

外資系企業における開発品目の傾向

~PhRMA/EFPIA合同調査結果より~



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PhRMA/EFPIAで実施した2022年度の合同調査結果は以下の通りであった

・2022年度は760 件のプロジェクトから回答が得られた。開発中品目で見ると疾患領域では例年どおり引き続き抗悪性腫瘍薬が最も多く、半数を占めていた。

・本邦で 2024年3月までに申請予定のプロジェクト(88 件、12%)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 42%であり、昨年の64%と比較し同時開発品目の減少傾向がみられた。

·新有効成分213件のうち第I相試験を実施せずに参加したプロジェクトは35件(16%)であり、それ以外はMRCT前または並行して、あるいは他効能で第I相試験を実施していた。

・致命的でない疾患に対し長期間の投与が想定され、希少疾病用医薬品に該当しない新医薬品で、国際共同試験が主たる試験となるプロジェクト(160件)のうち、日本人1年100例以上評価するプロジェク トの割合は32%で、100例未満のプロジェクトは52%であった。

・全プロジェクトの治験実施数は854件であり、そのうち約85%は国際共同試験であった。なお、本調査を開始した2015年からほぼ右肩上がりで治験実施数は毎年増加の傾向であったが、昨年の治験実施 数1043件に比べ、今回は大幅に減少した。

·FDAにおける抗悪性腫瘍薬の早期承認制度 (RTOR、Assessment Aid、Project Orbis)のいずれかの利用は82件と昨年67件に比べ増加傾向にあった。

・先駆的医薬品指定制度の利用は検討中も含めて全体の3%であり、昨年の2%と同様に少なかった。

ドラッグロスの要因として、薬価及び日本特有規制要件等の意見が挙げられた。

・全プロジェクトの27%(205/758プロジェクト)は小児開発が進められ、昨年の19%(164/884プロジェクト)より増加した。小児開発促進のために、小児に対する用法・用量の製造販売承認事項一部変更承認 申請に必要なデータの簡略化、薬価へのインセンティブを求める意見が多かった。

Therapeutic Area for Projects in FY2022



• The ratio of new MOA products is as many as 66%, of which innovative new MOA products (products significantly different pharmacological effecting compared with existing drugs) are 34%.



Peripheral nerve Immunosuppressan ■ Regenerative (cell) Regenerative (gene) Fixed Dose Combination Radiopharmaceutical

Submission lag (1)



The first submission region was the US in 75% of the cases. EU accounts for 22% and Japan accounts for 2%.

Submission lag (2)



First submission in Japan or same day submission with other regions is only 2%, but submission in Japan within 3 months is planned in around 42% projects (down from 59% in 2022 and 51% in 2021). It accounts for 56% in case of oncology drugs.

Submission lag (3)



processes that enable same-day submission. **r** . **r**... **r**.

$^{ m v}$ The main reasons for not filing first in Japan (or on sam	ne day) are that such submissions are
impossible or was a business decision. Japan specific r	egulatory requirements also account for 26%
Major Japan specific reasons which caused delay in	Development of companion diagnostics
Japan submission were: → • PMDA opinion affected submission timing (11/26)	 US/EU approval was a condition of approval in Japan Orphan drug designation timing (2 cases) Data available timing of clinical study in Japan
 Preparation of M2.3 or applicant form for Japan (8/26) 	 Considering approval timing in Japan Requires translation time for J-CTD Data error in a clinical study needed time for correction Miss reading of patient recruitment speed at interim analysis

Timing of MRCT participation New active ingredients (N=374)

Timing of Japanese Phase 1 implementation of new active ingredients

In-licensed products (N=86)

Whether or not there was any explanation by PMDA other than "In principle, it is necessary" or "We cannot



• Of the 760 products, 344 (45%) projects participated in MRCTs from P3 (P2/3). • Of the 374 new active ingredient projects, 126 (34%) participated from P3 (P2/3), followed by 87 (23%) from P2 study. • Of the 125 in-licensed product of new active ingredient, 58 (46%) participated from P3 (P2/P3), followed by 28 (22%) from P2. • More in-licensed products of new active ingredients participate in MRCTs from Phase 3 trials (46%) than whole new active ingredients (34%).

Is the development plan to include \geq 100-Japanese



than for those that participated in MRCTs from P3 (P2/3). Of the 172 products in which Phase 1 was conducted prior to MRCT participation (includes projects other than new active ingredients), 49 (28%) had PMDA consultations prior to Phase 1. In 38 of them (78%), PMDA provided no explanation other than "in principle, it is necessary" or "we cannot make a decision because there are no Japanese Phase 1 data ".

consultation

The extent of population exposure to assess clinical study (1)

(≥100 patients/one-year in Japanese population)



- Of 760 projects, 220 projects (29%) were applicable to ICH E1 and MRCT registration studies.
- Of 160 non-orphan projects, 52 projects (32%) were ≥100-Japanese population per year and 83 projects (52%) were <100-Japanese population per year.
- Of 60 orphan^{*} projects, one project were \geq 100-Japanese population per year.

The extent of population exposure to assess clinical study (2)

(≥100 patients/one-year in Japanese population)

Why is "≥100 Japanese population per year" <u>not</u> included in clinical data package? (multiple-answers)

Reasons	All (N=139)	Non-orphan (N=83)	Orphan* (N=56)
The safety in Japanese population can be evaluated based on consistency of results between overall and Japanese population	67 (48%)	40 (48%)	27 (48%)
Japanese population was calculated considering feasibility	118 (85%)	64 (77%)	54 (96%)
Already evaluated in other submission	4 (2.8%)	4 (4.8%)	0

How many Japanese population for long-term safety are evaluated in clinical data package?



The most common reason for "<100 Japanese population per year" in clinical data package was enrollment feasibility

Regarding number of Japanese population, 54 projects (65%) were less than 50 Japanese populations even if projects were non-orphan

Number of Clinical Studies (Global/ Domestic)





The total number of studies was 854 and the ratio of Global studies was 85% in FY2022.



The survey respondents only use/planned to use SAKIGAKE for 24 (3.2%) of the total projects, including those under consideration. Reasons for not using SAKIGAKE include that the projects do not meet the requirements or that it is difficult to submit applications in Japan before or at the same time as the first global application. More than half of the companies (57%, 13/23) believe that further relaxation of the criteria of simultaneous submission is necessary to promote utilization of the SAKIGAKE designation system.



	Eactors of Drug loss	
	Factors of Drug loss	N=20
Drug pricing system	 Drug pricing unpredictable Drug price adjustments with other countries New indication is not developed due to price reduction by market recalculation. 	expansion
lapan specific regulations	 <japanese data=""></japanese> Japanese data requirement for clinical data package Japanese P1 data requirement before MRCT <japanese language=""></japanese> Japanese is required in CTD M2 <regulation></regulation> Supplemental NDA is required for concomitant medications Post-market regulation requirement such as 14-day prescription, F 	PMS, etc
Prioritize other regions	Declining attractiveness of Japan marketPlanning initial development in US/EU.	
Expedited Program	 Differences in Orphan designation with US/EU. Differences in accelerated approval (US)/conditional approval (EU))
Development by Overseas Venture	Not developed for Japan	
Cooperation among regulators	• No cooperation of PMDA with FDA or EMA (e.g. Project Orbis, PGA	4)

Pediatric development drug



- Respondents had pediatric development plans for 205 of the 758 projects (27%), higher than in FY2022. In most instances the plan is to develop globally (79case, 80%) and in 43 cases (54%) there is a data package agreement with PMDA.
- Reasons for prioritizing include global plan, followed by IP and pricing incentives.
- Particularly desired measures to facilitate pediatric development are: 1: Simplification of data required for pediatric dosage and administration applications (e.g., review of requirements for approval of clinical trials for additional pediatric dosage, approval only for pharmacokinetic studies in pediatric patients by extrapolation from adult data); and 2: Additional incentives for drug price upon approval for pediatric dosage and administration (e.g., subject to additional new drug creation, subject to company index, etc.).

Plan for specific-use drug designation (SUDD)



Utilization of Real-World Data

Survey Respondents (N=760 projects)



Among 14 projects, 6 projects are proceeding with RWD as a result of PMDA consultation, 4 projects decided no-go after internal discussion and 4 projects will be consulted with PMDA. There was no project which gave up after PMDA consultation.