The 11th Joint Conference of Taiwan and Japan

Current Progress on New Drug Review Cooperation between Taiwan and Japan

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Activities under the Framework of the Cooperation on the Medical Products Regulation

Pharmaceuticals

- New Drug WG (New Drug/GCP)
- GBO WG (Generic/BE/OTC)
- Information sharing WG

Medical Devices

- QMS WG
- Product Registration WG
- Information sharing WG

Annual Meetings

Open conference

Sharing regulatory considerations and industry expectation on interest topics

Closed meeting

Experience sharing and opinion exchange on regulatory issues

New Drug Working Group

- 2017, Proposal of Japan-Taiwan Cooperation Scheme on Product Review
  - ***Utilization of English version of review report to promote Japan-Taiwan mutual understanding of review practices***.
  - Cooperation scheme will be initiated upon the applicant's request to both PMDA and TFDA.
  - Evaluation will be given on product basis
  - The applicant accepts utilization of the unmasked review report and its information. **PMDA and TFDA, applicant signed consent form to cope with pilot project**.
- Pilot cases for case study

Case Study: Case A (Pilot case)

- **Approved in Japan: 2014**
  - **NDA submitted in Taiwan: Apr. 2018**
  - **Approval letter issued in Taiwan: Aug. 2019**
- **Review pathway: Standard Review**
- Unmasked full review report received ~3 months later after NDA submission.
- NDA approved within a review period about 270 days (Standard review: 360 days)

Case Study: Case A –Discussion

- **Full review report provided after NDA review started.**
  - Review report was received after the first round of technical review, and the inquiries were already sent to the applicant.
  - ➡ **The consent for PMDA/TFDA/Applicant to share product review documents should be confirmed before NDA submission.**
- **Post-marketing safety reports were not included in the full review report.**
  - **A 3 year time gap** between the approval in Japan and NDA submission in Taiwan.
  - **Specific safety issue were identified** through the post-marketing safety report.
  - Additional documents and risk management activities were requested.
  - ➡ **This might limit the utilization of the full review report** provided from the Approved side.
- **Limited CMC information in the full review report.**
  - The CMC content in the full review report was a summary of submitted data, detailed information such as justification of specifications and analytical procedures were not included.
  - ➡ **CMC reviewer could request for detailed information from the Approved side** through Email.

Queries to the Review Side

Communication between PMDA and TFDA/CDE

- **Q: How was the review report been utilized?**
  - The unmasked PMDA review report was considered as reference, which **helped us to understand the review considerations of PMDA reviewers**
  - **The decision making is still based on review of the Dossier provided by the sponsor.**
- **Q: What are future challenges on this framework based on your experience of the pilot?**
  - The usability of the unmasked PMDA review report is **limited in CMC section.**
  - Although the PMDA report is good reference for review in TFDA/CDE, it is a one-way communication. **It would be benefit for both sides to build up mutual confidence and reach review consistency if we could exchange review reports, or have reviewers to discuss timely during an ongoing review process**.

The New Drug Review Scheme

- 2019, *"**Position Paper on New Drug Review Cooperation between Japan and Taiwan**" –"The New Drug Review Scheme"*
  - The New Drug Review Scheme is established as a review platform to exchange information and deepen understanding on new drug review issues.
  - To facilitate the review cooperation on NDA between PMDA and TFDA/CDE, the companies are encouraged to apply NDA under the Scheme.
  - The application on this scheme from companies needs to be adopted by PMDA and TFDA/CDE before starting collaborative activity in this Scheme.
  - The Company can decide type of information to be exchanged. Users of the information and control of confidential information need to be clarified in a signed Consent Document by the Company, PMDA and TFDA/CDE.

The New Drug Review Scheme

- **Step 1: Fulfil the criteria**
  - NDA from Companies that intend to obtain marketing approval of the drug product in Taiwan/Japan.
  - **The products of NDA that is already approved by either one and is planned to be applied to the other voluntarily**
  - The time gap between one approval date and the other NDA submission date is strongly recommended to **be less than one year**.
- **Step 2: Expresses interest** to join the Scheme through TFDA or PMDA.
- **Step 3: Sign the Consent form** for the use of review documents of the drug product by the Company, PMDA and TFDA/CDE.
- **Step 4: NDA dossier submission together with Unmasked full review report** (translated in English) to the Review side.
- **Step 5:** The Review side will inform the review progress to the Approved side. Performance and activities during the review will be presented in the Annual meeting.

The New Drug Review Scheme

- 2019, ***"Position Paper on New Drug Review Cooperation between Japan and Taiwan"***
- Case study:
  - CASE C, treatment of Parkinson's Disease
  - CASE D, treatment of insomnia
  - CASE E, treatment of hematological malignancies

Case Study: Case C

Background

- **Approved in Japan: Jan. 2020**
  - ➡ **NDA submission in Taiwan: Jul. 2020**
  - ➡ **Approval letter issued in Taiwan: Mar. 2021**
- **Review timeline: Abbreviated Review**
  - Already approved in US, EU and Japan
- **Waiver of bridging study** granted in 2018
  - With commitment to submit Japan Phase 3 study results with NDA dossiers.
- PMDA unmask review report (English version) provided by the applicant together with NDA package.
- **Review points:**
  - The US formulation is different from JP formulation
  - The pivotal study applied for NDA in US is different from the pivotal study applied in Japan.

Case Study: Case C

Results

- **Total review time: ~185 days**
  - The review timeline was delayed due to additional dossiers submitted by the applicant at the late stage of review process.
    - new stability data and editorial correction of CMC documents.
- **CTD differences between Taiwan and Japan**
  - An explanation letter summarizing the differences was provided by the applicant.
  - Differences: Packager, Packaging, Specification for dissolution test, Storage condition (stability tests), etc.
- **Utilization of PMDA full review report**
  - The full review report supported the review in several aspects, such as formulation, indications and other clinical parts.
    - Difference on pivotal trials and formulation used. PMDA report was used for reference to assess the connection by PK reviewers.

Case Study: Case D

Background

- **Approved in Japan: Jan. 2020**
  - **NDA submission in Taiwan: Jul. 2020**
  - **Approval letter issued: Oct. 2021**
- **Review Timeline: Standard Review**
  - **Already approved in Japan and US**
- **Bridging study was evaluated during NDA review.**

Case Study: Case D

Results

- **Total review time: 349 days**
- **No bridging study required.**
  - **Bridging study was waived due to minimally ethnic difference found in PK/PD profile**, as well as **similar trends in efficacy and relatively comparable safety results between East Asian and Non-East Asian subjects**
  - Commitment to submit final CSR of an on-going trial focused on East Asian population was listed as a condition for approval.
- **Utilization of PMDA full review report**
  - No further review issue were raised after the 1st inquiry been replied.
- **Reviewer communication between Taiwan and Japan**
  - Review considerations on clinical data requirements and MRCT issues regarding the indication for neuropsychiatric diseases.

Communication between Reviewers

Question from TFDA, for example

- Q: If both Japan and Taiwan join the global MRCT, do PMDA/MHLW accept pooling data of Japanese and Taiwanese subjects for subgroup analyses as bridging data?
  - Based on ICH E17 guideline, if **the intrinsic and extrinsic ethnic factors which are critical** to the assessment of the area of disease/ investigational drug are considered to be **sufficiently similar** between Japanese and Taiwanese subjects, it **may be considered that data from Japan and Taiwan would be "pooled regions"**.

Study Case: Case E

Background

- **Approved in Japan: Mar. 2020**
  - Orphan drug designation in Japan
  - ➡ **NDA submission in Taiwan: Nov. 2020**
  - ➡ **Approval letter issued in Taiwan: Nov. 2021**
- **Review Timeline: Priority Review**
  - Designation for *Accelerated Approval*.
  - Designation for *Pediatric or Minority Patient with Serious*.
- Efficacy of the drug was based on the results of a Japanese only phase 1/2 trial.

Case Study: CASE E

Results

- **Total review time: ~255 Days**
  - Review time was delayed due to some documents listed on pre-submission consultation meeting were not provided in the NDA dossier.
- **Clinical data differences in NDA dossier between Japan and Taiwan**
  - Due to numerous data correction in the erratum of one pivotal trial CSR, resubmission of a revised CSR was requested by TFDA/CDE.
- **Similar concern on safety issue between Japan and Taiwan**
  - Due to similar concerns on safety issue based on clinical study results, Risk Management Plan and Drug use-results survey protocols approved by PMDA were requested.

Summary

- ***Purpose of the New Drug Review Scheme is to promote Japan-Taiwan mutual understanding of review practices and to facilitate the review process through the utilization of unmasked full review report.***

- **Factors that affect reference value of the review report:**
  - **Timing** for providing the review report to the Review side.
  - **Similarity** of the CTD dossiers between the Approved side and the Review side.
  - **Post-approval changes** and **post-marketing safety issues**.
  - **Consistency in review considerations (dosage use, safety issue, clinical trial results, PK considerations)**

Challenges and Future Expectation

- **Increase review confidence between Japan and Taiwan**
  - More review experience and more communications are needed.
- **Extend the review cooperation** (On-going project)

- **Need inputs from industry**
  - Any suggestion or comment to current New Drug Review Scheme?
  - Any issue on review inconsistency between Japan and Taiwan that need to be solved?
- ***"Q&A for the New Drug Review Scheme", 2022***

  http://www.fda.gov.tw/TC/siteListContent.aspx?sid=2984&id=42341

THANK YOU!

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