独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

Regulatory approach to promote orphan drug development in Japan

Yoko Aoi, PhD
Principal Reviewer
Office of New Drug V, PMDA Japan

Legal basis of orphan drug designation

Legislation etc.	Corresponding part	Description
PMD Act	Article 77-2	Overview of orphan drug designation system
Regulation for Enforcement of PMD Act	Article 251	Upper Limit on the Number of Patients
PED/MDED Notification No.831-7	All	Details of designation criteria

Please see the following paper.

Orphan drug designation and development in Japan: 25 years of experience and assessment. Nat Rev Drug Discov. 2021

Orphan drugs – Designation system

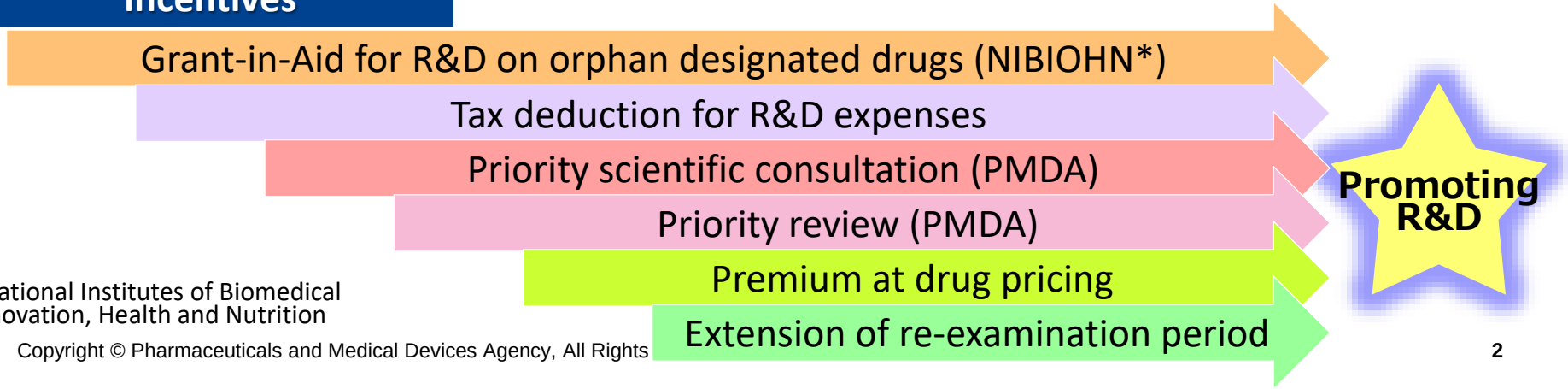
Aim

✓ To promote R&D on products for rare diseases, aiming to provide the people with the safe and effective medicines/medical devices as early as possible

Designation Criteria

1. Number of patients (that any of the followings is satisfied)
   - Less than 50,000 in Japan
   - The target disease is one of the designated intractable disease
2. Medical needs
   - For serious diseases with high medical needs
3. Feasibility of development

Incentives



*National Institutes of Biomedical Innovation, Health and Nutrition

Designated information

Name of pharmaceutical drug with a designation

Anticipated indications or diseases the orphan drug is intended to treat on the designation

Name of applicant receiving the designation

希少疾病用医薬品指定品目一覧表（令和2年9月1日以降）

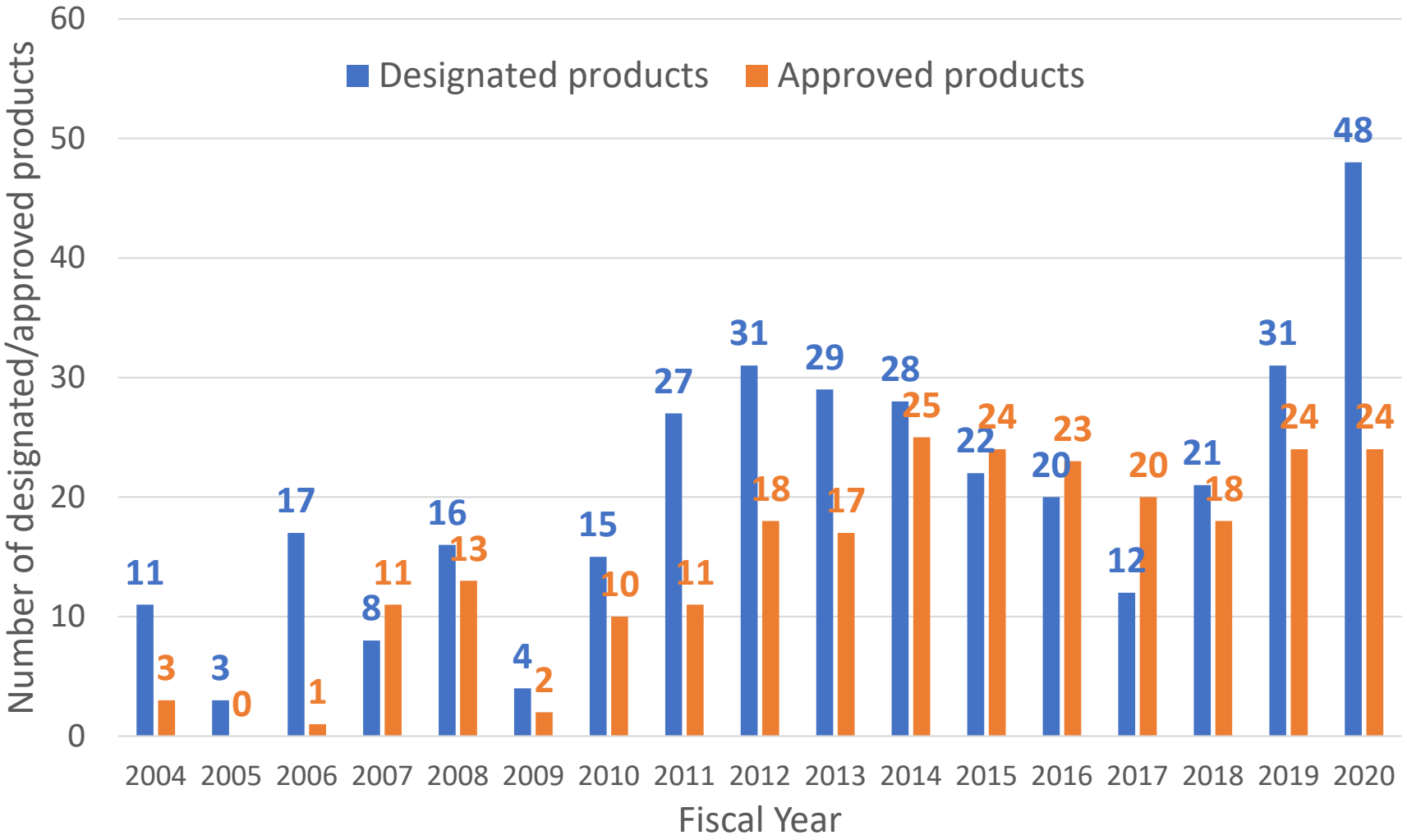
指定年度	指定日	指定番号	指定を受けた医薬品の名称	指定を受けた予定される効能又は効果	指定を受けた者の氏名又は名称	指定を受けた者の住所
R2	R2.9.18	（R2薬）第484号	サルグラモスチム（遺伝子組換え）	自己免疫性肺胞蛋白症	ノーベルファーマ株式会社	東京都中央区新川一丁目17番24号
R2	R2.9.18	（R2薬）第485号	イピリムマブ（遺伝子組換え）	悪性胸膜中皮腫	ブリストル・マイヤーズ スクイブ株式会社	東京都新宿区西新宿6-5-1
R2	R2.9.18	（R2薬）第486号	パビナフスプ　アルファ（遺伝子組換え）	ムコ多糖症II型	JCRファーマ株式会社	兵庫県芦屋市春日町3番19号
R2	R2.9.18	（R2薬）第487号	オリプダーゼ　アルファ（遺伝子組換え）	酸性スフィンゴミエリナーゼ欠損症	サノフィ株式会社	東京都新宿区西新宿3丁目20番2号東京オペラシティタワー
R2	R2.9.18	（R2薬）第488号	ミドスタウリン	*FLT3*遺伝子変異陽性の急性骨髄性白血病	ノバルティスファーマ株式会社	東京都港区虎ノ門1丁目23番1号
R2	R2.11.25	（R2薬）第489号	BIIB067	筋萎縮性側索硬化症	バイオジェン・ジャパン株式会社	東京都中央区日本橋一丁目4番1号 日本橋一丁目三井ビルディング14階
R2	R2.11.25	（R2薬）第490号	Rozanolixizumab	全身型重症筋無力症	ユーシービージャパン株式会社	東京都新宿区西新宿8-17-1
R2	R2.11.25	（R2薬）第491号	シロリムス	難治性脈管腫瘍・脈管奇形	ノーベルファーマ株式会社	東京都中央区新川一丁目17番24号
R2	R2.11.25	（R2薬）第492号	アバルグルコシダーゼ アルファ（遺伝子組換え）	糖原病Ⅱ型	サノフィ株式会社	東京都新宿区西新宿三丁目20番2号
R2	R2.11.25	（R2薬）第493号	ダラツムマブ（遺伝子組換え）・ボルヒアルロニダーゼアルファ（遺伝子組換え）配合注射剤	全身性ALアミロイドーシス	ヤンセンファーマ株式会社	東京都千代田区西神田3丁目5番2号
R2	R2.11.25	（R2薬）第494号	ボルテゾミブ	全身性ALアミロイドーシス	ヤンセンファーマ株式会社	東京都千代田区西神田3丁目5番2号
R2	R2.11.25	（R2薬）第495号	セルペルカチニブ	*RET*融合遺伝子陽性の切除不能な進行・再発の非小細胞肺癌 *RET*融合遺伝子陽性の根治切除不能な甲状腺癌 *RET*遺伝子変異陽性の根治切除不能な甲状腺髄様癌	日本イーライリリー株式会社	兵庫県神戸市中央区磯上通5丁目1番28号

https://www.mhlw.go.jp/content/11120000/000752896.pdf

- ✓ Designated information includes “Name of pharmaceutical drug with a designation”, “Anticipated indications or diseases the orphan drug is intended to treat on the designation” and “Name of applicant receiving the designation”.
- ✓ Orphan drug designation is granted for the combination of drug, indication and applicant.

Trend in designation and approval of orphan drugs in Japan

Designated products (343 in total) is counted based on designation from FY2004 to 2020.
Approved products (244 in total) is counted based on approval from FY2004 to 2020.



PMDA framework for orphan drugs

New Drug I

Category 1
Gastrointestinal drugs, immunosuppressive drugs etc

Category 6-2
Drugs for Diabetes mellitus, Osteoporosis, Gout etc

New Drug II

Category 2
Cardiovascular drugs, anti-Parkinsonian drugs, anti-Alzheimer's drugs

Category 5
Reproductive system drugs, drugs for urogenital system etc

New Drug III

Category 3-1
Central/peripheral nervous system drugs

Category 3-2
Anesthetic drugs, sensory organ drugs, narcotics

New Drug IV

Category 4
Antibacterial drugs, antiviral drugs

Category 6-1
Respiratory tract drugs, anti-allergy drugs

New Drug V

Oncology drugs
Antineoplastic drugs

[Others] Office of Cellular and Tissue-based Products, Office of Vaccines and Blood Products

PMDA framework for orphan drugs

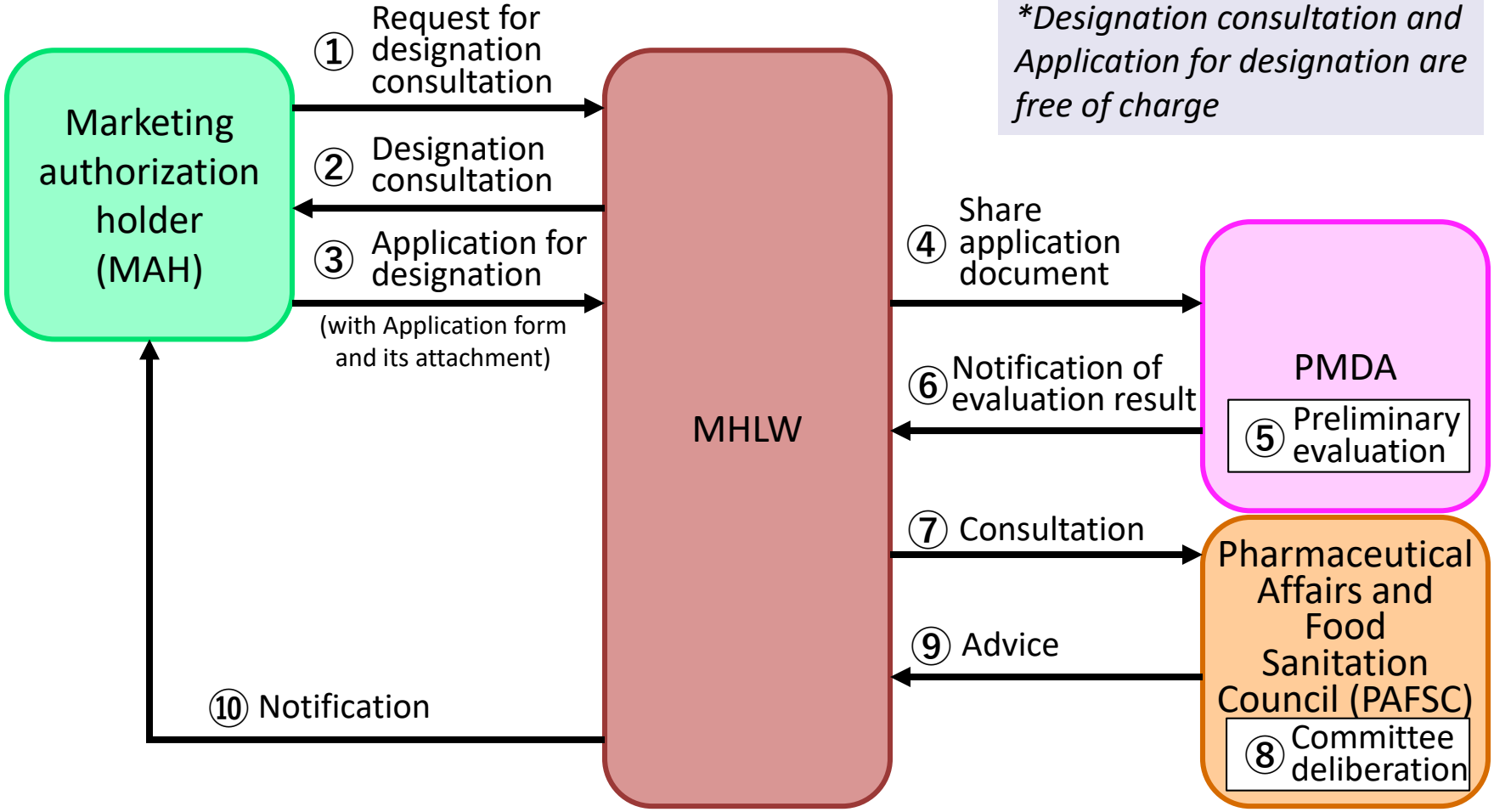
New Drug I	New Drug II	New Drug III	New Drug IV	New Drug V
Category 1 Gastrointestinal drugs,	**Category 2** Cardiovascular drugs, anti-Parkinsonian	**Category 3-1** Central/periph	**Category 4** Antibacterial	**Oncology drugs** Antineoplastic
Category 6-2 Drugs for Diabetes mellitus, Osteoporosis, Gout etc	**Category 5** Reproductive system drugs, drugs for urogenital system etc	**Category 3-2** Anesthetic drugs, sensory organ drugs, narcotics	**Category 6-1** Respiratory tract drugs, anti-allergy drugs	

Each review office responsible for review, scientific consultation and designation of orphan drugs

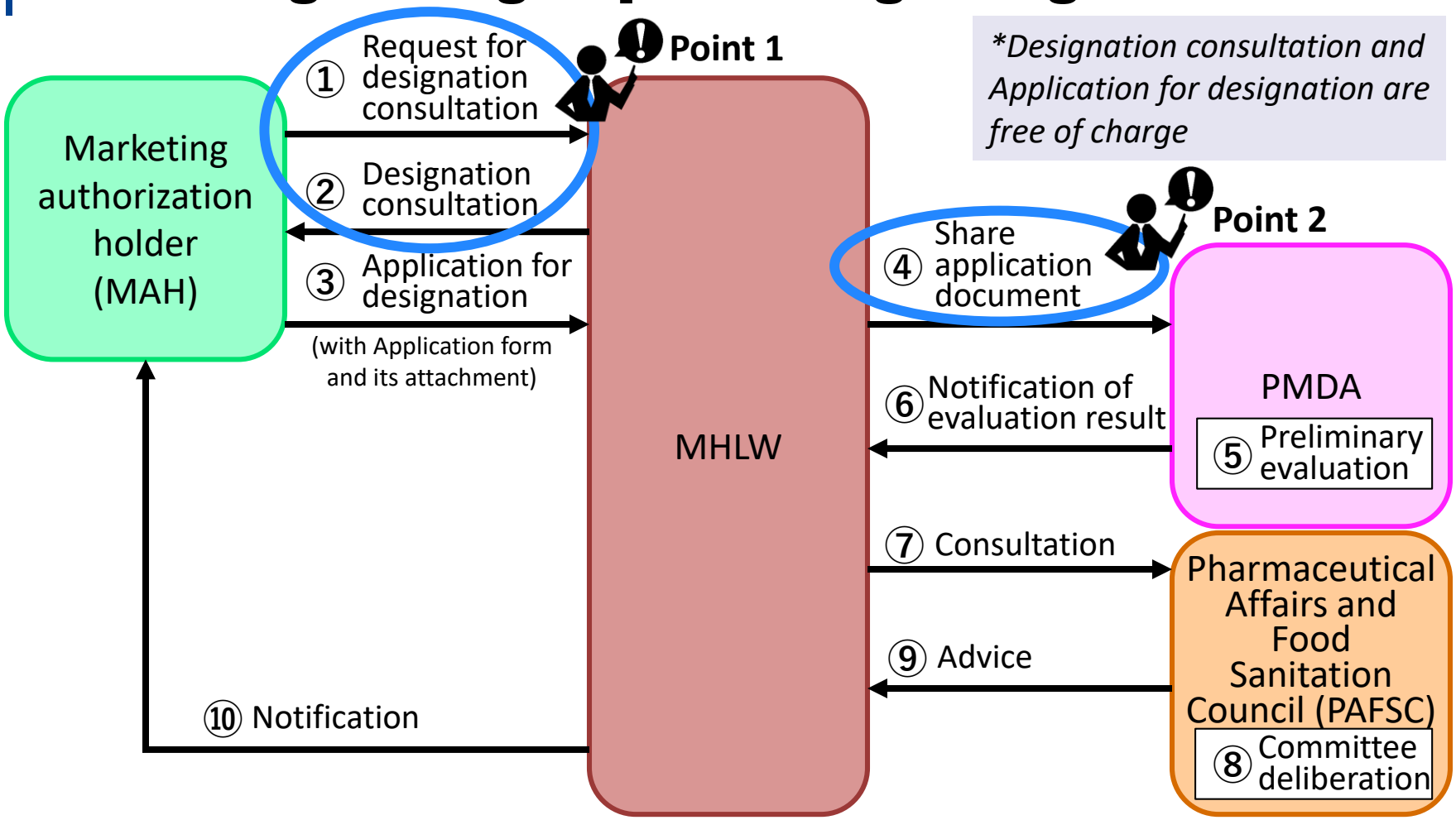
[Others] Office of Cellular and Tissue-based Products, Office of Vaccines and Blood Products

Flow for granting Orphan drug designation

**Designation consultation and Application for designation are free of charge*



Flow for granting Orphan drug designation



In order to expedite each timeline…

Point 1: <u>For designation consultation</u>

- MHLW carries out a “preliminary check” in order to exclude products that clearly do not meet the designation criteria.
- MHLW consults with PMDA about eligibility if needed.
- MHLW sometimes recommends MAH to have scientific consultations with PMDA if the consultations are likely to be helpful to fulfill designation criteria of “Feasibility of Development”. ➔This will bring benefits to both MAH and MHLW/PMDA.

For MAH:
Discussion points will be clarified in advance and predictability will be increased.

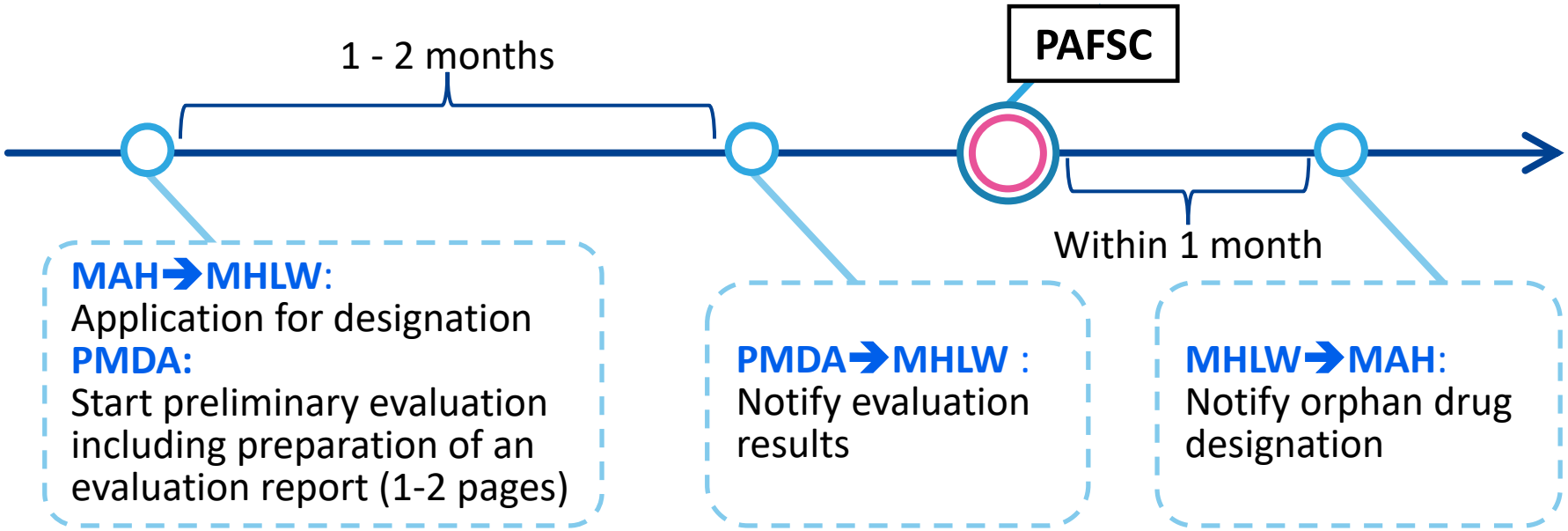
For MHLW/PMDA:
Preliminary evaluation of orphan drug designation and regulatory review will be smoothly conducted.

In order to expedite each timeline…

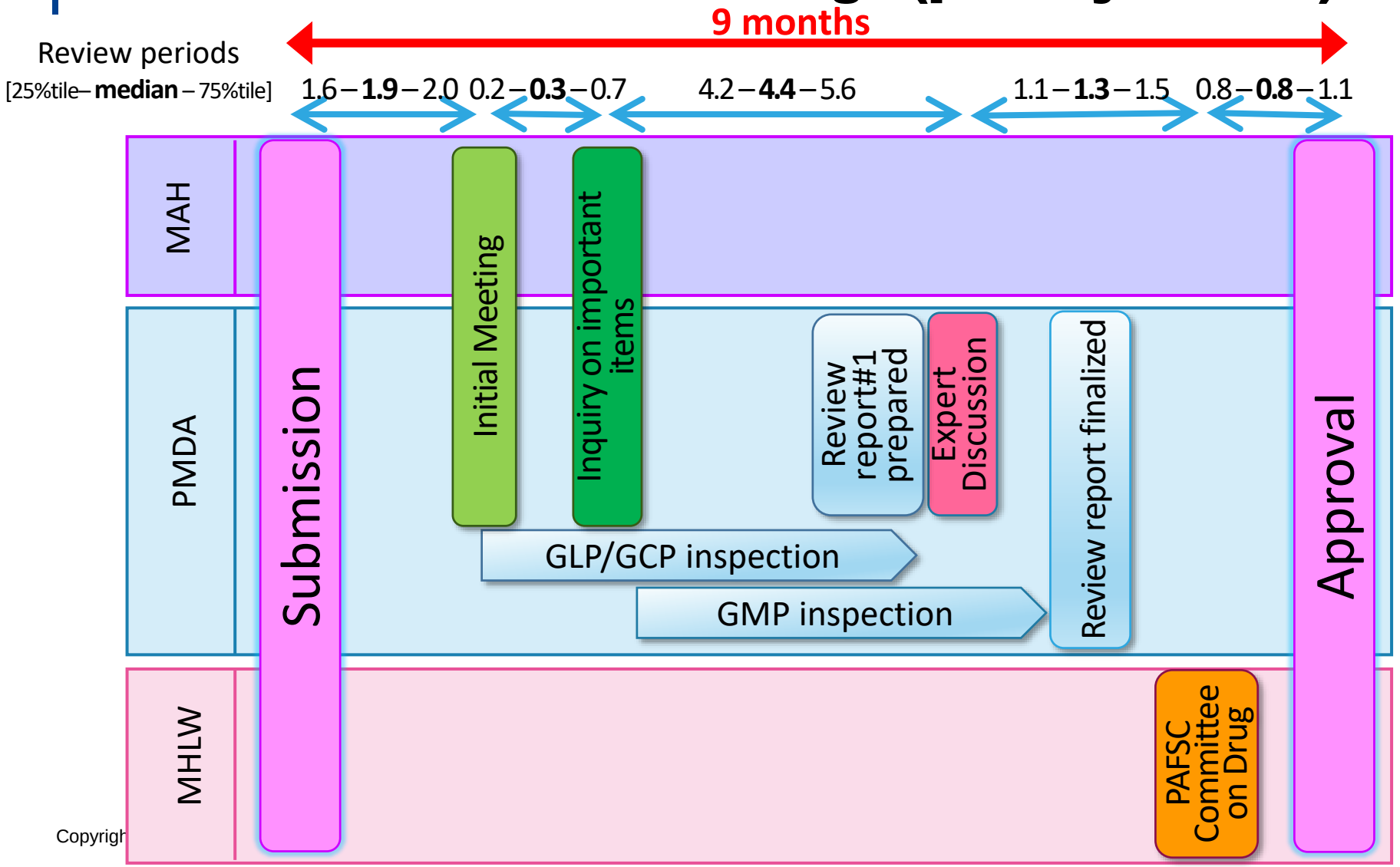
Point 2: For PMDA's preliminary evaluation

- Once draft of application document is prepared, MHLW checks sufficiency of explanation in the application document (usually about 30 pages).

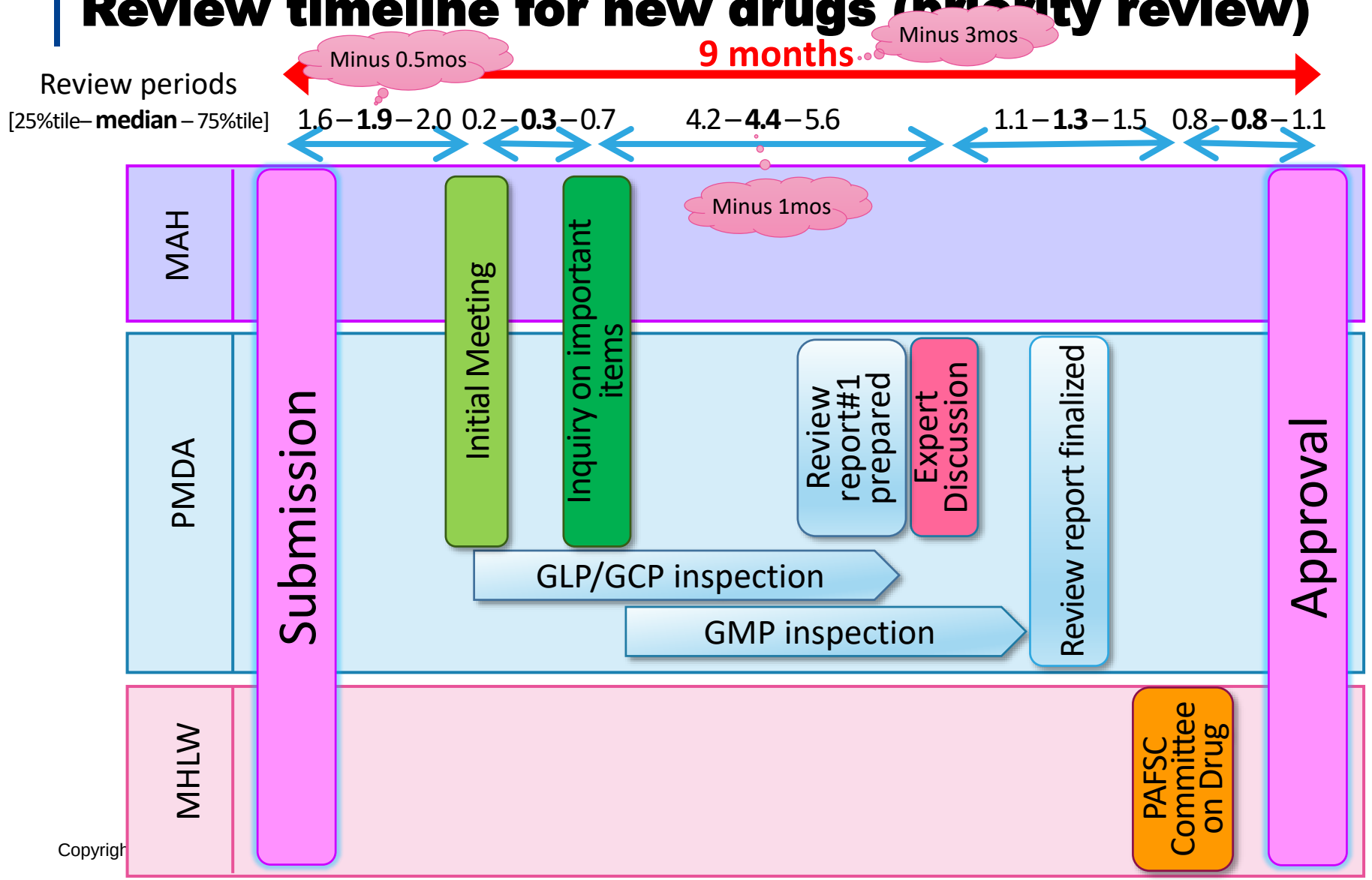
Example of timeline for orphan drug designation



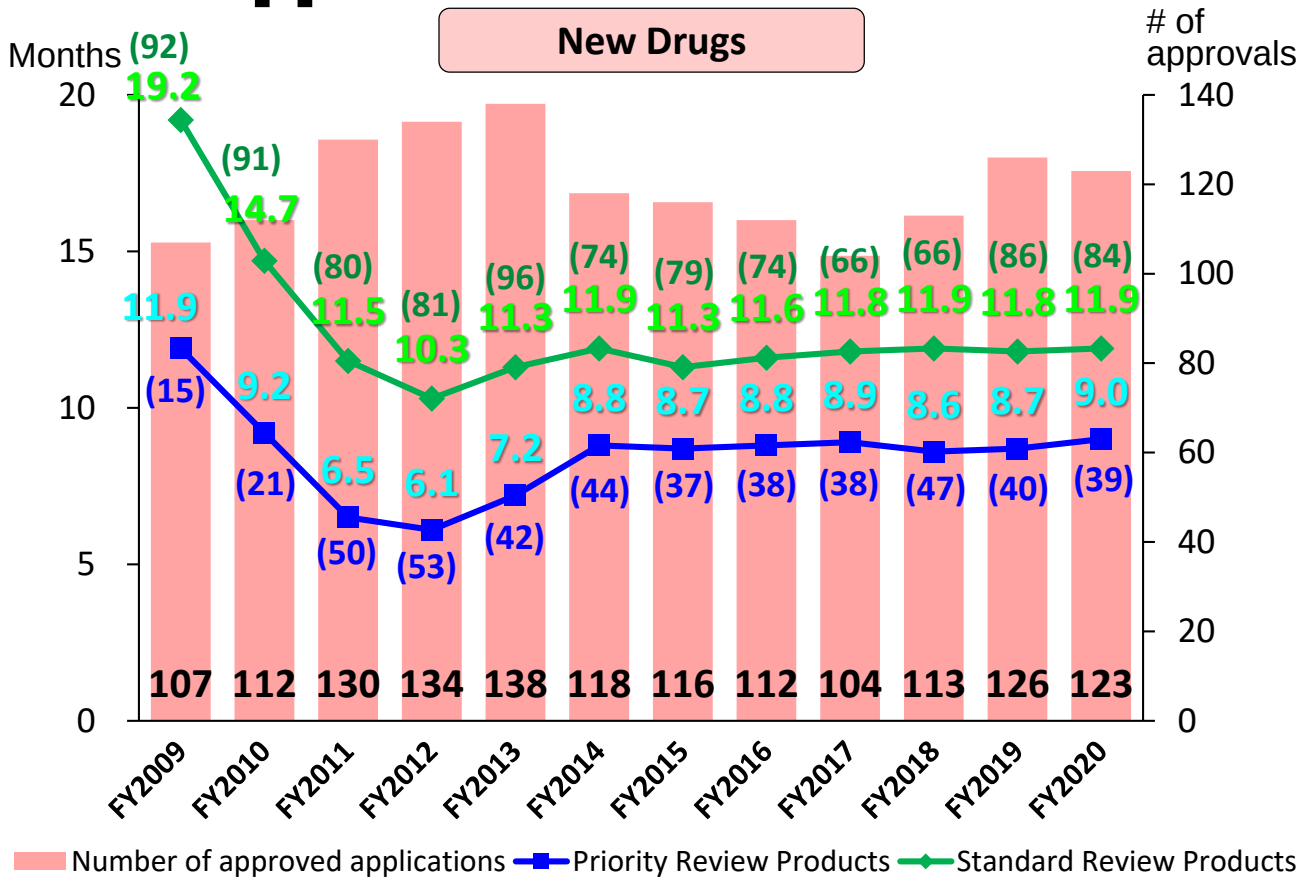
Review timeline for new drugs (priority review)



Review timeline for new drugs (priority review)



Number of Approvals and Review Periods



FY			'09	'10	'11	'12	'13	'14	'15	'16	'17	'18	'19	'20
Target median value (Month)	New Drugs	Priority	11	10	9	9	9	9	9	9	9	9	9	9
		Standard	19	16	12	12	12	12	12	12	12	12	12	12

Conclusion

- ✓ Taiwan and Japan are similar in terms of ethnicity including disease distribution and medical practice.
- ✓ If we could deepen understanding of legislation/regulation and cooperate each other, we would be able to further promote orphan drug development and supply in own regions and East Asia.

Work together for rapid availability of drugs with better quality to people