Experience in Japan
- PMDA perspectives -

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ICH Quality Strategy Workshop
June 1, 2014
A New Paradigm
in Brussels July 2003

☐ “Develop a harmonised pharmaceutical quality system applicable across the lifecycle of the product emphasizing an integrated approach to quality risk management and science”

☐ Pharmaceutical Quality System
Management system to direct and control a pharmaceutical company with regard to quality. (ICH Q10 based upon ISO 9000:2005)
History of implementing ICH Q8~10 in Japan

Q8, Q9

2006 2007 2008 2009 2010 2011 2012 2013 2014

Q8(R2)
Q&As
Q10
Q&As
Points to consider

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Q-IWG Training
EMA-FDA pilot program

Q-IWG Training Follow-up in Tokyo

*The number of approved products developed by QbD

ICH Quality Strategy Workshop June 1, 2014
MHLW-sponsored Health Science studies

- The group members are: researchers from the National Institute of Health Sciences (NIHS); reviewers and inspectors from PMDA; industries (ex. Daiichi-Sankyo, Astellas, Pfizer, GSK, Shionogi, Otsuka, Takeda, Chugai, etc.)

- **Sakura Tablet**: Pharmaceutical Development P2 with Enhanced Approach Mock

- **Sakuramil**: Manufacture S2 Mock
PMDA QbD Assessment Project

- In November 2011, PMDA launched a new project team to handle the participation in the EMA-FDA pilot program as an observer. (http://www.pmda.go.jp/english/service/qbd_e.html)

- The project team consists of reviewers, inspectors, etc..
  - Office of New drug I~V, GMP&QMS Inspection, International Programs, Standards and Guidelines Development, etc.

PMDA has been involved in:

- 1 parallel assessment application
- 1 biotech product that followed the consultative advice pathway
- 2 sets of Q&As that have been published
We have discussed since 2003

- Pharmaceutical Development
  - Process Understanding
  - Risk Management
  - Design Space and Real Time Release Testing
  - Control strategy etc.

- Pharmaceutical Quality System
  - Commercial Manufacturing
  - Batch Release Strategy
  - Technology Transfer etc.
Let’s look back at the original goal

What is the harmonised Pharmaceutical Quality System?

- What we expect
  - Continual improvement
  - Enhanced Quality Assurance by the company

Are there any unsolved issues or barriers?
Experience of QbD Assessment in PMDA (1)

- How to manage CPP
  - ICH Q-IWG PtC says that process parameter criticality can change as a result of risk management.
  - PMDA’s interpretation is that the level of criticality of PP can change as a result of risk management but “critical” pp should be stable.
  - PMDA’s concern is the statement that all parameters have become non-CPPs as a result of risk control.
Considerations (1)

- Cases where Edge of Failure (EOF) exist within the range of planned Design Space (DSp), and the end of DSp (the range of Process Parameters (PPs)) is close to EOF

The PP is CPP

Regulatory classification with high risk

Acknowledgement: Dr. Okuda et al.
Considerations (2)

- Cases where EOF exists within the range of planned DSp but the end of DSp is far from the EOF by setting the range of PPs to be smaller than DSp
  
  - The PPs are still CPPs
  - Risk Reduction
  
  The regulatory risk classification of the CPPs can be reduced.
Issues of QbD Assessment in PMDA (1)

- How to describe controlled CPPs in CTD.
  - Applicants should describe all PPs and evaluate each PP’s risk.
  - Regulators need to know where the risk is, and how industries can control the risk.

Should the controlled CPPs still be classified in the high risk category?
Experience of QbD Assessment in PMDA (2)

- Uniformity of Dosage Units – Criterion for a large sample size
  - It is not suitable to use the existing criterion for the uniformity of dosage units.
  - PMDA requests criterion 1 and 2 as done by EP/EDQM, for now.

- NIR
  - Japanese pharmacopoeia contains the Near Infrared Spectrometry (NIR) in the general information chapter.
Do we need collaboration with Pharmacopoeia?

- To harmonise the criterion for a large sample size of uniformity of dosage units.
- To harmonise the validation of the model and the system suitability for NIR.
What PMDA learnt from our experience

- Our concerns about QbD are basically the same as FDA and EMA.
- There are no great differences in the approaches of evaluating QbD applications, FDA, EMA or PMDA.
- Reviewers need a lot of time to assess the QbD approach even now and we tend to ask more questions than with traditional approach.
- Regulatory actions, especially post approval change actions, might be a little different because the regulatory framework of each jurisdiction is different.

But we have realized that ⋯
Challenges

☐ How to decrease our burdens?
  ■ To share our experience and knowledge
    ☐ QbD Pilot Programs, Workshops, Training…

☐ How to encourage continual improvement?
  ■ To increase flexibility in post approval changes
    ☐ ICH activity

Informal Quality Discussion Group Prioritized Quality Topics
Life-Cycle Management of CMC (Change Management)
Thank you for your attention