CMC Strategy Forum Japan 2023

Schedule

Monday, 4 December, 2023

07:30-08:30

Registration

08:30-09:00 North Ballroom

Welcome and Introductory Comments

CASSS Welcome and Introductory Comments (8:30 - 8:45)

Welcome to the CMC Strategy Forum Japan 2023 (8:45 - 9:00)

Session Speakers:

Wassim Nashabeh, *Genentech, a Member of the Roche Group*
Hiroshi Suzuki, *Pharmaceuticals and Medical Devices Agency (PMDA)*

09:00-10:20 North Ballroom

Session I - Recent Trends in the Regulation of Biopharmaceutical Products

Yoshiaki Maruyama, Cecilia Tami

Due to the influence of the COVID -19 pandemic, this will be the first in-person meeting since 2019. All the regulatory authorities have responded to the unexpected situation of the COVID -19 pandemic, and there are many types of lessons learned from the pandemic, and huge efforts and improvements in review and inspection activities.
In this session, regulators from each health authority will provide the recent regulatory updates and future perspective regarding biopharmaceutical products including regenerative medicine products. Furthermore, an industry representative will provide a case study from the ICMRA pilot on collaborative assessment.
The presentations will include information that will contribute to, and be further explored, in a panel discussion covering several themes, including:

Key Questions:
- Regulatory update on biopharmaceuticals products.
- Hot topics of CMC review / GMP inspection on biopharmaceutical products.
- Lessons learned from the COVID -19 pandemic and future initiatives.
- Progress on joint reviews/inspections and reliance for biopharmaceutical products, lessons learned from past experiences, and future perspectives and initiatives (e.g., ICMRA/PQKMS, ACCESS, Project OBIS)
- Modernization of marketing authorization application dossier in the future: for example, perspective for harmonization initiatives such as the ongoing M4Q revision and "Structured Product Quality Submissions" that are being carried out at ICH.
- Prospect and possibility for global submission by industry with same CTD, especially with same specification for drug substance and drug product.
- Progress, issues, and future perspective for ICH Q12 implementation: e.g., Established Conditions, PACMP, PLCM.
- Initiatives within health authorities and perspectives to industries for innovative technologies: e.g., continuous production, PAT.

Session Speakers:

Regulatory Updates and a Perspective on Biopharmaceuticals in Japan
Yasuhiro Kishioka, *PMDA*

Center for Biologics Research and Review (CBER) Updates
Ingrid Markovic, *CBER, FDA*

Advanced Manufacturing and Other Trends Supporting Access to Medicines for Patients
Hugo Hamel, *Health Canada*

10:20-10:50 South Ballroom Foyer

Networking Break

10:50-12:05 North Ballroom

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Session Speakers:

Regulatory Update From EU
Brian Dooley, *Europeans Medicines Agency (EMA)*

Current ATMP Regulation in China
Jiaqi Lu, *Center for Drug Evaluation (CDE)*

ICMRA PQKMS Pilots – the Roche Experience
Markus Goese, *F. Hoffmann-La Roche Ltd.*

12:05-13:30 South Ballroom

Lunch

13:30-14:30 North Ballroom

Session I - Panel Discussion

14:30-15:00 South Ballroom Foyer

Networking Break

15:00-16:45 North Ballroom

Session II - Stability of Biopharmaceutical Products: Topics about ICH Guideline Q1/Q5C Revision

Markus Goese, Akiko Ishii

ICH guideline Q1A is a stability guideline that reached Step 4 in 1993 and was established as one of the first guidelines finalized by the ICH. ICH guideline Q5C is a stability guideline for biopharmaceuticals that reached Step 4 in 1995.
Since the establishment of the guidelines, both industry and regulatory authorities have accumulated considerable experience and knowledge on the topic of stability, and concepts such as control strategy (ICH Q8/11), quality risk management (ICH Q9), and life cycle approach (ICH Q10/12) have been proposed. To align with some of these principles, Q1/Q5C revision is required to harmonize these existing stability guidelines, by incorporating science- and risk-based approaches, covering new modalities including ATMP and establishing a single integrated guideline. In line with the use of prior knowledge and applying a more risk-based approach, stability modeling is considered to be one of the ways to enable early patient access to medicines by predicting retest date and shelf-life.
In this session, scientific discussions will be held for the revision of ICH guideline Q1/Q5C based on challenges outlined concept paper and business plan. Expectations, requests and challenges from industries and regulators for the revision will be presented.

Key Questions
- Is there any expectation to ICH Q1/Q5C revision in terms of stability study programs, retest date and shelf-life from the viewpoint of regulator and industry?
- What are the challenges and expectations to predict stability profile, set retest date and shelf-life by using stability modeling?
- Are there any cases where different shelf-lives are approved for different countries, though the same stability data package is provided? How is Industry managing misalignments in Global expectations for shelf-life setting?
- Are there any cases of approved products with stability testing or shelf-life utilizing prior/platform knowledge? What are some of the challenges in proposing and adopting this strategy?
- In accelerated and early access programs (e.g., Sakigake Designation, FDA BTD, EMA PRIME), what approaches can be used for stability testing and shelf-life setting?
- What are special considerations to conduct stability study for personalized therapeutic products manufactured at a very small scale?
- What needs to be considered when evaluating the stability of products manufactured in continuous production?
- Are there any considerations to ensure holding and processing time for intermediates?

Confirmed Session Speakers:

Regarding Revisions of ICH Q1/Q5C Guidelines; Expectations and Concerns for Stability Assessment With Modeling-Type Extrapolation Methods in Biological Products
Takashi Kameda, *PMDA*

Current Situation and Issue on Stability Prediction of Biopharmaceuticals From Regulatory Perspective
Hiroko Shibata*, National Institiute of Health Science - Japan*

Modeling for Product-Specific Stability: A Regulatory Perspective
Paula Russell, *Health Canada*

Stability Predictions for mAbs Using Arrhenius-Based Kinetics
Mitja Zidar, *Novartis* (Presenting Virtually)

16:45-17:15 South Ballroom Foyer

Networking Break

17:15-18:15 North Ballroom

Session II - Panel Discussion

Additional Panelists:
Kousuke Tamura, Daiichi-Sankyo

18:15-19:30 North Ballroom

Networking Reception

Tuesday, 5 December, 2023

08:00-08:30 North Ballroom Foyer

Registration

08:30-10:15 North Ballroom

Session III - Challenges, Opportunities and Regulatory Expectations for CGT Product Comparability

Vandana Chauhon, Satoshi Yasuda

Comparability assessments based on product attributes is an important issue through all phases in the life of the Cell & Gene Therapy Products (CGTPs) from initial development through marketing, in order to improve and control the manufacturing process and/or products' quality. Meanwhile, there may be technical challenges for CGTPs to obtain comprehensive understanding of product characteristics and/or to identify potential product quality attribute, and to assess the comparability based on them, due to potential issues specific for CGTPs as follows.

- Wide variation in product quality among batches, due to characteristics of the cells as starting material.

- The impact of the manufacturing process on the product attributes is considered relatively high. In the meanwhile, the manufacturing process for CGTPs could be complex, for example using many kinds of reagents and/or ancillary materials, and so on.

- In order to understand the quality attributes of CGTPs, extensive analysis of the product characteristics may be preferable due to its complexity of the modality. Meanwhile, the availability of adequate samples for the analysis may be limited.

- The number of subjects of clinical study may be not adequate to evaluate the potential quality attributes correlate with efficacy.

In this session, regulatory expectations, technological challenges, and approach to measure the challenges for evaluating comparability of CGTPs, from initial development through marketing, will be discussed.

The presentation will include an introduction of Japanese draft guideline and lessons learnt from Industry's experiences for comparability assessment of CGTP.

Key Questions:

- It may be difficult to identify the potential critical quality attributes of CGTPs linked to safety and efficacy, especially in the preclinical or early clinical stages. From perspective of comparability assessment during development and/or post marketed, what is the points to consider on CMC development strategy including analytical development and evaluating product characteristics?

- In order to mitigate the potential risk or impact of manufacturing process changes on product quality, safety and/or efficacy, how could be risk assessment used?

- Are there any particular points to consider or recommendations on CMC development of CGTPs such as process development and analytical development? For example, are there any preferable approach for bridging strategy in before/after changes in process or analytical methods?

- What kinds of challenges in the process and/or analytical developments would be expected for comparability assessment of CGTPs? For example, the species difference in preclinical study, availability of human derived samples, and so on. And what kinds of approach would be expected to solve these challenges or limitation?

Confirmed Session Speakers:

Basic Approach for Comparability Assessment of Cell Therapy Products Subject to Changes in Their Manufacturing Process
Yoji Sato, *National Institiute of Health Science - Japan*

Change Management and Comparability for Cellular & Gene Therapy Products
Ingrid Markovic, *CBER, FDA*

Comparability of Autologous CAR-T Therapies in Development and Post-Approval
Edyta Pawelczyk, *Novartis*

Challenges in the Manufacturing Process of Autologous Regenerative Medical Products, and the Necessity for Post-Market Optimization
Yukio Mori, *Japan Tissue Engineering Co., Ltd.*

10:15-10:45 South Ballroom Foyer

Networking Break

10:45-11:45 North Ballroom

Session III Panel Discussion

Panelists:
Akiyoshi Kunieda, *PMDA*
Yuki Miyatake, *Bristol-Myers Squibb Company*

11:45-13:00 South Ballroom

Lunch

13:00-14:45 North Ballroom

Session IV: A Strategy for the Quality Control of Antibody-Drug Conjugates (ADCs) Throughout the Entire Life Cycle of the Product

Motonori Kidokoro, Helen Louis Newton

Antibody-drug conjugates (ADCs) are truly complex molecules that combine an antibody with a drug via a specific linker and are a promising new modality that offers a unique and unprecedented mechanism of drug action. ADCs combine the specificity of an antibody with the efficacy of a drug, enabling targeted and effective therapy. However, ADCs require alternative approaches to quality control compared to other antibody products because of their different nature and aspects that directly affects the efficacy, pharmacology, and toxicity of the product. In addition, since additional quality control measures are required for both biopharmaceuticals and small molecules, the level of regulatory requirements is inevitably more complex. Stability issues are also an important consideration, such as the tendency of ADCs to form aggregates compared to non-conjugated antibodies. The impact of these impurities on toxicity is also not fully understood.
This session will focus on the quality requirements of ADCs and discuss quality control strategies throughout the life cycle of ADC products, from preclinical through clinical development to commercial manufacture. In particular, this session will address the specific analytical issues of ADC products, quality control strategies during ADC product development (Critical Quality Attributes, impurity control, stability study, etc.) and the management of post-approval changes (raw material and process change control, comparability assessment, etc.). Additionally, the session will consider the documentation required when preparing the CTD/application for marketing authorization, review points and requirements in other countries.

Key questions
- What quality characteristics from each component (Antibody, Linker and Drug), for Drug substance and Drug product should be paid special attention to in ADC products? Are there any differences in the approach to quality requirement from countries?
- What ideas and concepts could be used to set the specification of ADC products (e.g., DAR, HMWS)?
- What quality characteristics are required for antibodies used as raw materials for ADC products (e.g., glycosylation)?
- ADC products consist of three components (antibody, linker, and drug), which increases complexity when managing change. How should comparability assessments be conducted?
- What are the points to consider when preparing the documentation required for the CTD/application, and what are the points for review by the regulatory authorities in other countries?

Session Speakers:

Quality Assessment of Antibody Drug Conjugate
Ayuki Nakano, *PMDA*

Aggregation of Antibody-Drug Conjugates Could Be a Hazard Related to Off-Target Toxicity
Michihiko Aoyama, *National Institiute of Health Science - Japan*

Challenges of Analytical Development and Control Strategy for Antibody-Drug Conjugate (ADC)
Yuki Shioiri, *Daiichi-Sankyo*

Navigating Global Regulations for Antibody Drug Conjugates (ADCs): A CMC Perspective
Vandana Chauhan, *Gilead Sciences*

14:45-15:15 South Ballroom Foyer

Networking Break

15:15-16:15 North Ballroom

Session IV - Panel Discussion

16:15-16:30 North Ballroom

Closing Remarks

Session Speaker:
Jamie Moore