Peer Review in Toxicologic Pathology

10th ESTP Congress 2012
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Current Situation for Pathology Peer Review in Japan

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Outline of Presentation

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1. Regulatory Agencies in Japan

Subjects	Guidelines	Risk Assessment
Pharmaceuticals:		
Synthetic	MHLW (2000)	PMDA
Herb	MHLW*	PMDA
Food additives:	MHLW (1996)	Food Safety Commission
Health foods:	MHLW*	MHLW subcommittee
Agrochemicals:		
Synthetic	MAFF (2000)	Food Safety Commission
Microbial	MAFF (1997)	Food Safety Commission
Veterinary drugs	MAFF (1985)	Food Safety Commission
Industrial chemicals:	METI/MHLW/ME (2001)	Food Safety Commission

* : Not specified, determined on case-by-case basis
MHLW = Ministry of Health, Labor and Welfare
MAFF = Ministry of Agriculture, Forest and Fisheries
METI = Ministry of Economy, Trade and Industry
ME = Ministry of the Environment
PMDA = Pharmaceuticals and Medical Devices Agency

2. Current Pathology Peer Review in Japan

- Pathology peer review (PPR) is recommended to be conducted but not required by any of regulatory agencies in Japan.
- Only Pharmaceutical and Medical Devices Agency (PMDA) proposed a guidance in 2006, “PPR by pathologists from sponsors should be conducted after data locking”.
- Consequently, sponsor PPR for pharmaceuticals has been being conducted after pathology data is fixed in accordance with the proposed guidance 2006 by PMDA.

Current PPR Procedures in Japan

Study Pathologist (SP)
(reads slide)

Findings

Work sheet

Internal PPR

Data locking

Findings

Work sheet signed and dated by SP (Raw data)

Sponsor PPR

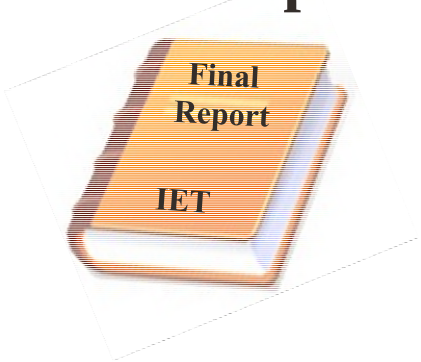
Revised version

Findings

If any changes, Document the history

Study Director (SD)

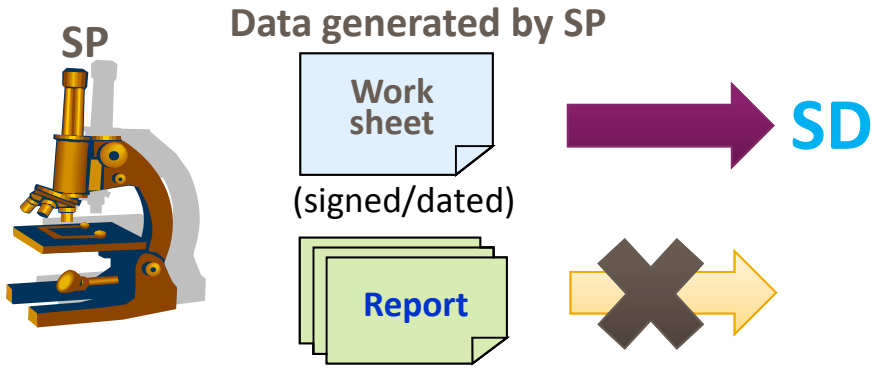
Final Report



3. Current Definition of Pathology Raw Data in Japan

- Pathology raw data is defined as findings described in the work sheets signed and dated by Study Pathologist (SP) in Japan.

- SP submits incidence data (Tables) and individual findings (Appendices) to Study Director after the data is finalized. However, pathology report singed and dated by SP is customarily not issued.



4. Current Reporting Procedures in Japan

- All the data generated during the conduct of a toxicological study are submitted to the Study Director (SD). Only SD prepare the final report based on the results gathered from each section.

- Therefore, Study Pathologist (SP) is not required to prepare a pathology report. Only pathology data singed and dated by SP is required to be submitted to SD.

5. JSTP Actions to Pathology Peer Review

- International panel discussion on regulatory perspective for pathology data was held at the 25th JSTP Annual Meeting in 2009. It was recognized that the timing of PPR and definition of raw data considerably differ among US, Europe and Japan.

- After a draft OECD guidance on PPR was proposed, the JSTP Peer Review Ad hoc Working Group discussed about the content with all members of the JSTP and consequently decided to endorse the STP position.

- In 2010, the JSTP and other relevant parties had a couple of face to face meetings with PMDA and recommended that PPR prior to data locking would be more suitable to improve the quality of pathology data.

6. New Draft Proposal for PPR by PMDA

- PPR is not mandatory to nonclinical studies of pharmaceutical products, but if PPR is carried out, then it is subject of GLP inspection.
- At the moment, PMDA considers that pathology raw data is the report or data signed and dated by the study pathologist.
- PPR before or after data locking would be acceptable either way, but PPR by pathologists outside from sponsors or academia may be required to ensure the transparency of review process and to be described in the protocol if the conduct is scheduled in advance.
- In that case, the name of the pathology peer reviewer and reviewed organs with disagreement should be described in the final report.
- The report or data generated by the peer reviewer should be archived together with other study documents.

7. JSTP Position on Pathology Peer Review

- The JSTP basically agrees with the new draft proposal by PMDA, although we need further discussions in details before it is finalized.

- In principle, the JSTP position is consistent with that of STP which is shown in "Recommendations for Pathology Peer Review" published in *Toxicologic Pathology* in 2010.

Dream forever