
R&D Head Club Survey in 2021 additional research 2022

NDA Lag

- Survey in RDHC member companies -

April 2023

CT Performance Survey Working Group

In this document, NDA (New Drug Application) refers to the marketing application of a drug, and MAA (Marketing Authorization Application) is a synonymous term.

- This report has been prepared a result of research conducted by member companies of R&D Head Club for research discussion.
- This report is current as of April 2023 and will be updated if any corrections are made.
- Costs related to this report were borne by R&D Head Club.
- See page 26 for the secondary use of this document.

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(alphabetical order)

1. Survey Overview (1)

[Objective]

Confirm the timing of NDA in Japan (application lag)

- There are multiple comparative data of drug lag (date of marketing approval) in Japan, but data showing application lag are limited.
- Since the comparison of the date of marketing approval includes the review period, it is important for pharmaceutical companies to compare the NDA lag focusing on the date of application.
- Since concurrent application in the US or Europe and Japan or preceding application in Japan is expected in the future, it is beneficial to confirm the past data as a benchmark.
- Partial disclosure will contribute to the further acceleration of drug development in Japan.

[Objective of the additional survey in 2022: To investigate the influential factors in the analysis of 2021 NDA Lag survey]

1. Whether global simultaneous development [simultaneous application] was scheduled at the time of planning the development (NDA lag is expected to differ depending on the development strategy. It is a key performance factor.)
2. [For global simultaneous development] Whether additional studies, etc. are conducted in Japan after the pivotal studies in Europe and the US (confirm the actual status because the NDA lag will be extended by additional studies, etc.)

[Participating companies]

Investigation requested to 20 member companies of R & D Head Club [Table 1]

[Period]

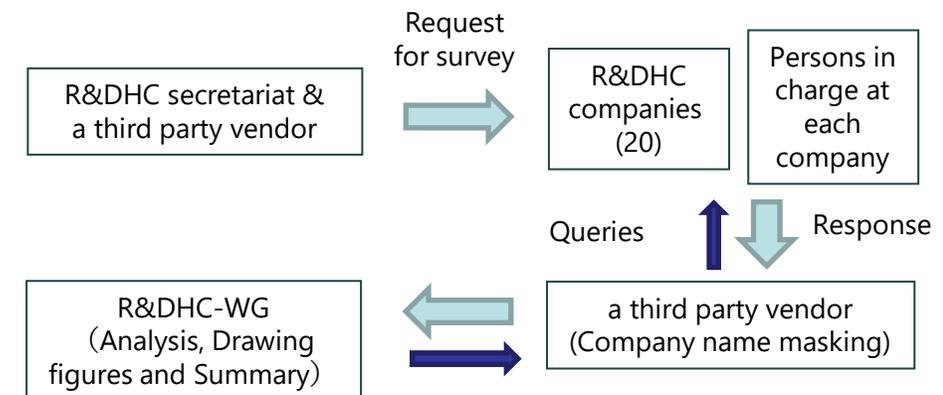
2021 survey: Aug 6 (Fri) - Sep 10 (Fri), 2021

2022 additional survey: Nov 2 (Wed) - Nov 18 (Fri), 2022

[Implementation method]

Questionnaire survey by Excel data collection

Company name, etc. is masked so that the responding company will not be identified by a third party vendor



1. Survey Overview (2)

[Subjects]

Projects where the NDA was submitted by the company to MHLW between Apr 1, 2016 and Mar 31, 2021

- ✓ Survey on the past 5 years
- ✓ including NDA for additional indication
- ✓ Projects for which NDA is submitted in Japan only (projects for which NDA has not been submitted in countries other than Japan at the time of inspection) are excluded

[2022 additional survey]

- No changes in the subjects of the survey.
- If omission of submission was found in the 2021 survey, submission of data was requested.
- If error was found in the data submitted for the 2021 survey, submission of corrected data was requested.

1. Survey Overview (3)

[Survey details] [(1) to (7) are survey items for 2021]

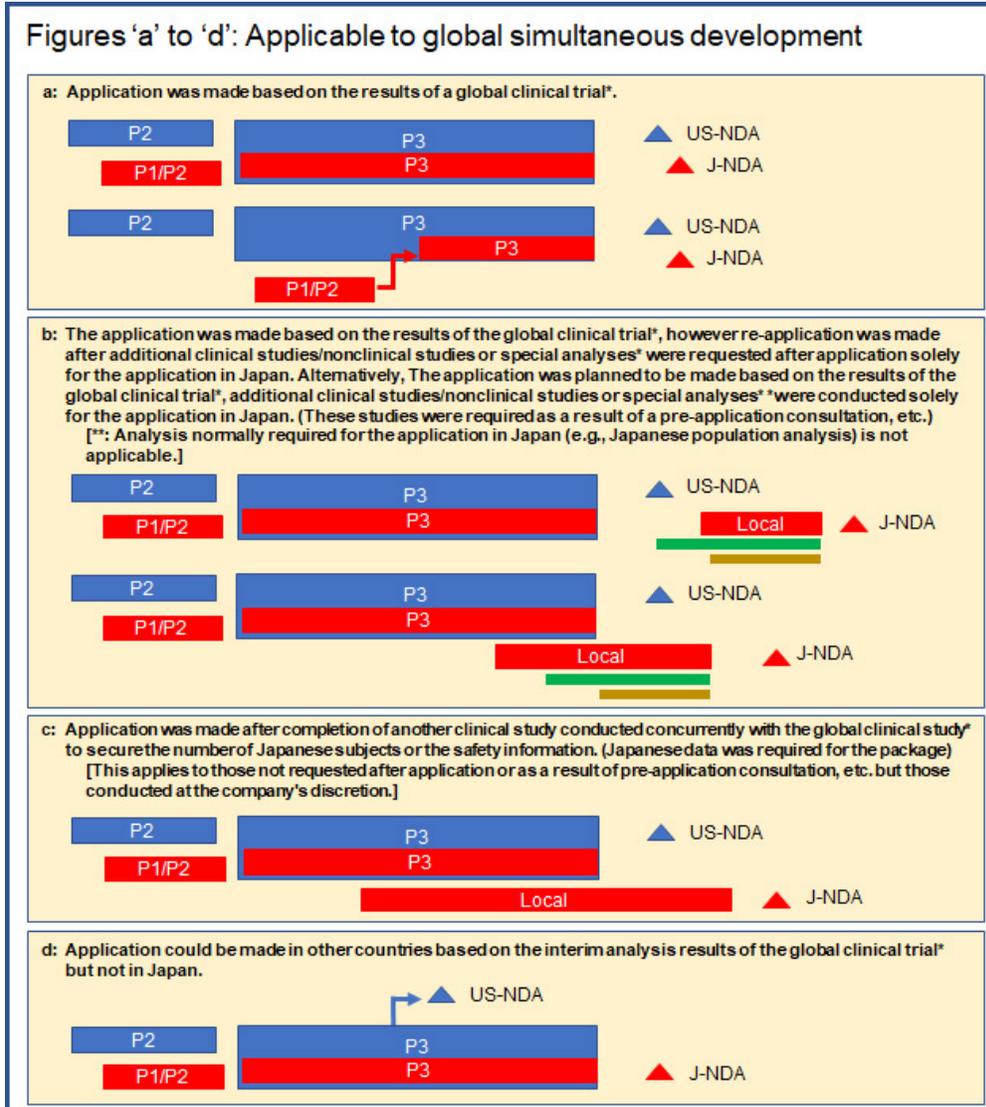
- (1) J-NDA or J-sNDA [NDA date in Japan]
- (2) G-NDA (MAA) or G-sNDA (sMAA) [Initial NDA date globally excluding Japan]
- (3) Country name [Country of the first NDA (MAA) globally excluding Japan]
- (4) If "EU" or "Other" is selected for (3), enter the country name
- (5) Target disease area
[Options: Infection, malignancy (cancer), musculoskeletal disorder, neuropsychiatric disorder, gastrointestinal/metabolic (including diabetes mellitus) disorder, cardiovascular disorder, respiratory disorder, other]
- (6) NME (New Molecular Entity) / Non-NME*
*: New ethical combination drug, drug with a new route of administration, drug with a new indication, drug with a new dosage form, drug with a new dosage, biosimilar drug, ethical combination drug with similar formulation, etc.
- (7) If "Non-NME" is selected for (6), select all that apply.
[Options: additional indication, additional indication (public knowledge-based application), additional dosage and administration, new combination drug, new route of administration, additional dosage form, biosimilar drug, other]

[2022 additional survey]

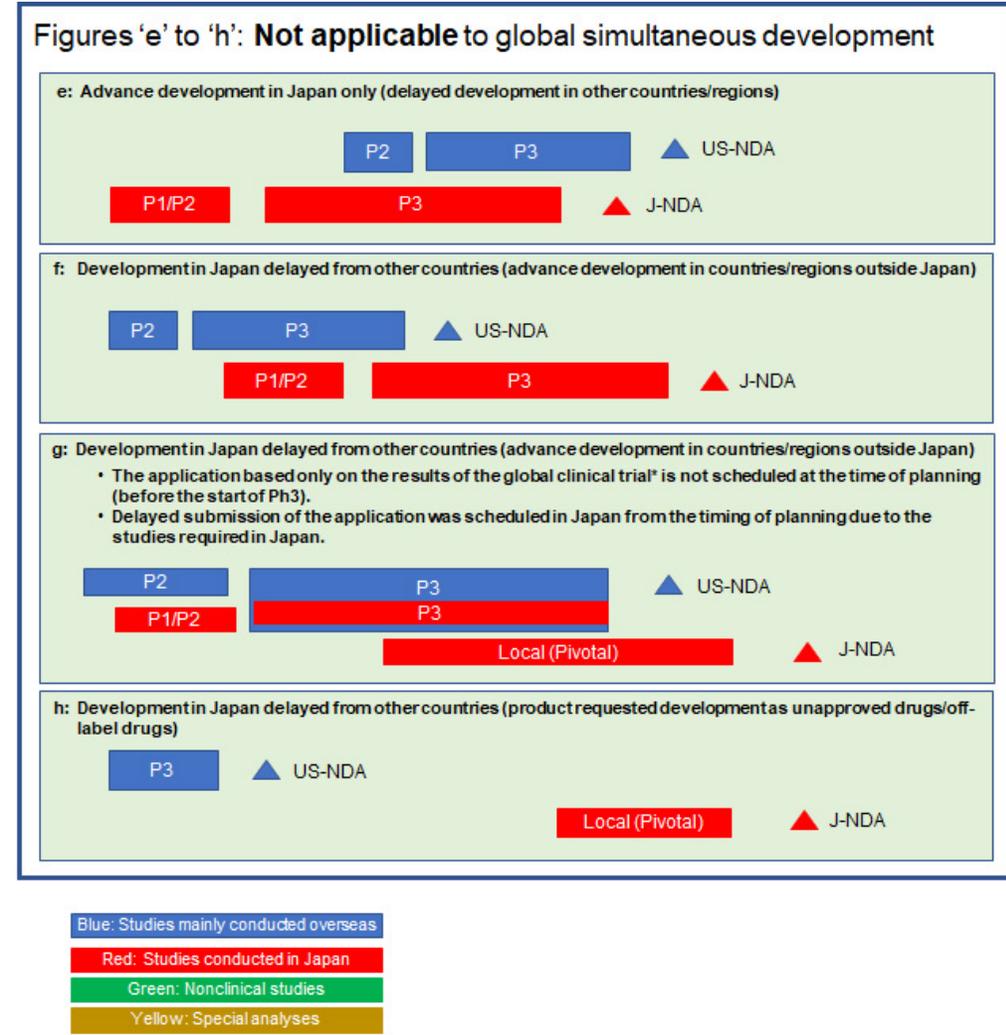
- Additional survey 1) Development strategy [Options: global simultaneous development, not applicable to global simultaneous development, other]
- Additional survey 2) If "global simultaneous development" is selected for Additional survey 1), select the relevant figure [Options: See page 6]
- Additional survey 3) If "b" is selected in Additional survey 2), select the requested/required item [Options: clinical study, nonclinical study, special analysis, unknown]
- Additional survey 4) If "not applicable to global simultaneous development" is selected for Additional survey 1), select the relevant figure [Options: See page 6]
- Additional survey 5) Attribute (origin) [Options: In-house item, license-in item (1), license-in item (2), license-in item (3), license-in item (4)]
- Additional survey 6) Low molecular, bio, etc. [Options: low molecular products, bio products, vaccines, other]

1. Survey Overview (4)

Additional survey 2) Options



Additional survey 4) Options



*: Global clinical studies that are positioned as pivotal studies globally

1. Survey Overview (5)

Table 1: R&D Head Club Companies (2021/2022) List

	Company Name		Company Name
1	AbbVie GK	11	Janssen Pharmaceutical K.K.
2	Amgen K.K.	12	Japan Tobacco Inc.
3	Astellas Pharma Inc.	13	MSD K.K.
4	AstraZeneca K.K.	14	Nippon Boehringer Ingelheim Co., Ltd.
5	Bristol-Myers Squibb K.K.	15	Novartis Pharma K.K.
6	Chugai Pharmaceutical Co., Ltd.	16	Otsuka Pharmaceutical Co., Ltd.
7	Daiichi Sankyo Co., Ltd..	17	Pfizer R&D Japan G.K.
8	Eisai Co., Ltd.	18	Sanofi K.K.
9	Eli Lilly Japan K.K.	19	Shionogi & Co., Ltd.
10	GlaxoSmithKline K.K.	20	Takeda Pharmaceutical Co., Ltd.

(alphabetical order)

2. Investigation results [2022 additional survey]

Table 2: Background

Number of responses	246	
Number tabulated	214	<ul style="list-style-type: none"> Additional submission in 2022 survey: 1
Number not tabulated	32	<ul style="list-style-type: none"> Difference in the number of days cannot be calculated as [Initial NDA date globally excluding Japan] is "unknown": 20* Product requested development as unapproved drugs/off-label drugs: 9* (*: 1 duplicate) Not approved in countries other than Japan at the time of survey: 2 Medical device (this investigation is limited to drugs): 1 Additional submission in the 2022 survey but was out of the scope of the survey period: 1

Number tabulated		214
NDA fiscal year	2016	33 (15.4%)
	2017	43 (20.1%)
	2018	53 (24.8%)
	2019	46 (21.5%)
	2020	39 (18.2%)
NME/ non-NME	NME	70 (32.7%)
	non-NME	144 (67.3%)
Development strategy at the time of planning development	Global simultaneous development	159 (74.3%)
	Not applicable to global simultaneous development	51 (23.8%)
	Other	4 (1.9%)

Number tabulated		214
Disease area	Infection	15 (7.0%)
	Malignancy (cancer)	105 (49.1%)
	Musculoskeletal disorder	6 (2.8%)
	Neuropsychiatric disorder	11 (5.1%)
	Gastrointestinal and metabolic disorder	17 (7.9%)
	Cardiovascular disorder	11 (5.1%)
	Respiratory disorder	17 (7.9%)
	Other	32 (15.0%)

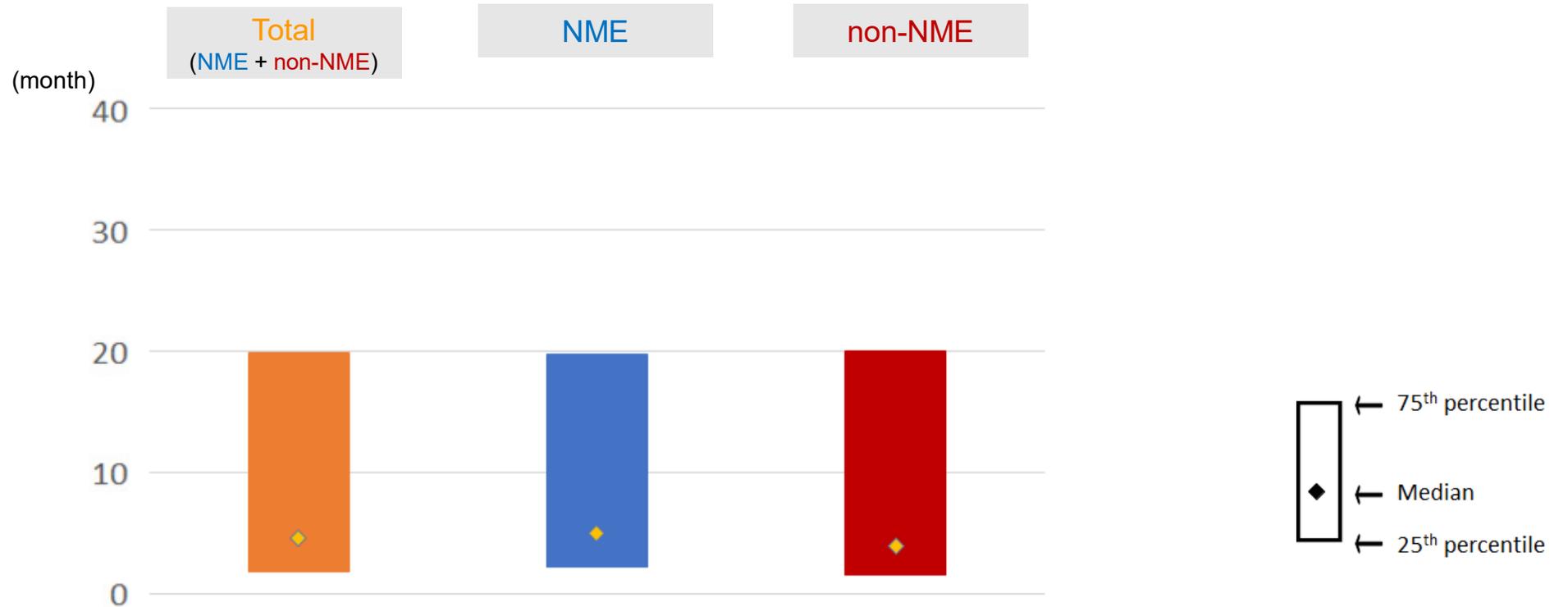
NME: New Molecular Entity

Non-NME** (**: New ethical combination drug, drug with a new route of administration, drug with a new indication, drug with a new dosage form, drug with a new dosage, biosimilar drug, ethical combination drug with similar formulation, etc.)

2. Investigation results

Figure 2-1: NDA lag comparison [NME / non-NME]

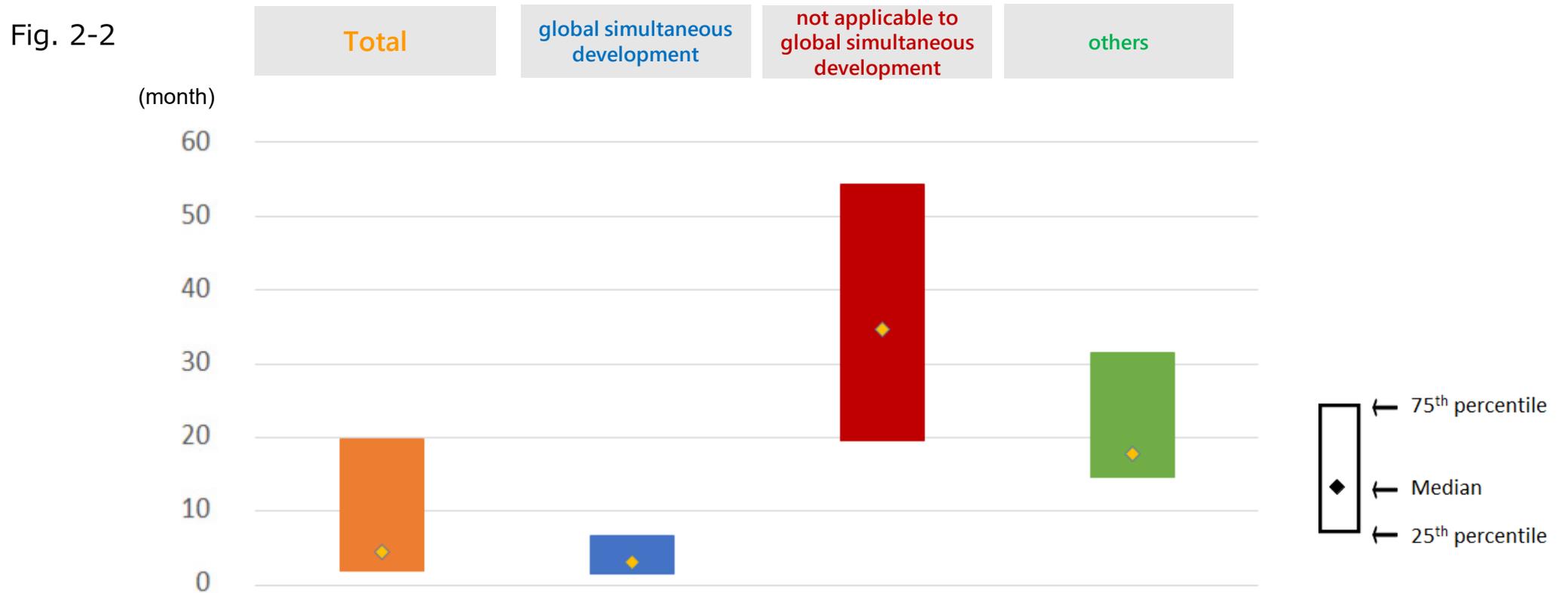
Fig. 2-1



	Total	NME	Non-NME
n	214	70	144
Median (month)	4.59	5.04	3.96
25th percentile (month)	1.91	2.30	1.64
75th percentile (month)	19.87	19.75	20.04

2. Investigation results

Figure 2-2: NDA lag comparison [global simultaneous development / not applicable to global simultaneous development]

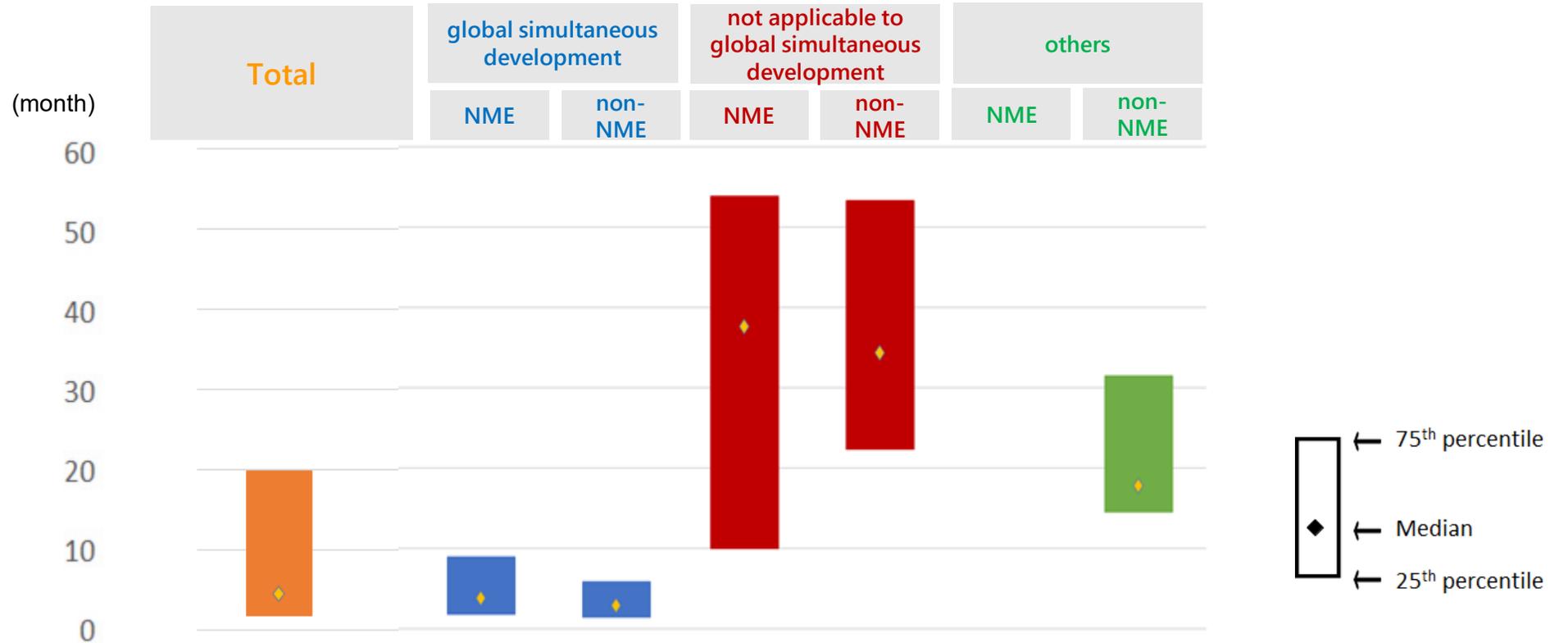


	Total	global simultaneous development	not applicable to global simultaneous development	others
n	214	159	51	4
Median (month)	4.59	3.12	34.74	17.88
25th percentile (month)	1.91	1.51	19.59	14.58
75th percentile (month)	19.87	6.66	54.31	31.40

2. Investigation results

Figure 2-3: NDA lag comparison [global simultaneous development / not applicable to global simultaneous development × NME / non-NME]

Fig. 2-3

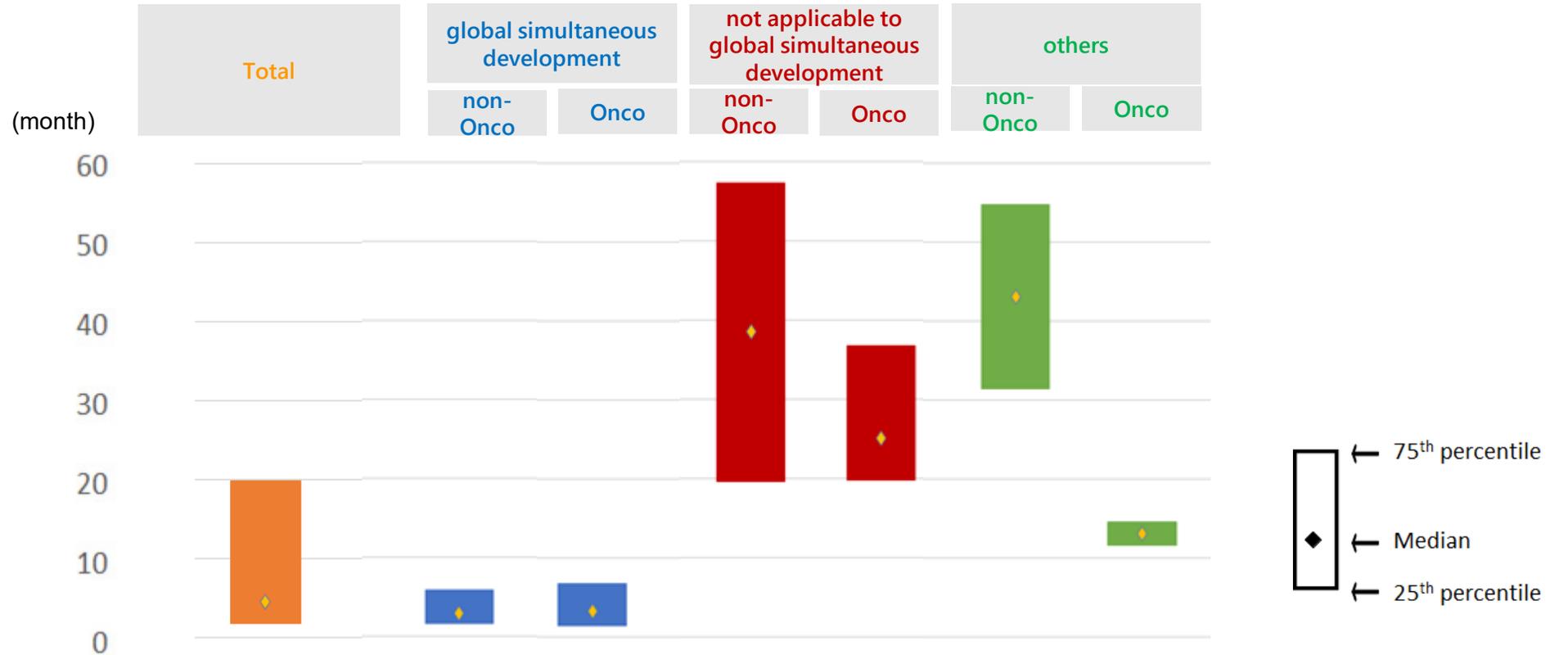


	Total	global simultaneous development		not applicable to global simultaneous development		others	
		NME	Non-NME	NME	Non-NME	NME	Non-NME
n	214	50	109	20	31	-	4
Median (month)	4.59	3.82	2.99	37.64	34.47	-	17.88
25th percentile (month)	1.91	1.89	1.48	10.06	22.39	-	14.58
75th percentile (month)	19.87	8.93	5.86	53.75	53.24	-	31.40

2. Investigation results

Figure 3-2: NDA lag comparison [global simultaneous development / not applicable to global simultaneous development
× non-oncology drugs / oncology drugs]

Fig. 3-2

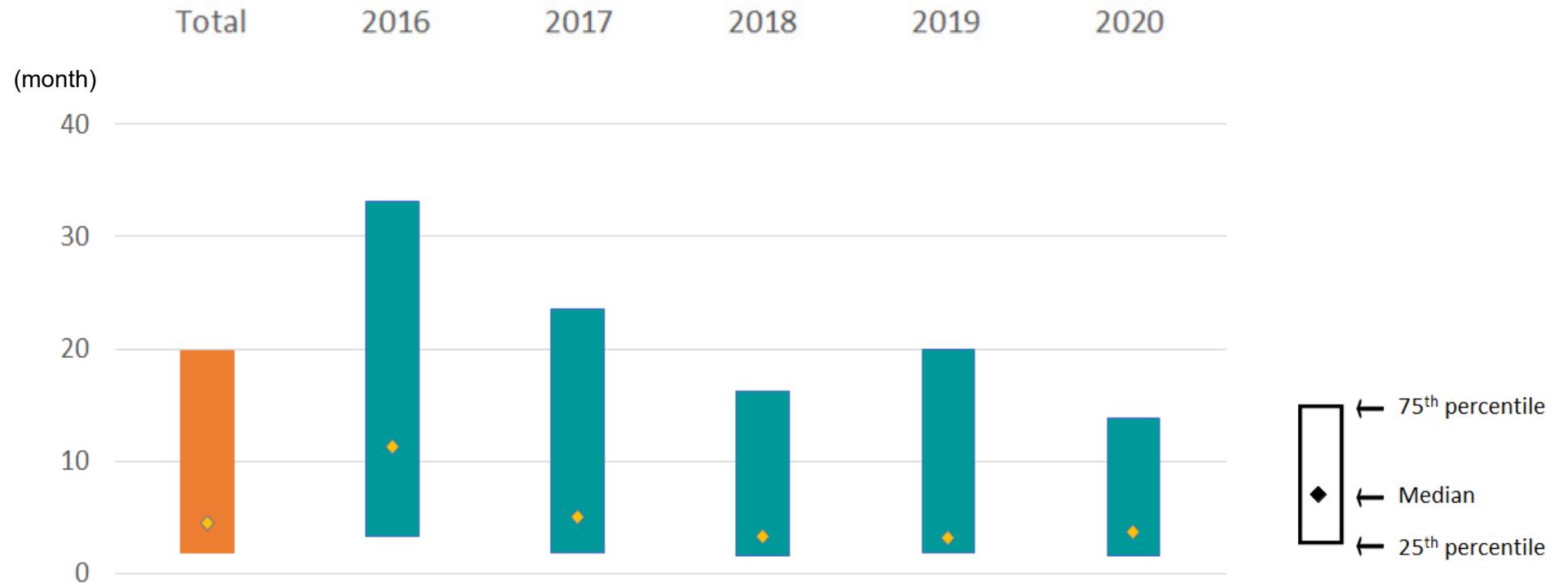


	Total	global simultaneous development		not applicable to global simultaneous development		others	
		Non-Onco	Onco	Non-Onco	Onco	Non-Onco	Onco
n	214	69	90	38	13	2	2
Median (month)	4.59	3.03	3.26	38.52	25.13	43.03	13.18
25th percentile (month)	1.91	1.64	1.51	19.68	19.90	31.40	11.77
75th percentile (month)	19.87	5.86	6.70	57.35	36.78	54.65	14.58

2. Investigation results

Figure 4-1: NDA lag comparison, comparison by NDA fiscal year

Fig. 4-1



	Total	2016	2017	2018	2019	2020
n	214	33	43	53	46	39
Median (month)	4.59	11.28	5.10	3.29	3.18	3.78
25th percentile (month)	1.91	3.32	1.84	1.64	1.91	1.55
75th percentile (month)	19.87	33.12	23.57	16.18	19.89	13.79

2. Investigation results

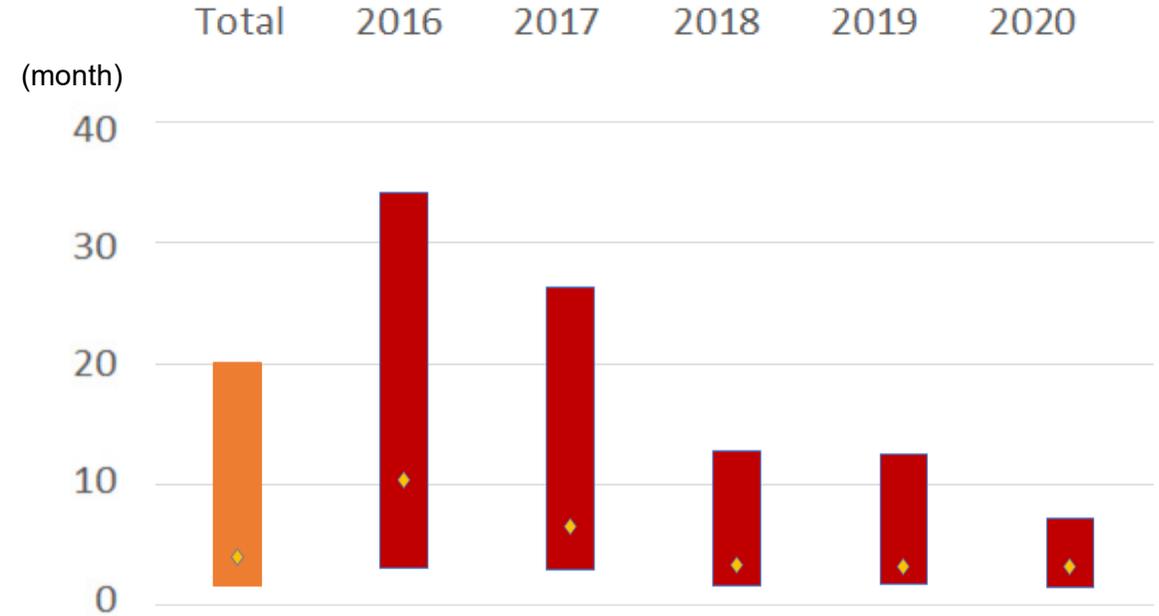
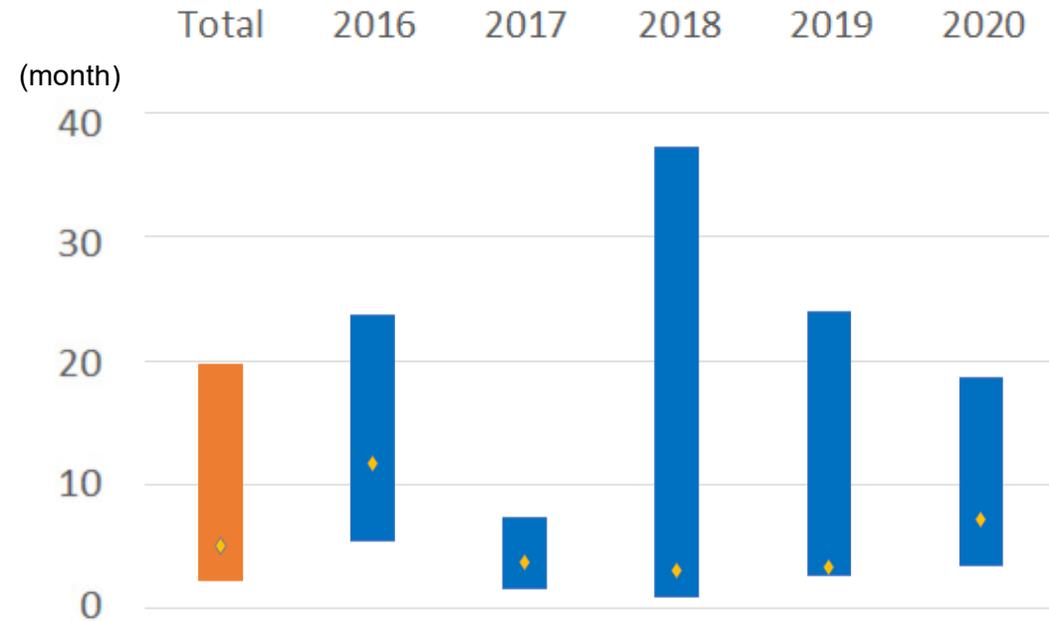
Figure 4-2: NDA lag comparison, comparison by NDA fiscal year [NME / non-NME]

Fig. 4-2-1

NME

Fig. 4-2-2

non-NME



Total	2016	2017	2018	2019	2020		Total	2016	2017	2018	2019	2020
70	14	16	12	12	16	n	144	19	27	41	34	23
5.04	11.66	3.72	3.08	3.34	7.25	Median (month)	3.96	10.33	6.58	3.29	3.18	3.19
2.30	5.51	1.61	0.93	2.73	3.42	25th percentile (month)	1.64	3.08	2.96	1.64	1.71	1.42
19.75	23.62	7.30	37.21	23.98	18.59	75th percentile (month)	20.04	34.18	26.35	12.76	12.55	7.24

2. Investigation results

Figure 4-3: NDA lag comparison, comparison by NDA fiscal year

[global simultaneous development / not applicable to global simultaneous development]

Fig. 4-3-1

global simultaneous development
(NME+non-NME)

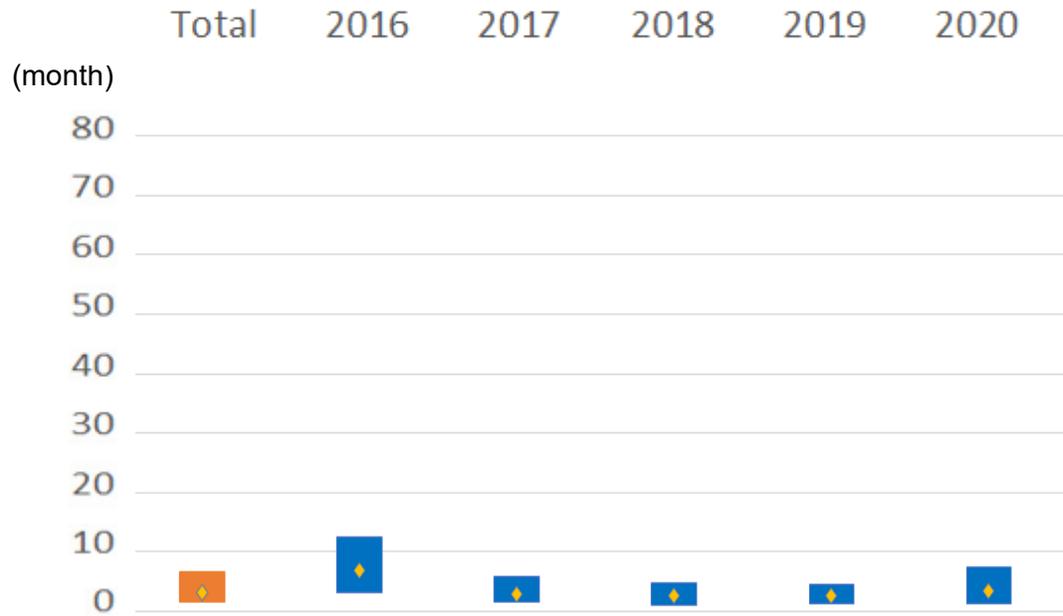
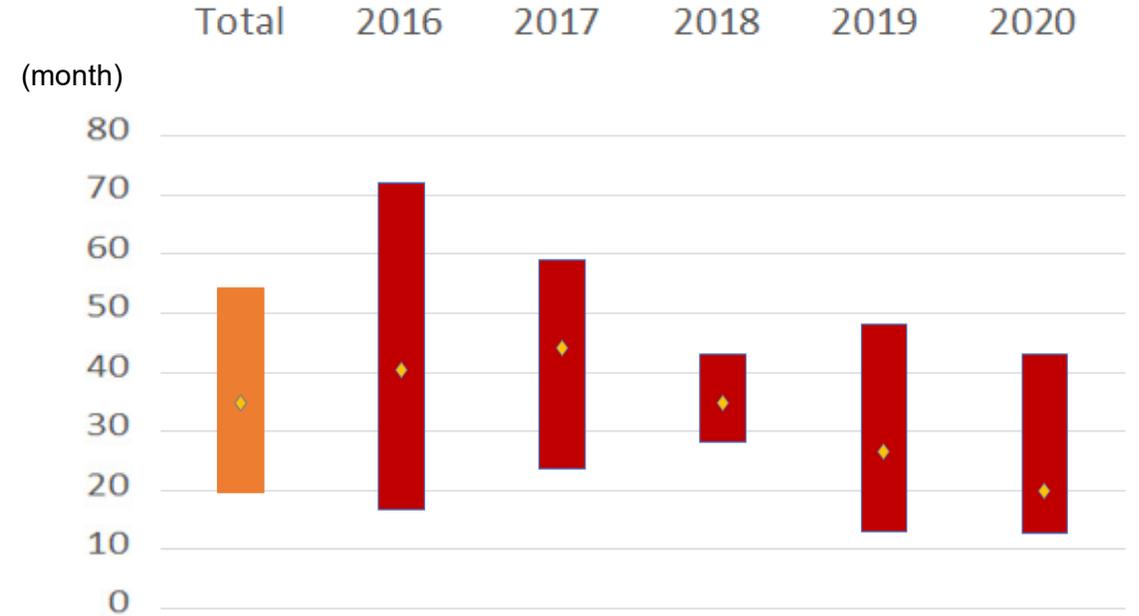


Fig. 4-3-2

not applicable to global
simultaneous development
(NME+non-NME)

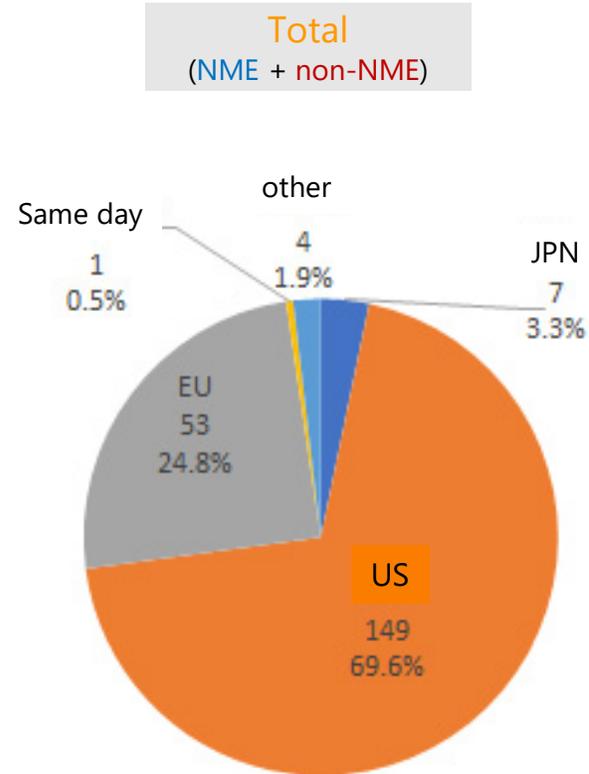


Total	2016	2017	2018	2019	2020		Total	2016	2017	2018	2019	2020
159	23	29	39	36	32	n	51	10	11	13	10	7
3.12	6.81	2.99	2.80	2.57	3.36	Median (month)	34.74	40.35	44.05	34.74	26.53	19.90
1.51	3.27	1.51	1.04	1.45	1.45	25th percentile (month)	19.59	16.74	23.64	28.16	13.09	12.85
6.66	12.45	5.86	4.90	4.43	7.50	75th percentile (month)	54.31	71.99	58.93	43.06	48.25	42.98

2. Investigation results

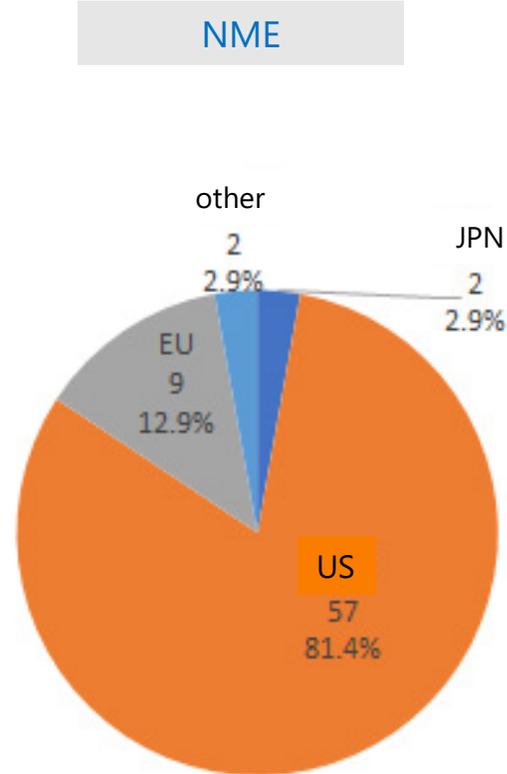
Figure 6-1: Country of initial NDA [NME / non-NME]

Fig. 6-1-1



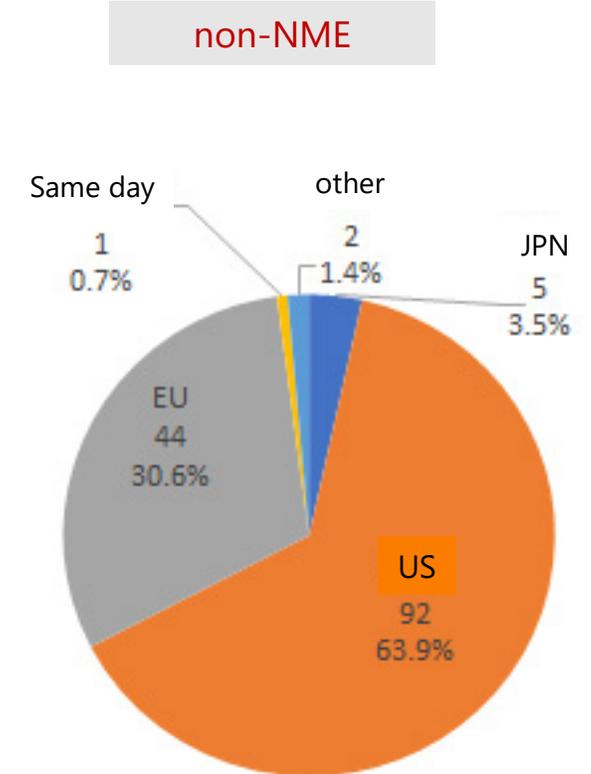
	JPN	US	EU	same day	other	Total
n	7	149	53	1	4	214

Fig. 6-1-2



	JPN	US	EU	same day	other	Total
n	2	57	9	0	2	70

Fig. 6-1-3



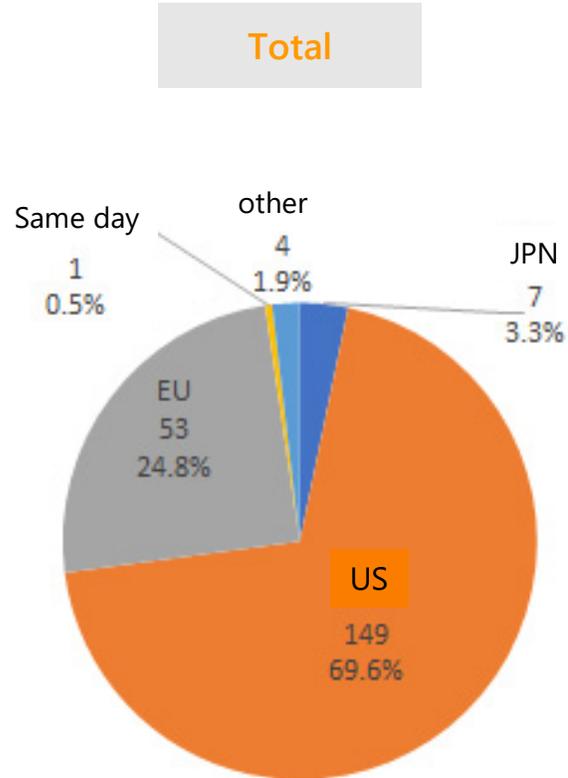
	JPN	US	EU	same day	other	Total
n	5	92	44	1	2	144

other: China, Canada, Russia

2. Investigation results

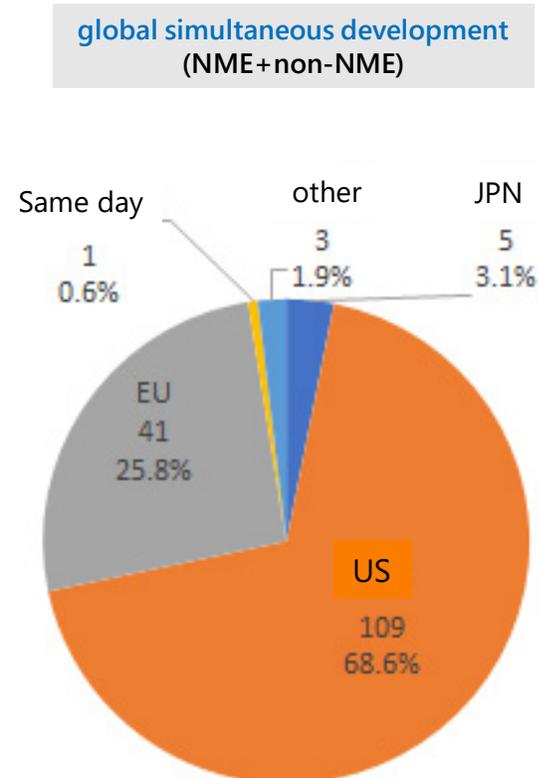
Figure 6-2: Country of initial NDA [global simultaneous development / not applicable to global simultaneous development]

Fig. 6-2-1



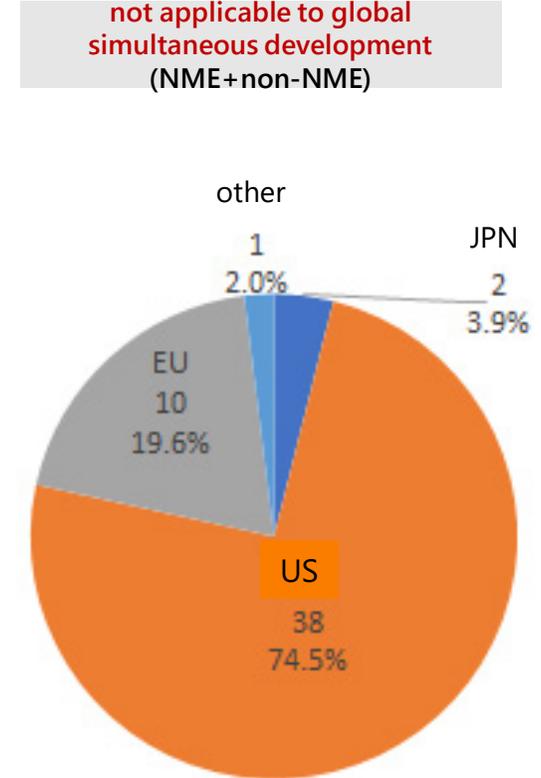
	JPN	US	EU	same day	other	Total
n	7	149	53	1	4	214

Fig. 6-2-2



	JPN	US	EU	same day	other	Total
n	5	109	41	1	3	159

Fig. 6-2-3



	JPN	US	EU	same day	other	Total
n	2	38	10	0	1	51

other: China, Canada, Russia

2. Investigation results

Figure 7-1: NDA lag, comparison by timing

Fig. 7-1-1

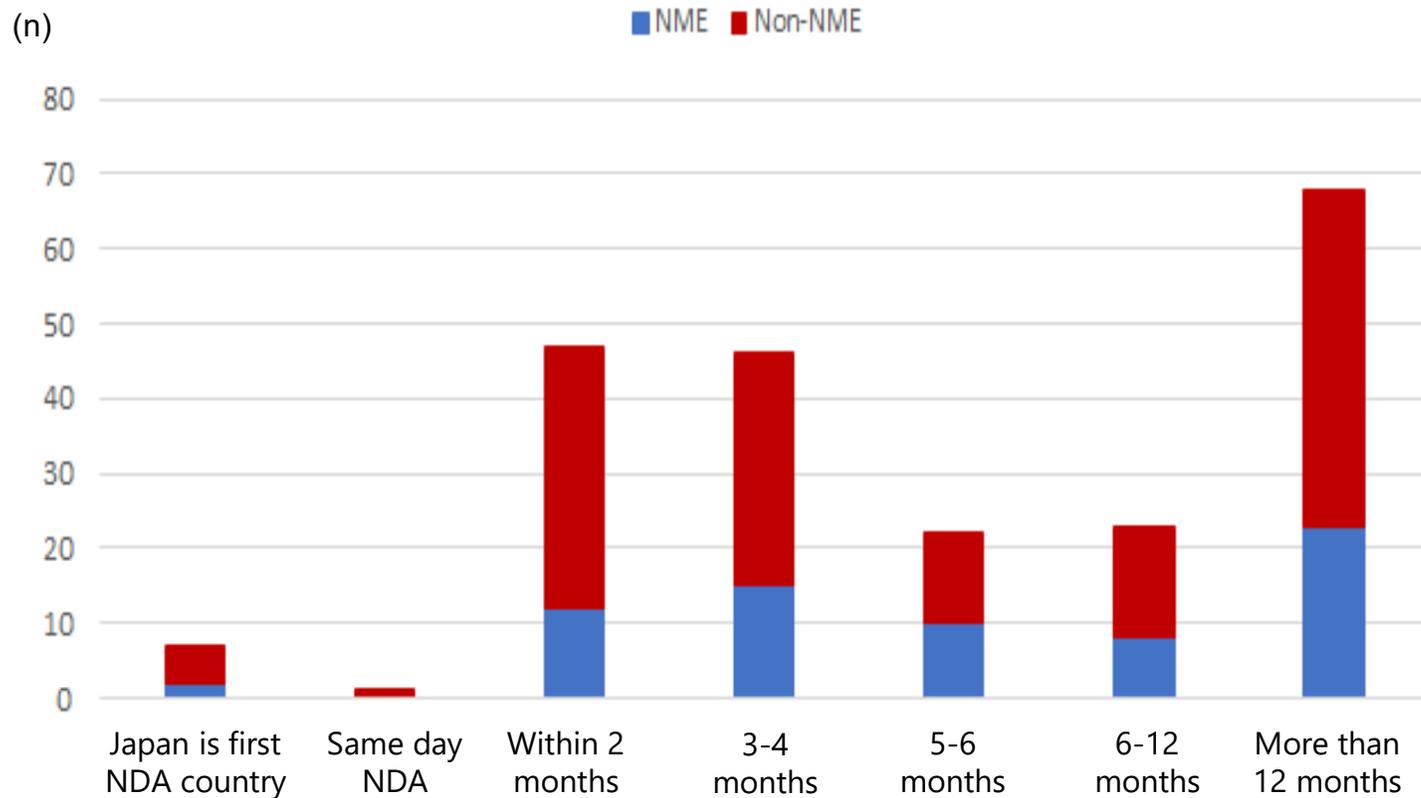
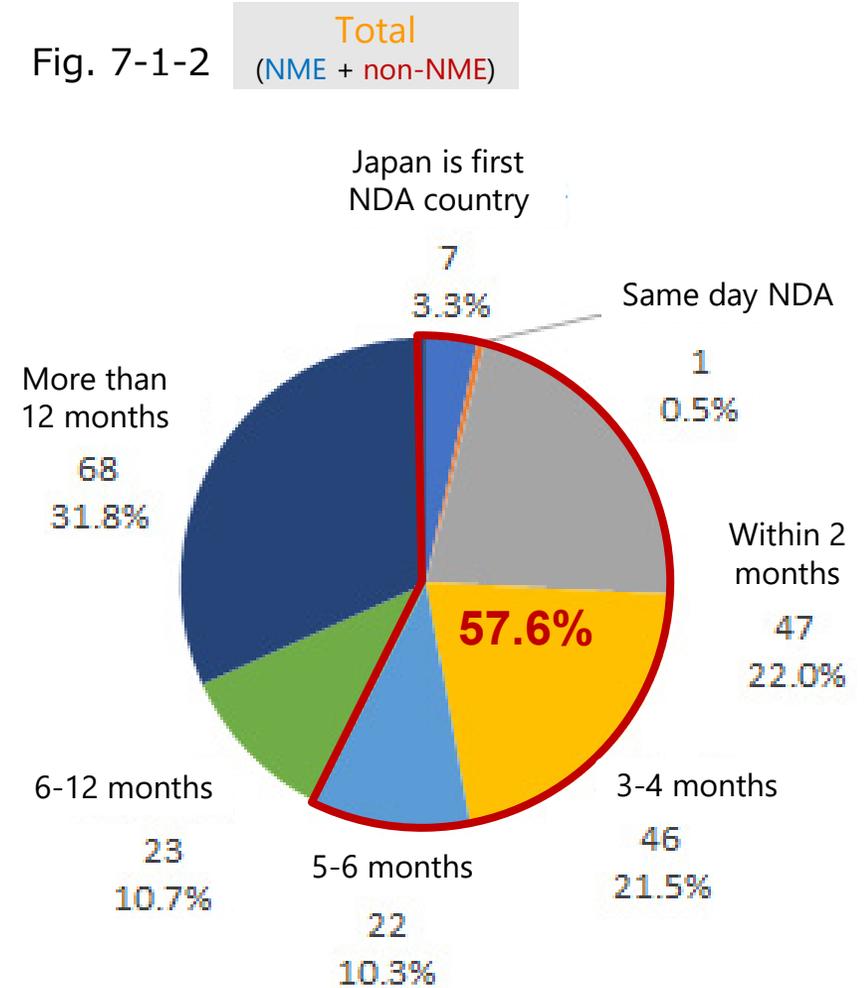


Fig. 7-1-2

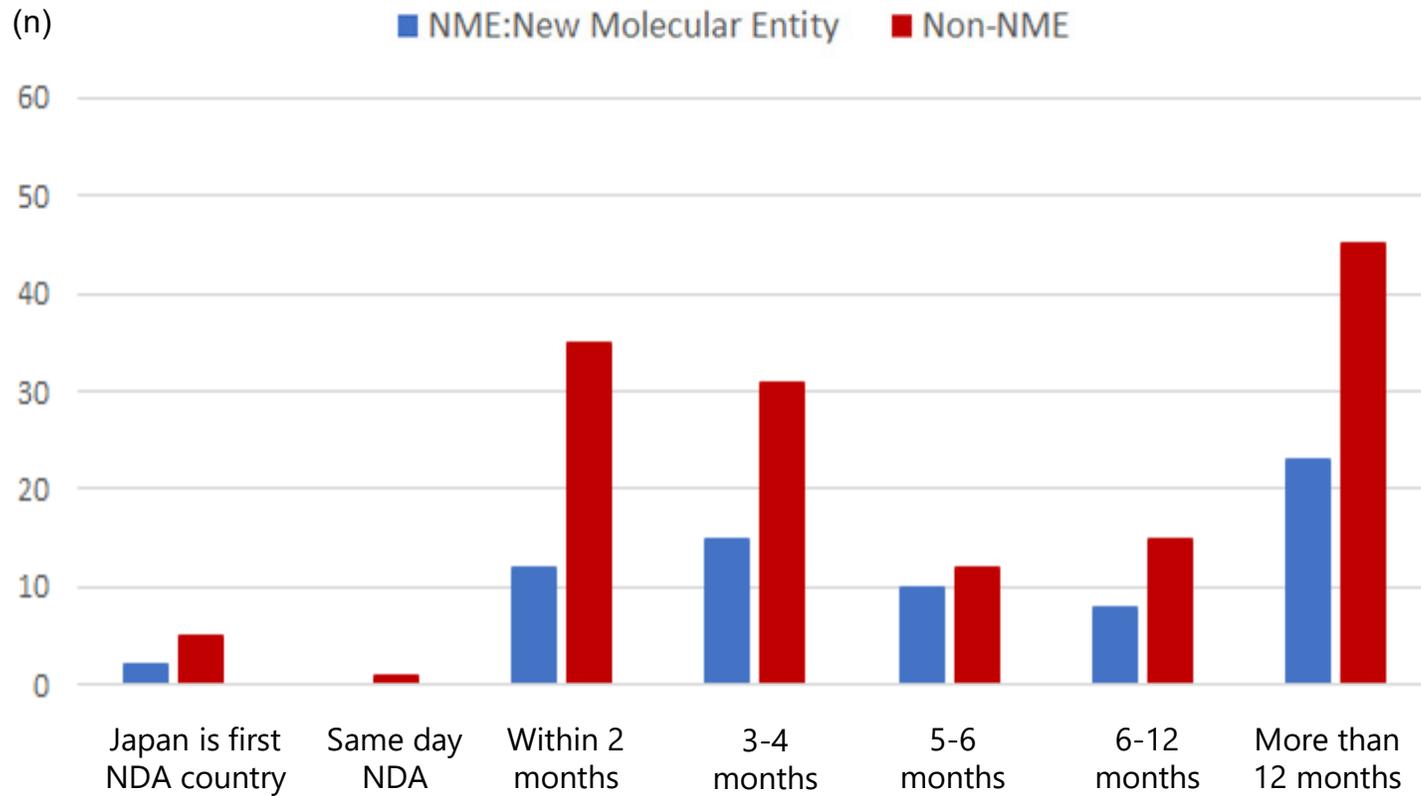


With concurrent application defined as "within 6 months from the initial application in another country" : 57.6%

2. Investigation results

Figure 7-2: NDA lag, comparison by timing [NME/non-NME]

Fig. 7-2-1



With concurrent application defined as "within 6 months from the initial application in another country" :
 NME : 55.7%、 non-NME : 58.3%

Fig. 7-2-2

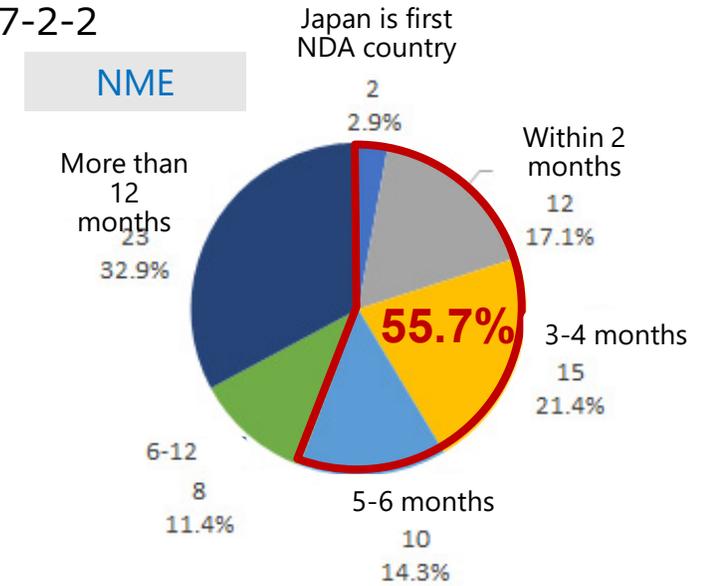
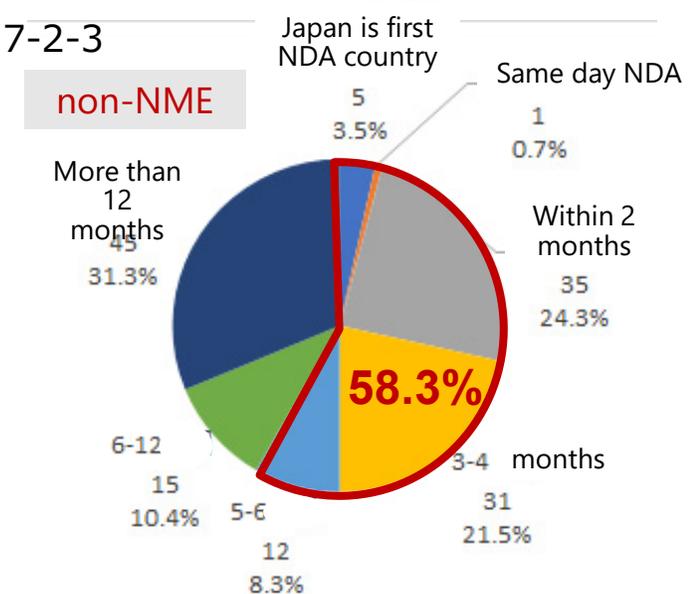


Fig. 7-2-3

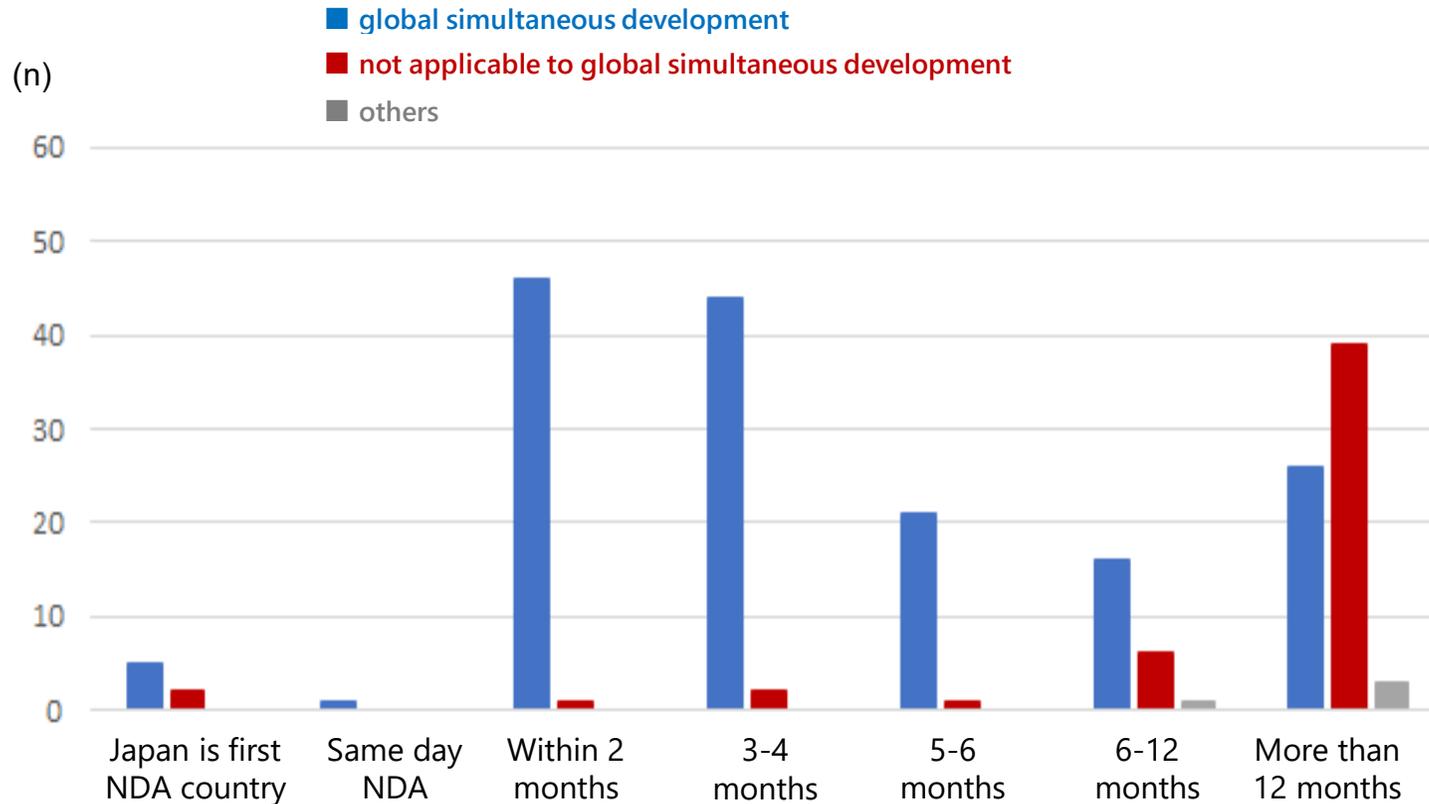


2. Investigation results

Figure 7-3: NDA lag, comparison by timing

[global simultaneous development / not applicable to global simultaneous development]

Fig. 7-3-1



With concurrent application defined as "within 6 months from the initial application in another country" :
 global simultaneous development : 73.5%
 not applicable to global simultaneous development : 11.8%

Fig. 7-3-2 **global simultaneous development**

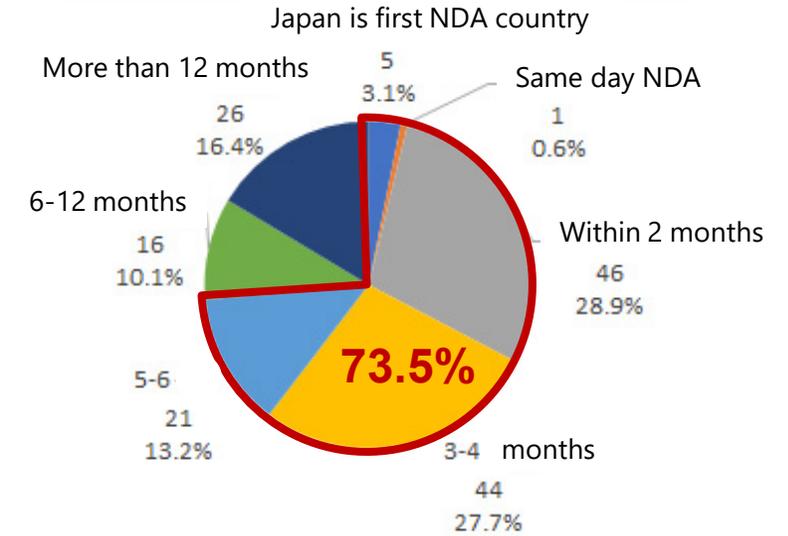
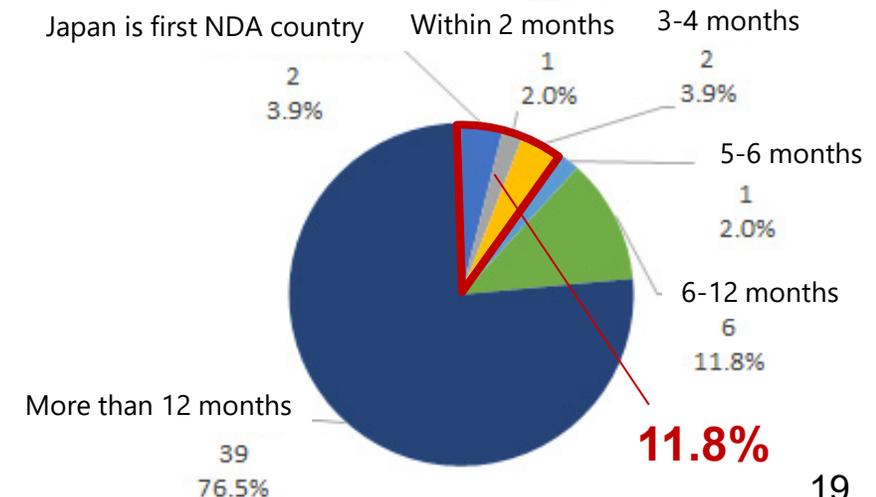
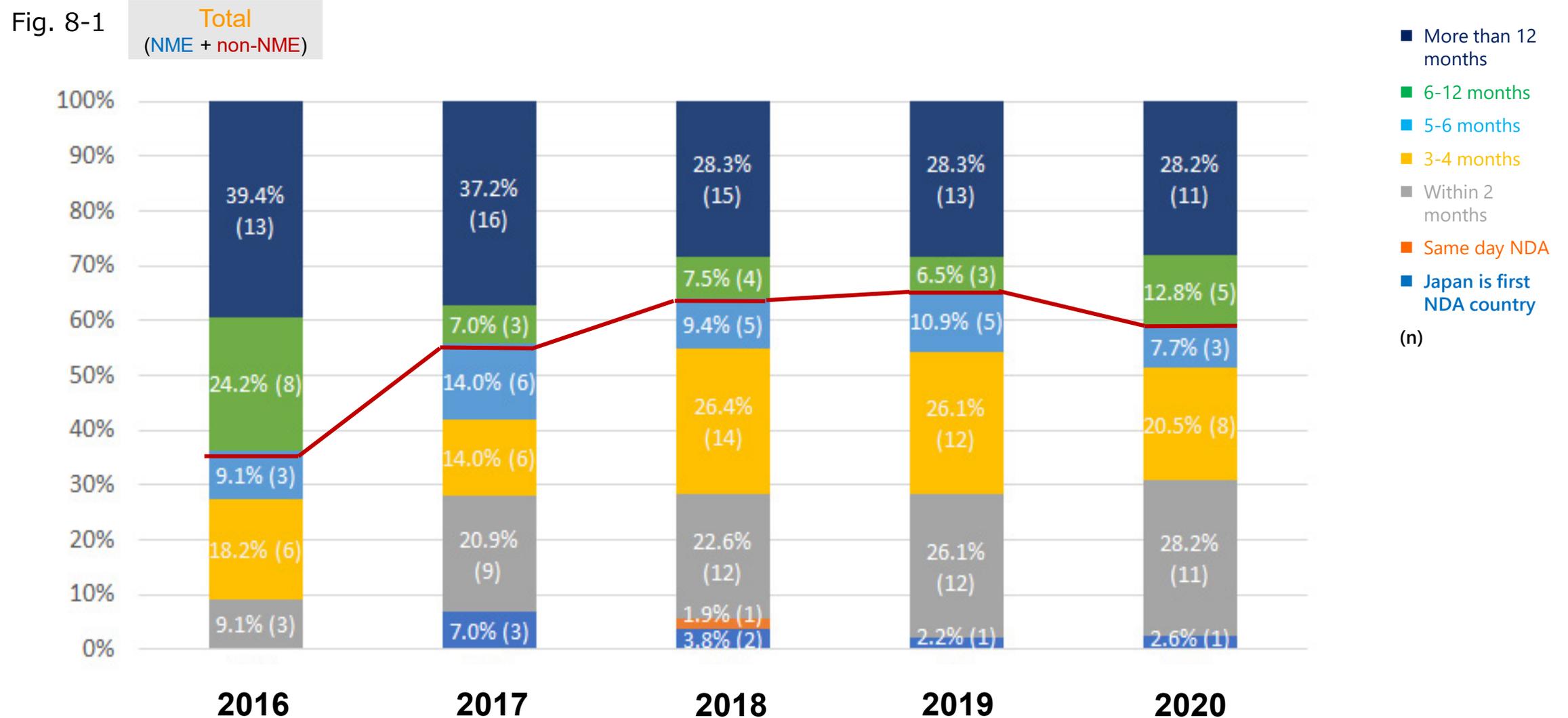


Fig. 7-3-3 **not applicable to global simultaneous development**



2. Investigation results

Figure 8-1: NDA lag, comparison by timing [NDA fiscal year]



— : With concurrent application defined as "within 6 months from the initial application in another country"

2. Investigation results

Figure 8-2: NDA lag, comparison by timing [NDA fiscal year × NME / non-NME]

Fig. 8-2-1 NME

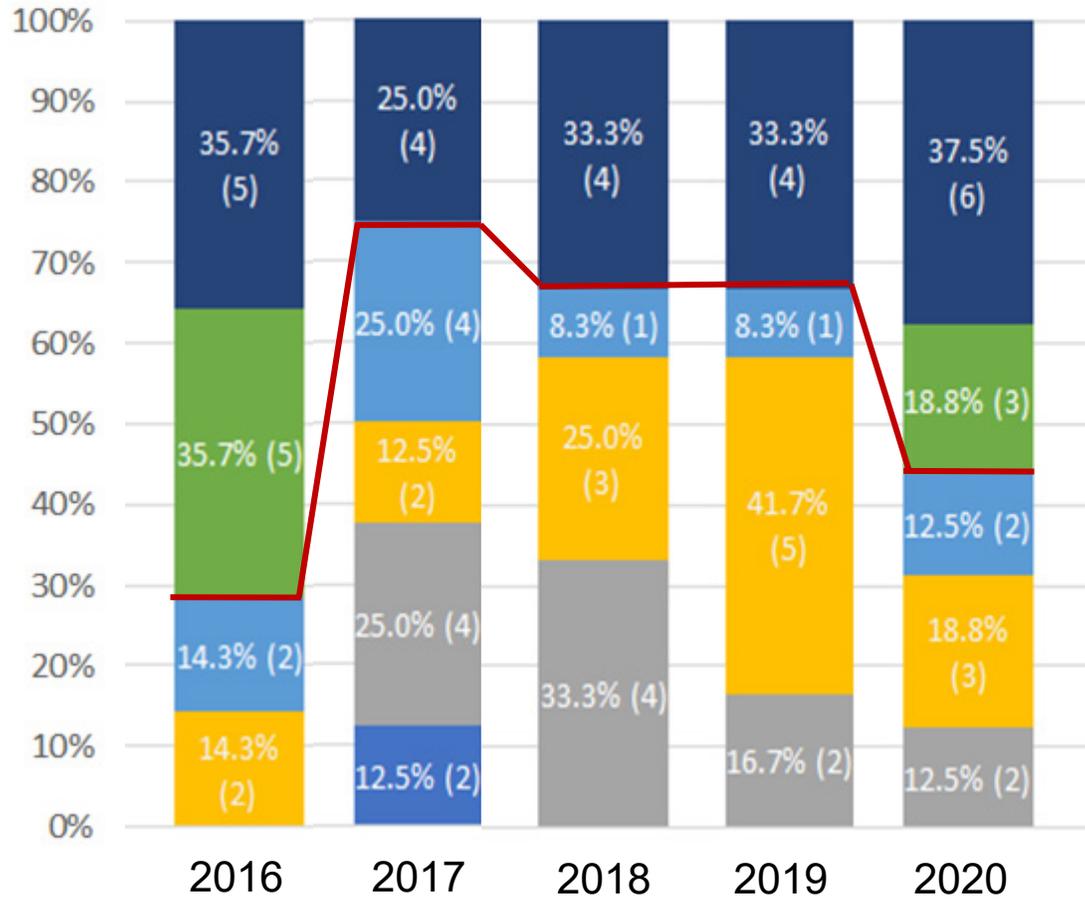
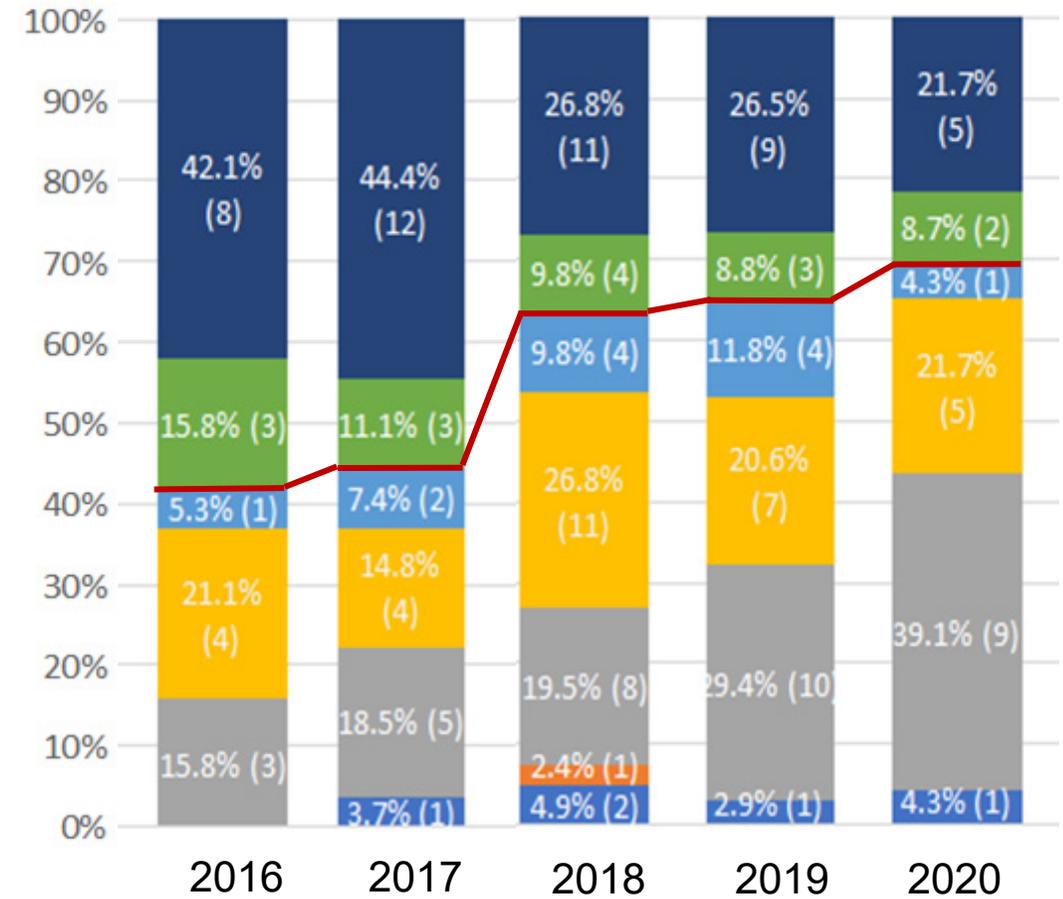


Fig. 8-2-2 non-NME



- More than 12 months
 - 6-12 months
 - 5-6 months
 - 3-4 months
 - Within 2 months
 - Same day NDA
 - Japan is first NDA country
- (n)

— : With concurrent application defined as "within 6 months from the initial application in another country"

2. Investigation results

Figure 8-3: NDA lag, comparison by timing

[NDA fiscal year × global simultaneous development / not applicable to global simultaneous development]

Fig. 8-3-1

global simultaneous development
(NME+non-NME)

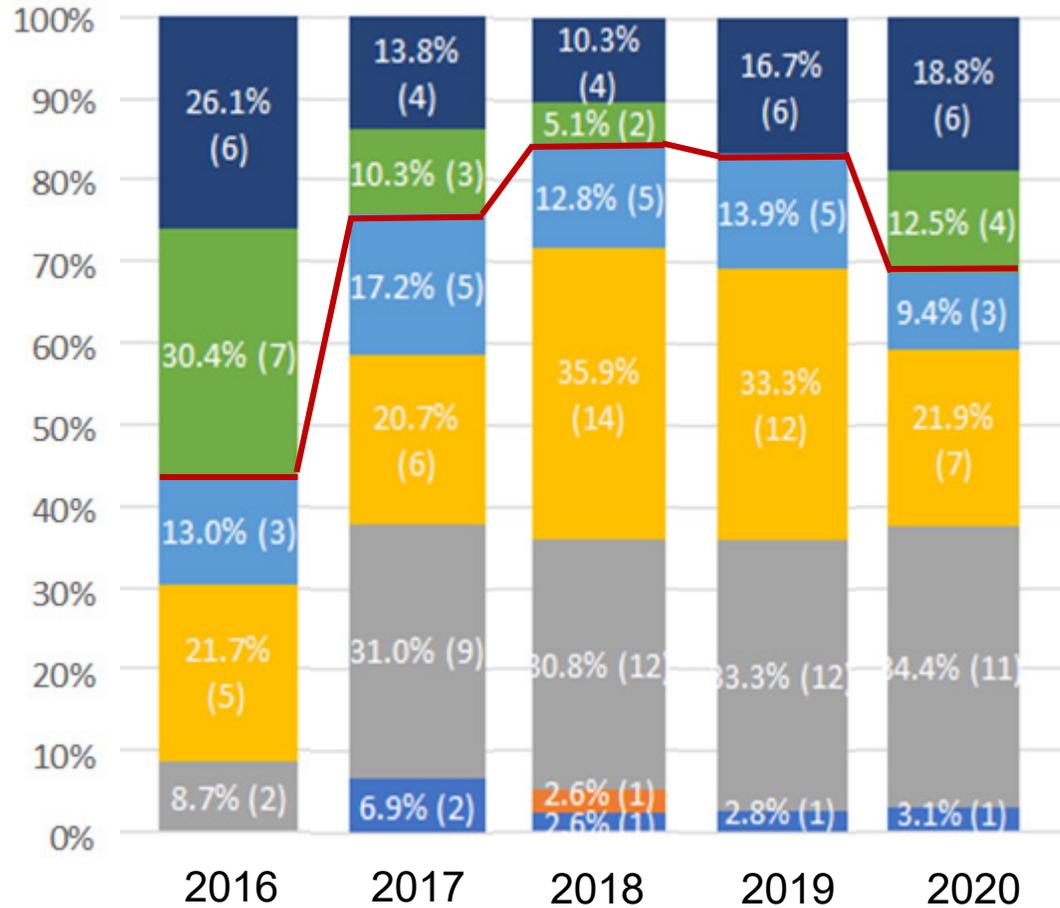
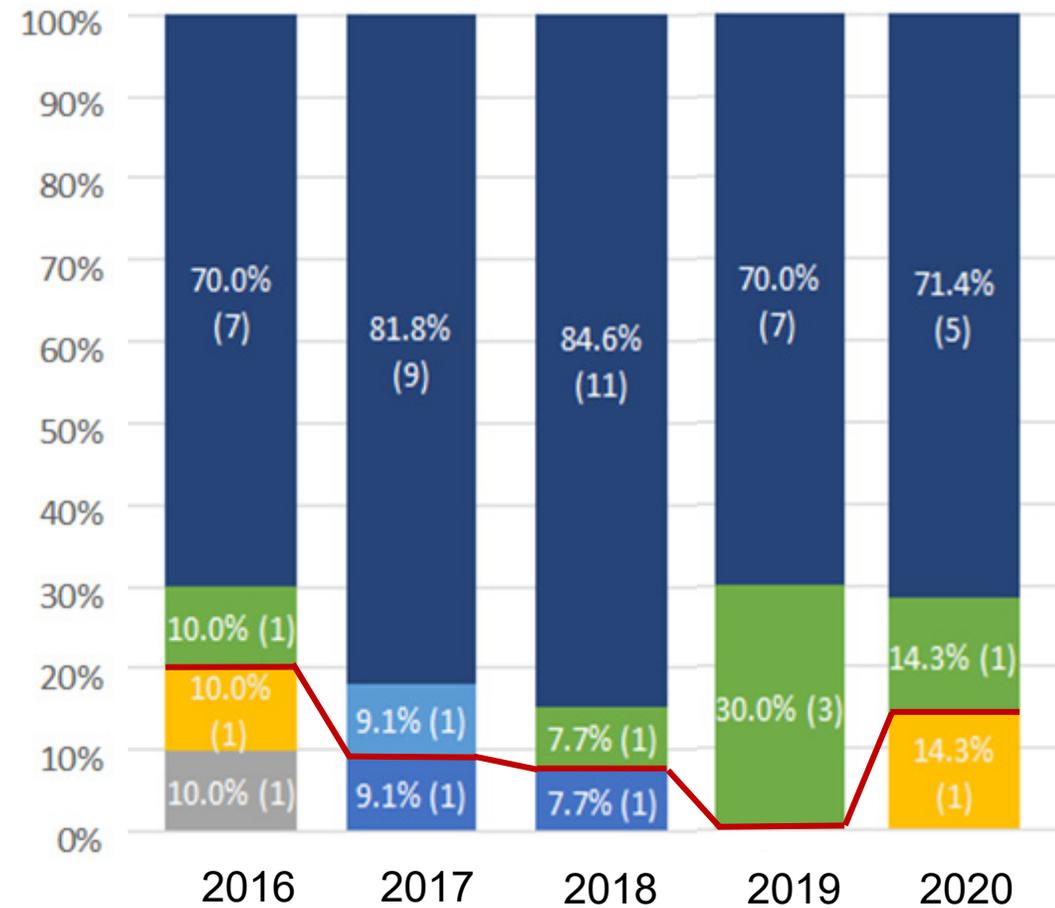


Fig. 8-3-2

not applicable to global simultaneous development
(NME+non-NME)



- More than 12 months
 - 6-12 months
 - 5-6 months
 - 3-4 months
 - Within 2 months
 - Same day NDA
 - Japan is first NDA country
- (n)

— : With concurrent application defined as "within 6 months from the initial application in another country"

2. Investigation results

Table 3-1: Development patterns for [global simultaneous development] and items requested/required if [b] was selected

global simultaneous development 159 (71.62%)	not applicable to global simultaneous development 59 (26.58%)	others 4 (1.80%)
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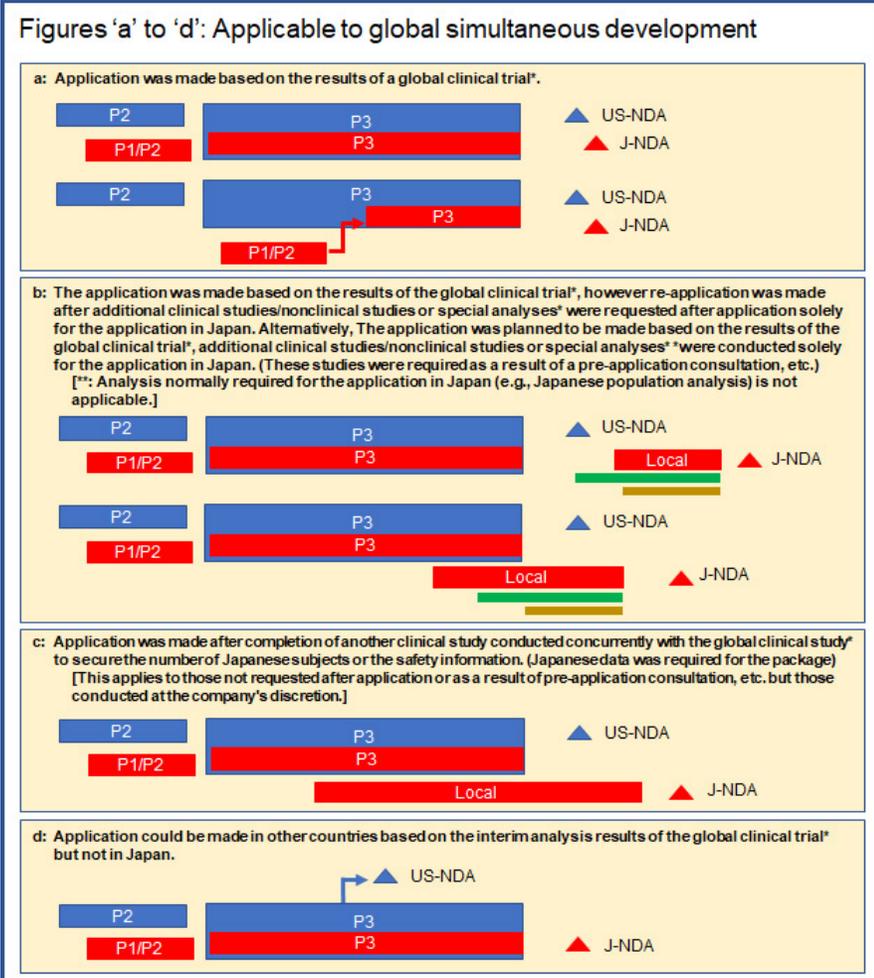


Table 3-1-1: [global simultaneous development] pattern of development

	n	%
a	129	81.13
b	4	2.52
c	9	5.66
d	3	1.89
Not applicable to a-d	12	7.55
unknown	2	1.26

Table 3-1-2: Requested items when 'b' selected

項目	n
Clinical studies	3
Non-clinical studies	0
Special analyses	1
unknown	0

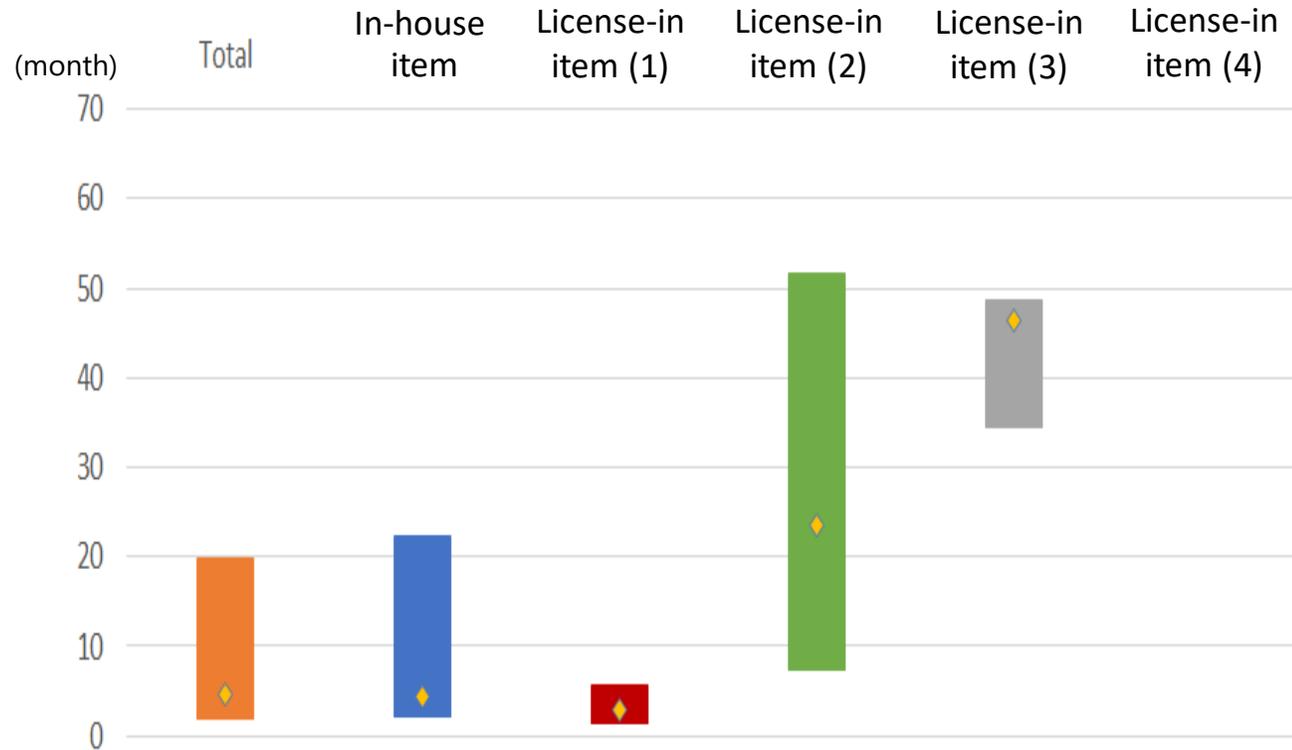
- Blue: Studies mainly conducted overseas
- Red: Studies conducted in Japan
- Green: Nonclinical studies
- Yellow: Special analyses

*: Global clinical studies that are positioned as pivotal studies globally

2. Investigation results

Figure 10-1: NDA lag, comparison of attributes (origin)

Fig. 10-1



Definitions

- **In-house item**
- **License-in item (1):**
Introduced before overseas application and participated in the pivotal study from Japan
Introduced before the first overseas application outside Japan and participated from Japan in the study positioned as pivotal study globally (including participation from halfway during the study).
- **License-in item (2):**
Introduced before overseas application but not participated in the pivotal study from Japan
Introduced before the first overseas application outside Japan but was unable to participate from Japan in the study positioned as pivotal study globally (including participation from halfway during the study).
- **License-in item (3):**
Introduced after overseas application
Introduced after the first application in globally excluding Japan.
- **License-in item (4):**
Overseas development status at the time of introduction is unknown.

	Total	In-house item	License-in item (1)	License-in item (2)	License-in item (3)	License-in item (4)
n	214	139	54 *	18 *	3	-
Median (month)	4.59	4.51	2.81	23.64	46.35	-
25th percentile (month)	1.91	2.08	1.34	7.48	34.53	-
75th percentile (month)	19.87	22.37	5.58	51.74	48.65	-

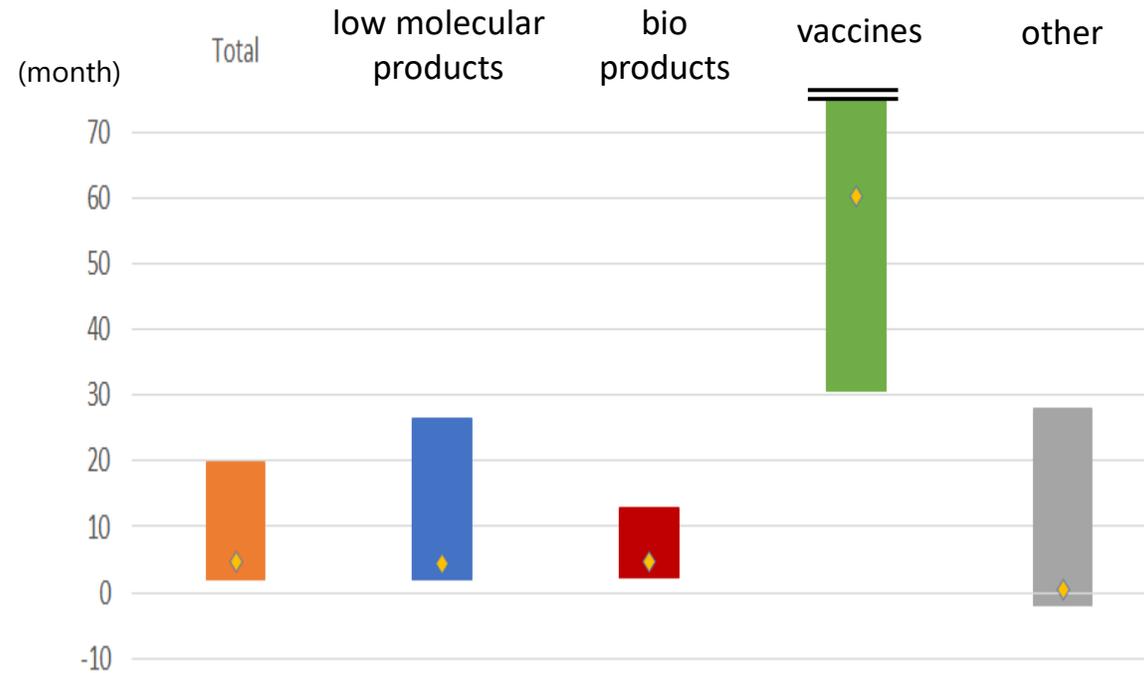
Note: During the analysis for this survey, discrepancy was found between the responses to “product attribute (origin)” and “development patterns” in the responses to license-in items (1) and (2). [*License-in item (1): 2 cases, license-in item (2): 8 cases]

The 10 applicable cases were not excluded for Fig. 10-1.

2. Investigation results

Figure 11-1: NDA lag, comparison by low molecular, bio, etc.

Fig. 11-1



	Total	low molecular products	bio products	vaccines	other
n	214	104	105	2	3
Median (month)	4.59	4.26	4.70	60.30	0.36
25th percentile (month)	1.91	1.83	2.30	30.61	-1.83
75th percentile (month)	19.87	26.47	12.76	89.98	27.95

3. Secondary use of this result

This report has been prepared by R&D Head Club member companies by bringing together data in order to understand current clinical trial environment in Japan. Please note the following instruction when you use this material for the secondary use.

Preliminary actions for secondary use

- Please let the R&D Head Club secretariat know below contents by contact form in the R&D Head Club home page (<https://rdhead-club.com/contact/>)
 - User (name, affiliation, opportunity to use)
 - Where used (applicable pages and purpose of use*)

Ex.)
 Name : Ichiro Club
 Affiliation : ABC Pharma K.K.
 Purpose for use : Oral presentation in OOO annual meeting, MMM/DD/YYYY
 Data of use : Slide #9
 Introduction on current NDA Lag in Japan

How to describe Source Data

- Source: R&D Head Club NDA Lag Survey in 2022 <https://rdhead-club.com/>

*: It is to confirm that there is no discrepancy with the perception of R&D Head Club, and does not restrict secondary use