外資系企業における承認及び開発品目の傾向
～PhRMA/EFPIA合同調査結果より～

PhRMA RESEARCH + PROGRESS = HOPE

efpia European Federation of Pharmaceutical Industries and Associations

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PhRMA/EFPIAで実施した2018年度の合同調査結果は以下の通りであった。

審査期間と承認品目

- 2018年度（2018年4月～2019年3月）にPhRMA及びEFPIA加盟会社で承認された新医薬品は59品目で、そのうち通常審査品目は30品目であり、審査期間は80%tileで11.8カ月であった。公知申請を含む優先審査品目は29品目で、80% tileで8.7カ月であった。
- 日米欧の審査期間はほぼ同じであり、審査期間のラグは解消されていることが示された。よって、日本における承認時期の欧米との差は、申請時期の差によるものとみられた。
- 日米欧での先駆け審査指定制度、Breakthrough指定制度、PRIME指定制度等の利用状況については、FDAで一番多く複数の制度が利用されており、制度の利用状況には当局別で差があった。

開発品目

- 2018年度に開発中のプロジェクト数は674であり、792試験が実施されていた。全試験のうち、第Ⅱ相、第Ⅲ相試験では国際共同試験が80%を占めており、多くの品目で海外と同時に開発が進められ、60%以上の品目で同時申請を予定していることが示された。疾患領域として抗悪性腫瘍薬が多く、全体の55%を占めていた。
- 外資系企業における先駆け指定を希望する品目は5%と低かった一方で、3カ月以内の申請予定は6割以上であった。
- 小児開発については、全プロジェクトのうち18%で開発が進められており、うち約40%が同時開発であった。

PMS

- PMSは承認品目の75%（44品目でPMS49件）で実施され、うち全例調査は31%であった。データベースを用いた調査はPMS全体の18%を占めており、昨年度と比較し増加していた。これは改正GPSPの浸透に伴うものであると推察される。

PhRMA-EFPIA Joint Survey 2019

- Review Period
  - Review time for new drug approvals in FY2018
  - Submission/approval gap
  - Utilization of expedited program
- Clinical Studies and Development Plan
  - Projects ongoing in FY2018
  - Filing gap
  - Global and local studies ongoing in FY2018
  - Interaction with the agency for global studies
- PMS
  - PMS in approved new drugs

Companies involved:

PhRMA (12 companies)

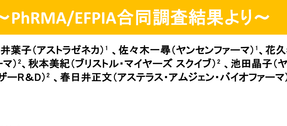
- Abbvie, Alexion, Amgen Astellas BioPharma, Biogen Japan, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Mundipharma, Pfizer, and Gilead Sciences

EFPIA (17 companies)

- Actelion, AstraZeneca, Bayer, CHUGAI, CSL Behring, Ferring, GlaxoSmithKline, Janssen, LEO, Lundbeck, Merck Biopharma, Boehringer Ingelheim, Novartis, Novo Nordisk, Sanofi, Shire, and UCB

Review period

Review Time for Standard Review



	FY2010	FY2011	FY2012	FY2013	FY2014	FY2015	FY2016	FY2017	FY2018
	Median	Median	Median	Median	60%tile	70%tile	70%tile	80%tile	80%tile
ALL (PMDA)	14.7	11.5	10.3	11.3	11.9	11.3	11.6	11.8	11.9
PhRMA+EFPIA						11.1	11.4	11.3	11.7

Key findings: Both review time for "Standard Review" in FY2018 were less than 12 months in 80%tile.

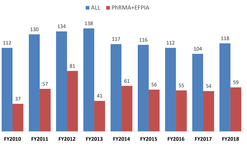
Review Time for Priority Review

Including Paper JNDAs

	FY2010	FY2011	FY2012	FY2013	FY2014	FY2015	FY2016	FY2017	FY2018
	Median	Median	Median	Median	60%tile	60%tile	70%tile	70%tile	80%tile
ALL (PMDA)	9.2	6.5	6.1	7.2	8.8	8.7	8.8	8.9	8.6
PhRMA+EFPIA						9.2	8.3	8.8	8.7

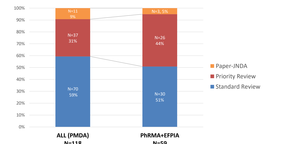
Key findings: Both review time for "Priority Review" in FY2018 were less than 9 months in 80%tile.

The Number of New Drug Approvals in Japan



Key findings: In FY2018, approvals of EFPIA+PhRMA (59) account for 50 % of ALL (118).

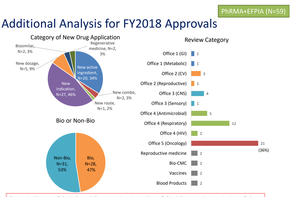
Proportion of Review Category for FY2018 Approvals



Key findings: Proportion of Priority Review (including Paper-JNDA) in PhRMA+EFPIA accounts for 49%, which is larger than the one in ALL 41%.

PhRMA+EFPIA (N=59)

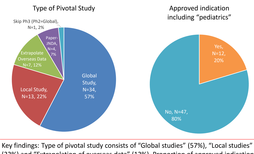
Additional Analysis for FY2018 Approvals



"New indication" (46%) and "new active ingredient" (34%) were the majority of the category of the NDA.
Oncology (36%) was the largest review category.

PhRMA+EFPIA (N=59)

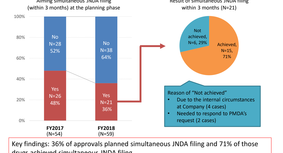
Additional Analysis for FY2018 Approvals



Key findings: Type of pivotal study consists of "Global studies" (57%), "Local studies" (22%) and "Extrapolation of overseas data" (12%). Proportion of approved indication with pediatrics accounts for 20%.

PhRMA+EFPIA

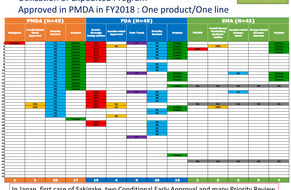
Simultaneous JNDA filing



Key findings: 36% of approvals planned simultaneous JNDA filing and 71% of those drugs achieved simultaneous JNDA filing

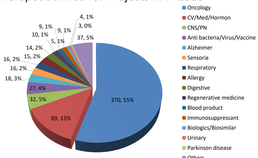
PhRMA+EFPIA

Utilization of Expedited Program
Approved in PMDA in FY2018 : One product/One line



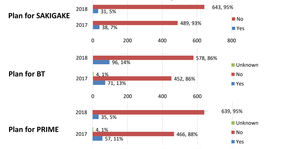
In Japan, first case of Sakigake, two Conditional Early Approval and many Priority Review as well as Orphan drugs were utilized. Expedited program is widely granted in the US.

Submission/Approval Gap of 18 NMEs (New Molecular Entities)



The timing when to submit filing seems to contribute the approval timing.
The review time of PMDA is almost same as one in FDA and EMA, some are faster than other HAs.

Submission/Approval Gap of 24 LCMs (Life Cycle Managements)



The timing when to submit filing seems to contribute the approval timing.
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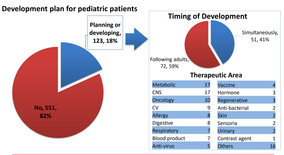
Clinical Studies and Development Plan

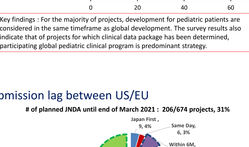
Total Projects in FY2018

EFPIA + PhRMA 674 projects



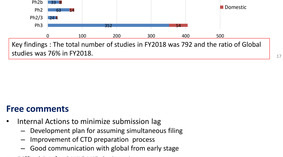
Key findings : In FY2018 the total number of ongoing projects are 674 . The ratio of new MOA increased from 54% (FY2017) to 72% in FY2018 . The products with plan of simultaneous submission are 63%, slightly increased from 61% in FY2017.

Therapeutic Area for Projects in FY2018



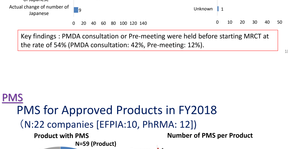
Key findings : Oncology is a major focused area and the proportion of projects regarding oncology accounts for 55% of the total projects in FY2018.

Plan for SAKIGAKE/Breakthrough(BT)/PRIME



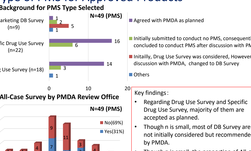
Key findings : In FY2018, the number of projects with plan for SAKIGAKE designation is 31 (5%). The number of projects with BT planned is highest (14%) among three expedited programs.

Plan for Pediatric Development



Key findings : 18% of projects have a plan for the development for pediatric patients. Roughly 60% of projects are planning to develop for pediatric patients following the development for adults.

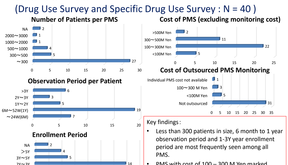
Plan for Pediatric Development



Key findings : For the majority of projects, development for pediatric patients are considered in the same timeframe as global development. The survey results also indicate that if projects for multi clinical data package has been determined, participating global pediatric clinical program is predominant strategy.

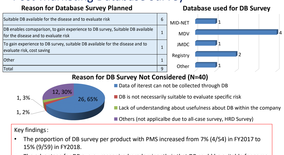
Number of Clinical Studies (Global/ Domestic)

EFPIA + PhRMA 792 studies



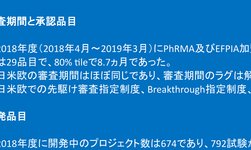
Key findings : The total number of studies in FY2018 was 792 and the ratio of Global studies was 76% in FY2018.

PMDA Consultation for MRCT



Key findings : PMDA consultation or Pre-meeting were held before starting MRCT at the rate of 54% (PMDA consultation: 42%, Pre-meeting: 12%).

Submission lag between US/EU



Free comments

- Internal Actions to minimize submission lag
  - Development plan for assuming simultaneous filing
  - Improvement of CTD preparation process
  - Good communication with global from early stage
- Difficulties for SAKIGAKE designation
  - Conflict with expedited scheme in US/EU
  - Human resources for JNDA preparation
  - Understanding and getting support from global
  - Unclear benefit to drug pricing system

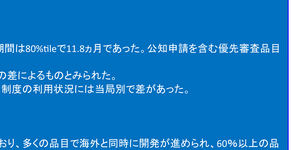
Overall findings and discussions

The followings are considered as the background to lead the result;

- It is necessary to secure additional time and resources for JNDA preparation.
- NDA timing in US/EU is decided first and then decide JNDA timing. For "Japan First" and " on the Same Day" submission in Japan, tough negotiation between global is needed to get agreement to give priority to Japan
- Up-to 3 months lag is considered "simultaneous filling" internally and 3 months is reasonable for JNDA preparation.

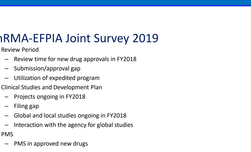
PMS

PMS for Approved Products in FY2018
(N:22 companies [EFPIA:10, PhRMA: 12])



Key findings : PMS is conducted for almost all of NCE products. Products without PMS are predominately those approved for new indication.

Type of PMS for Approved Products



Key findings :

- Regarding Drug Use Survey and Specific Drug Use Survey, majority of them are accepted as planned.
- Though n is small, most of DB Survey are not initially considered but recommended by PMDA.
- Though n is small, the proportion of All-case surveys for products reviewed by Office 4 is relatively high (7/16; 43%).

Details of PMS

(Drug Use Survey and Specific Drug Use Survey : N = 40)

Key findings :

- Less than 300 patients in size, 6 month to 1 year observation period and 1-3Y year enrollment period are most frequently seen among all PMS.
- PMS with cost of 100 – 300 M Yen marked highest number and majority costs more than 100 M Yen.

Post-Marketing Database Survey

Reason for Database Survey Planned	
Suitable DB available for the disease and to evaluate risk	4
DB enables comparison, to gain experience to DB survey, Suitable DB available for the disease and to evaluate risk	1
To gain experience to DB survey, suitable DB available for the disease and to evaluate risk, cost saving	1
Other	1
Total	5

Key findings :

- The proportion of DB survey per product with PMS increased from 7% (4/54) in FY2017 to 15% (9/59) in FY2018.
- The advantage for DB survey recognized predominantly is that DB could be suitable for some specific diseases and to evaluate specific risks
- Among reasons why DB was no considered, the majority is that DB does not necessarily suitable to collect data of interest.