology: 15%(6/41) {This is almost the same as last year.（last year 9 % (8/43)）}

Pediatric Development

Pediatric Development

Target of the approved indication (N=68)

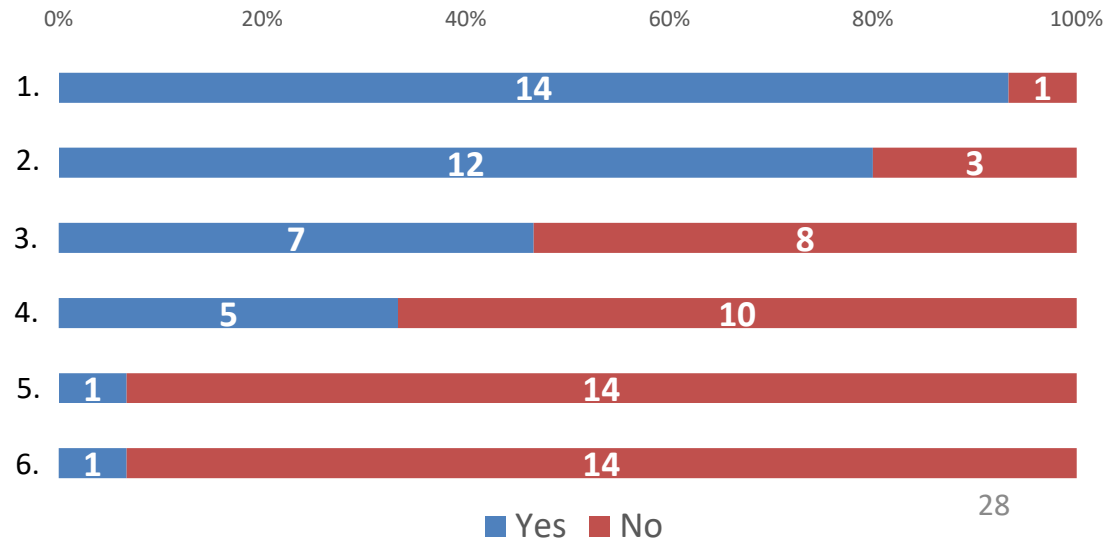


- ＜12 years old children only
- Children only (incl. adolescents [12-17 years old])
- Adults and children (incl. adolescents)
- Adults and adolescents
- Adults and ＜12 years old children
- Adults only (already approved for at least either of ＜12 years old children and adolescents)
- Adults only (Not approved for children or adolescents)

(N=15)

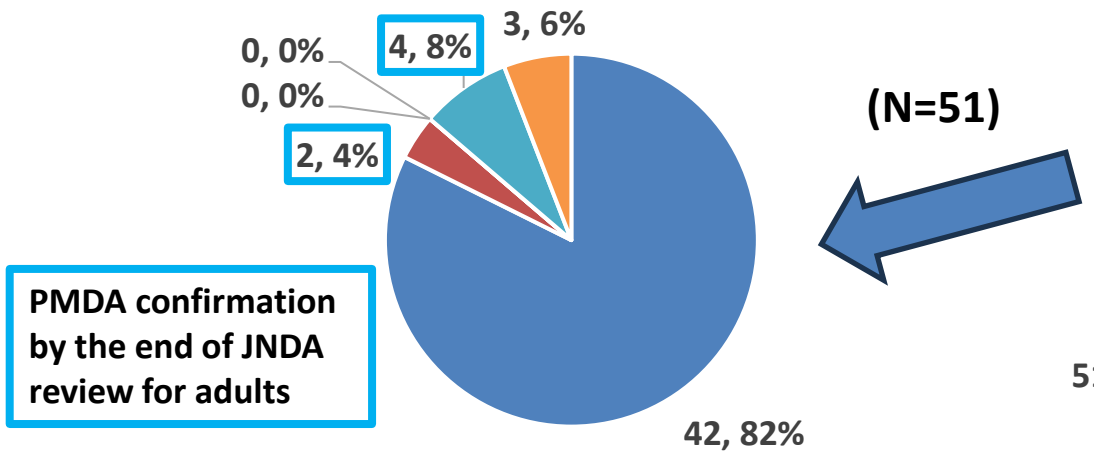
The reason of development for pediatrics (multiple answers allowed)

1. For therapies (drugs) for diseases including children
2. To align with the global development schedule
3. For therapies (drugs) that can be evaluated with adults
4. Because the pediatric premium can be obtained
5. Because the re-examination period for adults can be expected to be extended
6. Because the request from the Evaluation Committee on Unapproved or Off-label Drugs or academic societies, etc.



Pediatric Development

Planning of pediatric development of approved indication only for adults



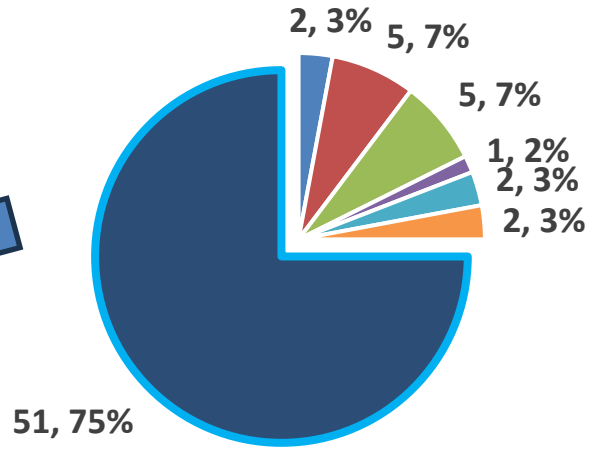
PMDA confirmation by the end of JNDA review for adults

- No plan for pediatric development
- Pediatric development is planned with PMDA confirmation at End of Phase 2 consultation for pediatric drug development＊1
- Pediatric development is planned with PMDA confirmation on Consultation on Confirmation of the Pediatric Drug Development Program
- Pediatric development is planned with PMDA confirmation on the other consultation (except for the above two consultations)
- Pediatric development is planned with PMDA confirmation in CTD M1.5 of JNDA review for adults
- Pediatric development is planned without PMDA confirmation by the end of JNDA review for adults

＊1 presumed from the timing of JNDA for adults

(N=51)

Target of the approved indication (N=68)



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- 15 (22%) of the 68 products were approved including pediatric use, with disease characteristics and global development being the primary reasons for pediatric development.
- Of the 68 products, 51 (75%) have only been approved for adults. 9 of the 51 products are planning for pediatric use, and 6 products have received PMDA confirmation about the plan by the end of JNDA review for adults (FY2023: 0 product).
- Since the products of JNDA were submitted before or shortly after the notification ＊2 was issued, the impact of the notification is considered to be limited, but it is expected to promote pediatric development from an earlier stage of development in the future.

＊2 Notice on the pediatric drug development issued on Mar 29 ,2024