外資系企業における製造販売後調査（PMS）の傾向
～PhRMA/EFPIA合同調査結果より～

〇穂積香織(アッヴィ)[2]、今井景子(ヤンセンファーマ)[1]、小川嘉正(フェリング ファーマ)[1]、佐藤夫美(ファイザー)[2]、仙田雅之(サノフィ)[1]、塚本はるな(日本イーライリリー)[2]
[1] 欧州製薬団体連合会（EFPIA）　[2] 米国研究製薬工業協会（PhRMA）

・2021年度にはPMSは承認品目66品目中48品目（73%）で実施され、昨年に比べ実施品目の割合は少し増えているが、大きな傾向の違いはなかった。うち一般使用成績調査は35%、特定使用成績調査は48%、使用成績比較調査は2%、データベース調査は15%であり、この割合も2020年度と同様の傾向であった。
・PMSの実施計画書については、初回面談時までに40%の製品で実施計画書を提出しており、PMSに関連する初回問合せも70%が初回面談後の問合せ時までに来ており、PMSの検討が早くから始まっていることが認められる。一方でPMDAとの実施計画書等の合意は74%の調査で専門協議後に至っている。
・PMSの実施体制は、8割強の会社で実施計画書の内容についてグローバルの承認が必要であった。また照会事項の回答も、全ての事項ではないが9割近くの会社でグローバルの確認を必要としており、PMSは日本独自の制度に従って実施するが、グローバルが一定の関与をしていることがわかる。
・また、同意取得の状況は、89%の会社でなんらかの同意取得を行っており、そのうち64%の会社では、全例調査においても同意取得を行っていた。
・PMSの結果公表に関し、94%の会社で実施計画書又は実施要綱に調査結果の公表について記載されていた。再審査を目的としての実施が中心であったが、適正使用情報を早期に提供することやデータジェネレーションといった点から中間や最終報告を含め、積極的にPMSのデータが公表されていた。グローバルの関与や、同意の取得が進んでいる点からも今後もPMSのデータ活用の傾向は強くなっていくと考えられた。
・なお、2020年、2021年はコロナ禍での調査実施であったことも踏まえ、PMDAへの対応についても報告する。

PhRMA-EFPIA Joint Survey 2021

- Review Period
  - Review time for new drug approvals in FY2021
- PMS
  - PMS in approved new drugs in FY2021
  - PMS plan PMDA interaction/agreement timing
  - PMS organization and global interaction
  - PMS trend informed consent and disclosure
  - PMS under Covid-19

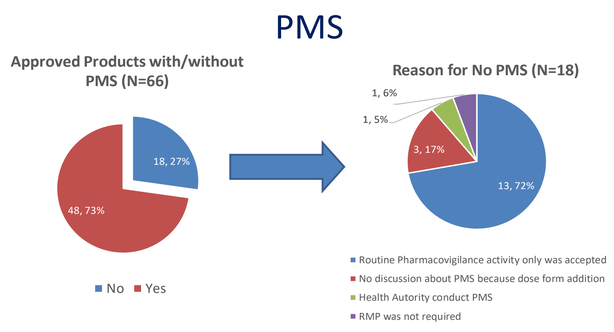
This results of analysis is based on the following companies, and the result of three overlapping companies are counted as one time

Participating companies:

- PhRMA (11 companies)
  - Abbvie, Amgen, Biogen Japan, Bristol-Myers Squibb, CSL Behring*, Eli Lilly, GlaxoSmithKline*, Janssen*, MSD, Pfizer, and Gilead Sciences
- EFPIA (15 companies)
  - AstraZeneca, Bayer, CHUGAI, CSL Behring*, Ferring, GlaxoSmithKline*, Janssen*, LEO, Lundbeck, Merck Biopharma, Boehringer Ingelheim, Novartis, Novo Nordisk, Sanofi, and UCB

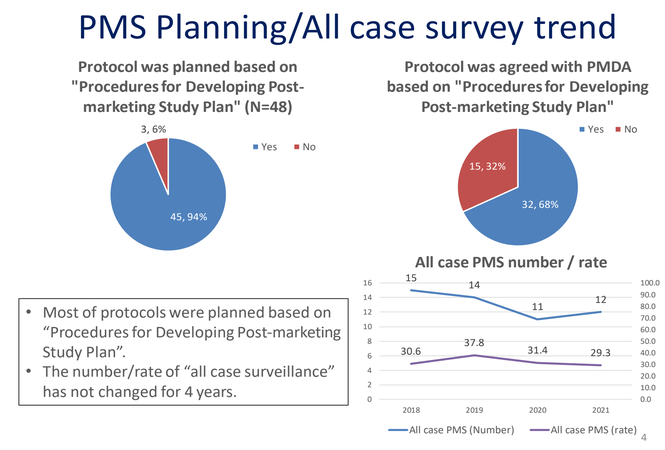
*: Companies participating in both of PhRMA and EFPIA

PMS



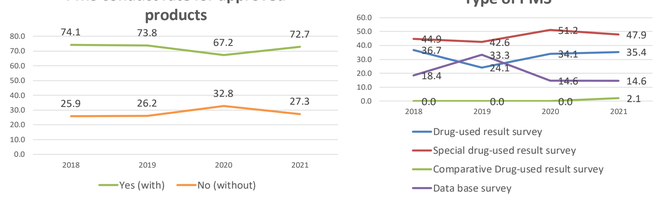
- PMS was conducted for all NCE/innovative biologics products.
- There were 27% of approved drugs which did not conduct PMS.
- For most products without PMS, they were accepted that routine pharmacovigilance activities suffice.

PMS Planning/All case survey trend



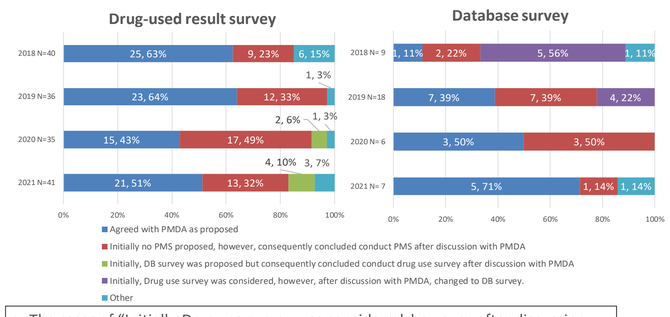
- Most of protocols were planned based on “Procedures for Developing Post-marketing Study Plan”.
- The number/rate of “all case surveillance” has not changed for 4 years.

PMS type trend



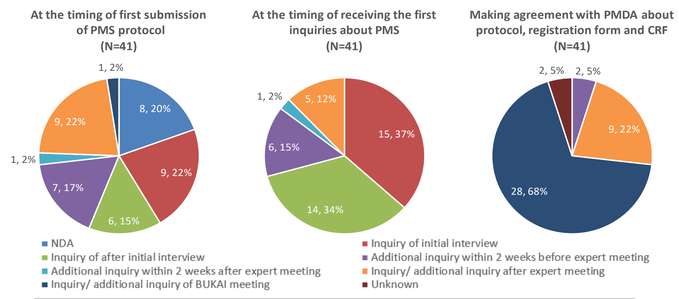
- The implementation rate of post-marketing surveillance for approved products remained unchanged during the past 4 years.
- The proportion of database surveys decreased in 2020 and remained in 2021.

Background of PMS



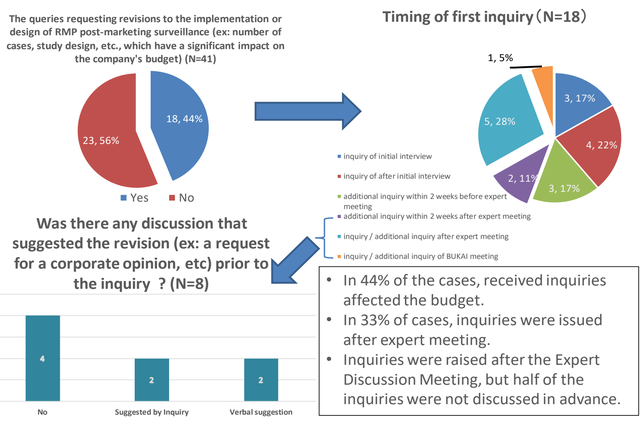
- The cases of “Initially, Drug use survey was considered, however, after discussion with PMDA, changed to DB survey.” were decreased year by year and stays zero since 2020.
- On the other hand, the cases of “Initially, DB survey was proposed but consequently concluded conduct drug use survey after discussion with PMDA” were increased.

Drug-used result survey PMDA interaction -agreement timing-



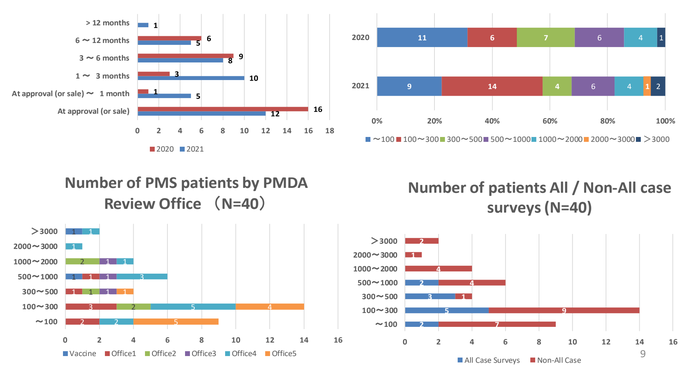
- 42% of the surveys had submitted protocols by the time of the initial interview.
- 71% of the first inquiries related to PMS were issued by the time of inquiries after initial meeting.
- However, in 68% of the surveys, the protocols, registration forms, and survey forms were agreed with PMDA after the BUKAI meeting.

Drug-used result survey PMDA interaction -inquiries timing-

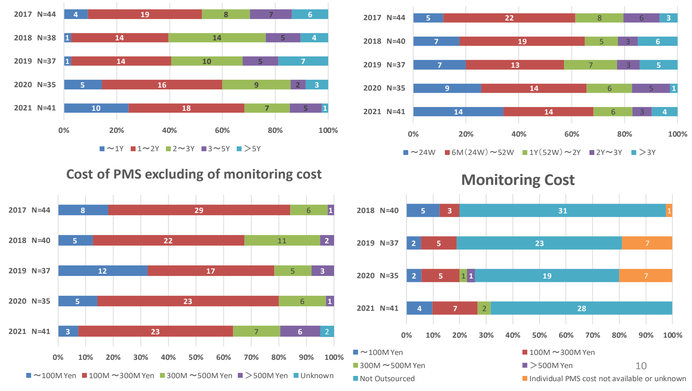


- In 44% of the cases, received inquiries affected the budget.
- In 33% of cases, inquiries were issued after expert meeting.
- Inquiries were raised after the Expert Discussion Meeting, but half of the inquiries were not discussed in advance.

Drug-used/Special Drug-used result survey -Survey details-



Drug-used/Special Drug-used result survey -Survey period and cost-



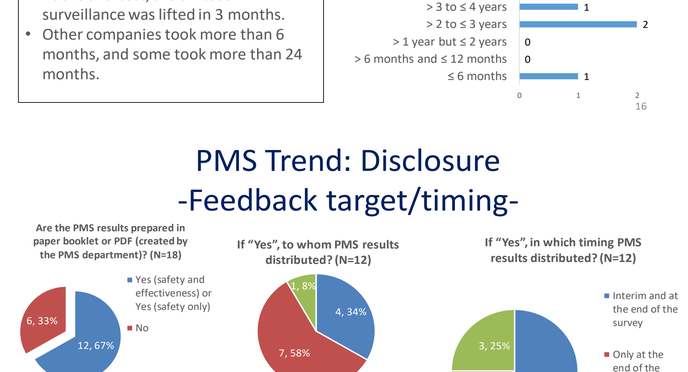
Drug-used/Special Drug-used result survey -Survey tools-

- The percentage of Electric data capture （EDC） is clearly increasing.
- In the all-case survey, Hybrid is the most.

Database Survey

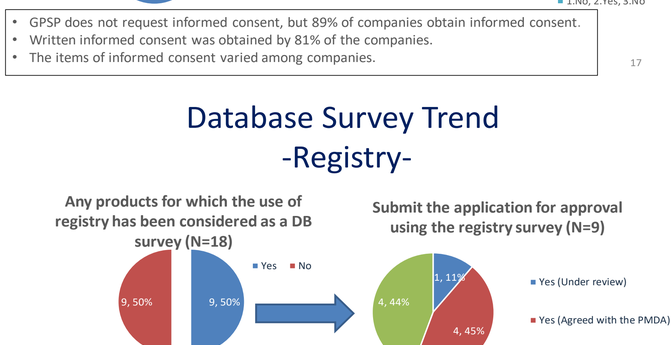
- 15% of all surveys were DB surveys.
- The main reason for selecting the DB surveys was “Suitable DB available for the disease and risk”.
- 85% of all surveys were Drug-used result surveys.
- The main reason for not selecting the DB survey was “Data can not be collected through DB”.

Database Survey -type, agreement timing and cost-



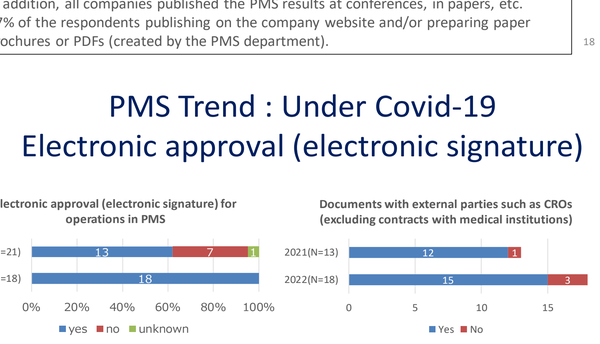
- 43% of Database survey reached to agreement with PMDA inquiry of after initial interview.
- 70% of Database Survey shows over 100 M cost in assumption base.

Global interaction on PMS protocol approval



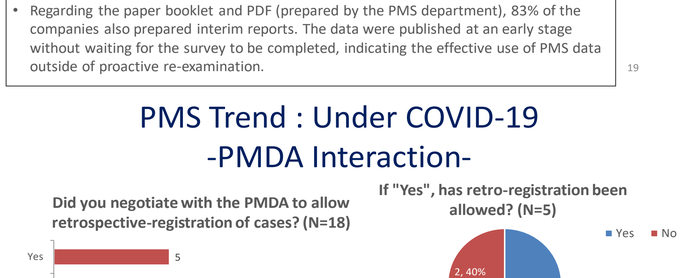
- About 60% of companies, there was no global contact point for PMS departments.
- More than 80% of companies required approval from Global for the contents of the PMS protocol
- About 90% of the companies needed to confirm the answer of PMDA inquiries before submission..
- Although GPSP is a local regulation in Japan, Global was involved.

Organization for DB study management



- Mainly, DB study was managed by safety Department in Japan.
- Slim majority, global epidemiologist participated in the planning of DB Study concepts.

PMS Trend -Termination of all-case surveillance-



- All-case surveillance was cancelled for 6 products in FY 2021.
- At the shortest, the all-case surveillance was lifted in 3 months.
- Other companies took more than 6 months, and some took more than 24 months.

PMS Trend -Obtaining Informed Consent-

- GPSP does not request informed consent, but 89% of companies obtain informed consent.
- Written informed consent was obtained by 81% of the companies.
- The items of informed consent varied among companies.

PMS Trend: Disclosure

- Although PMS was mainly conducted for the purpose of re-examination under the GPSP, 94% stated disclosure in the implementation plan or implementation guidelines beside re-examination .
- In addition, all companies published the PMS results at conferences, in papers, etc.
- 67% of the respondents publishing on the company website and/or preparing paper brochures or PDFs (created by the PMS department).

PMS Trend: Disclosure -Feedback target/timing-

- In the case of paper booklet or PDF (created by the PMS department), 58% were distributed only for medical institutions participating in the survey, and 42% were distributed for all medical institutions to which they deliver or without restrictions.
- Regarding the paper booklet and PDF (prepared by the PMS department), 83% of the companies also prepared interim reports. The data were published at an early stage without waiting for the survey to be completed, indicating the effective use of PMS data outside of proactive re-examination.

Database Survey Trend -Registry-

- A half of the companies have considered the utilization of registries.
- The reasons for not applying were “the quality cannot be assured, ”“ there is no registry that can be utilized, ” and “there is no understanding within the company.”

PMS Trend : Under Covid-19 Electronic approval (electronic signature)

PMS Trend : Under COVID-19 -PMDA Interaction-

- 5 companies consulted with PMDA to conduct a retrospective-registration, only 3 companies was admitted.
- Of these, two related to COVID-19 and non-COVID-19 drugs and three related to COVID-19 drugs only.
- 4 companies consulted PMDA about the difficulty of completing the survey within the re-examination period due to the impact of the COVID-19 pandemic.
- As a result, 3 companies were instructed to continue the survey after the re-examination period.