CMC Strategy Forum Japan 2024

Schedule

Monday, 9 December, 2024

06:30-11:00 Lounge and Dining G (Floor 1)

Buffet Breakfast

Breakfast will be available until 11:00am and is included for all CMC Japan registrants who are hotel guests of the Tokyo Marriott Hotel located in the Lounge and Dining G on Floor 1.

07:30-08:30 Foyer

Registration for CMC Strategy Forum Japan

Registration will be open until 16:30.

07:30-08:30

Coffee Service

Coffee service will be available all day.

08:30-08:45 Ballroom North AB

CASSS Welcome and Introductory Comments

08:45-09:00 Ballroom North AB

CMC Strategy Forum Japan 2024 Welcome and Introductory Comments

09:00-10:40 Ballroom North AB

Session I - Recent Trends in the Regulation of Biopharmaceutical Products

Andrew Chang, Yasuhiro Kishioka

Session Chairs:
Yasuhiro Kishioka, *Pharmaceuticals and Medical Devices Agency* (*PMDA)* and Andrew Chang*, Novo Nordisk Inc.*

In this session, regulators from each health authority will provide the recent regulatory updates and future perspective regarding biopharmaceutical products including regenerative medicine products.

Due to the unexpected situation of the COVID-19 pandemic, the health authority has made many improvements in review and inspection activities. Lessons learned from not only ICMRA pilot on collaborative assessments but also ASEAN joint assessment will be provided. 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/ Gene and Cell therapy products including the latest Guideline (e.g. Platform Technology Designation Program for Drug Development)
- Hot topics of CMC review / GMP inspection on biopharmaceutical products.
- Progress on joint reviews/inspections and reliance for biopharmaceutical products, lessons learned from past experiences, and future perspectives and initiatives (e.g., ICMRA/PQKMS, ASEAN, ACCESS, Project OBIS)
- Prospects and challenges to expand the scope for joint reviews/inspections based on the experience up this point.
- Future perspective on AI/digitalization.
- 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.
- Future perspective for setting globally harmonized Patient Centric Specification.
- 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
Akira Sakurai, *Pharmaceuticals and Medical Devices Agency* (*PMDA)*

ICMRA Efforts to Achieve Regulatory Convergence and Reliance in Quality CMC Assessment – A Progress Report on the Collaborative Assessment and Hybrid Inspection Pilots
Stelios Tsinontides, *CDER, FDA*

Update on the Initiatives at the Center for Biologics Evaluation and Research (CBER), U.S. FDA
Ingrid Markovic, *CBER, FDA*

Regulatory Update From Europe
Brian Dooley, *European Medicines Association (EMA) - Virtual Presentation*

10:40-11:10 South Ballroom Foyer

Morning Networking Break

11:10-12:25 Ballroom North AB

Session I: Continued

Andrew Chang, Yasuhiro Kishioka

Session Chairs: Yasuhiro Kishioka, *Pharmaceuticals and Medical Devices Agency* (*PMDA)* and Andrew Chang*, Novo Nordisk Inc.* .

Session Speakers:

Introduction to ICH Q6B and Considerations for Implementation in China
Dongchen Jia, *Centre for Drug Evaluation (CDE) - Virtual Presentation*

Regulatory Updates from Singapore
Subin Sankarankutty, *Health Sciences Authority (HSA), Singapore*

Malaysian Regulatory Updates & Initiatives on Biopharmaceutical Products
Prasad Narayanan, *National Pharmaceutical Regulatory Agency (NPRA)*

12:25-13:45 Ballroom South CD

Buffet Lunch

13:45-15:00 Ballroom North AB

Session I - Panel Discussion: Questions & Answers

Andrew Chang, Yasuhiro Kishioka

Session Chairs: Yasuhiro Kishioka, *Pharmaceuticals and Medical Devices Agency* (*PMDA)* and Andrew Chang*, Novo Nordisk Inc.*

15:00-15:30 South Ballroom Foyer

Afternoon Networking Break

15:30-16:25 Ballroom North AB

Session II - CTD Quality part of Biopharmaceutical Products: Topics about ICH Guideline M4Q Revision and Structured Application

Takao Kojima, Ingrid Markovic

Session Chairs: Takao Kojima, *AbbVie, Japan Pharmaceuticals Manufacturing Association (JPMA)* and Ingrid Markovic, *CBER, FDA*

ICH guideline M4Q (R1) introduced in 2002 provides a harmonized format of quality information in the Common Technical Document (CTD) for the registration of pharmaceuticals for human use. After approximately 20 years from the introduction, the concept paper for revision of this guidance was released in 2021, and the concept paper describes the following specific drivers for this revision:
- To align with modern quality guidelines Q8-Q14, and other relevant ICH guidelines
- To support multicomponent and/or complex products such as ADC, vaccines, ATMPs/Cell & Gene Therapies and Tissue Engineered Products or combination products, continuous manufacturing techniques.
- To leverage digital tools

In this session, discussion on the current status of M4Q(R2), expectations for M4Q(R2), harmonization with other quality guidelines, and utilization way of digital technologies for structured application will be held. For this discussion, related information will be presented.

Key Questions:

- Which new concepts in M4Q(R2) will offer benefits to industry, regulators, patients, and consumers most?
- Is there any challenge to incorporate the concept of Q12 guideline into M4Q?
- One of main points for M4Q(R2) is to introduce “Core Quality Information (CQI)” in Module 2. How will be the relationship between CQI in Module 2 and the existing local regally binding document in Module 1 (e.g. Approval Application Form in Japan)?
- Currently, how to utilize Module 2 and Module 3 seems to be different among regions (e.g. Module 2 is mainly reviewed in Japan, but Module 3 in US/EU). Will this be harmonized by M4Q (R2)?
- Is there any modality for which it may be difficult to introduce M4Q(R2) format?
- What impact is expected for leveraging digital tools on the structure and handling of the current CTD?
- Is there any consideration/discussion in terms of Structured Product Quality Submissions (SPQS)?
- How will ICH M4Q(R2) contribute to collaborative assessment initiative like ICMRA?
- Is there any particular expectation to ICH M4Q(R2) revision from the viewpoint of regulators and industry?

Session Speakers:

Update on ICH M4Q(R2)
Yasuhiro Kishioka, Pharmaceuticals and Medical Devices Agency (*PMDA)*

Expectations for M4Q(R2) from an Industry Point of View
Hiroshi Ohtsuka*, Japan Pharmaceuticals Manufacturing Association (JPMA), Bayer Yakuhin, Ltd.*

16:25-17:40 Ballroom North AB

Session II - Panel Discussion: Questions and Answers

Takao Kojima, Ingrid Markovic

Session Chairs: Takao Kojima, *AbbVie, Japan Pharmaceuticals Manufacturing Association (JPMA)* and Ingrid Markovic, *CBER, FDA*

Additional Panelists:

Andrew Chang, *Novo Nordisk Inc.*
Stelios Tsinontides, *CDER, FDA*
Stephan Roenninger, *Amgen (Europe) GmbH*

17:40-19:10 Ballroom South CD

Networking Reception

Tuesday, 10 December, 2024

06:30-08:45 Lounge and Dining G (Floor 1)

Buffet Breakfast

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07:30-08:45 Foyer

Registration for CMC Strategy Forum Japan

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07:30-08:45

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08:45-10:55 Ballroom North AB

Session III - Unveiling the Latest Updates: Regulatory Landscape and Changes in ICH Guideline Q6 for Biological Products

Andrew Chang, Akiko Ishii

Session Chair: Akiko Ishii, National Institute of Health Sciences (NIHS) and Andrew Chang, Novo Nordisk Inc.

ICH Q6B was established in 1999 (Step 4) and 2001 (Step 5) in Japan to define test procedures and acceptance criteria for biotechnological/biological products. However, after two decades, advancements in analytical technology and the significant progress of innovative new modalities have rendered the current guideline obsolete. Additionally, various environmental changes have occurred, including advances in manufacturing technologies, analytical capabilities and predictive modelling/statistic approaches, adoption of new ICH topics and/or significant updates to existing guideline (e.g., ICH Q2, Q3C-D, Q8-Q14, and M7), development of advanced therapeutic modalities, and increased propensity for expedited development of new product. The Concept Paper and Work Plan for revision of ICH Q6A and Q6B have been approved by ICH Management Committee. This revision aims to achieving more consistent international harmonization in setting specifications including but are not limited to 1) develop unifying principles that apply to all modalities, 2) modernize the old guidelines by aligning with relevant ICH guidelines (e.g., Q8-14) and advanced tools, 3) update specification during product lifecycle, e.g., change of test methods for drug substances and drug products based on scientific and risk-based approaches.

In this session, industry experts and regulators will engage in discussions to anticipate the expectations and challenges of the upcoming ICH Q6 revision, with a particular focus on ICH Q6B for biological products. The revised guideline will address several important aspects, including:

- Appropriate use of prior knowledge
- Appropriate use of pharmaceutical development data
- Prospective process and product (Critical Quality Attributes, CQA and Critical Process Parameters, CPP) understanding
- Considerations of the overall control strategy
- Appropriate use of modelling tools and statistical evaluations
- Non-clinical and clinical relevance
- Impact to the safety and efficacy of the drug product

We hope the outcome of these discussions would be helpful to assist current effort to modernize ICH Q6 guideline on specifications, to make it more effective and relevant in the biological field with rapid growth of different modalities, while ensuring innovation, e.g., test methods and harmonizing international quality standards.

Key Questions:

- Challenges and Expectations for setting specifications for biological products in the current context: What are the challenges faced in setting specifications for biological products, and what are the expectations for the revision of ICH Q6?

- Setting Specifications for New Modalities: Is there any unique challenge for setting specifications for Cellular and Gene Therapy (CGT) product? How should specifications be established for innovative new modalities, using traditional vs. enhanced approach, or both?

- Setting Specifications based on clinical data and other evidence: What are the expectations and challenges in setting specifications using clinical data and other supporting evidence?

- Flexibility in Specifications throughout Development and Product Life Cycle: How can specifications be made flexible to adapt to different stages of development and the life cycle of the product?

- Challenges in making post-approval changes of Specifications: What are the challenges encountered when making post-approval changes on specifications during product lifecycle? Can risk-based approach introduced in ICH Q12 guideline be

used for changing specifications, for example, adopting a new analytical mothed with advanced technologies, or setting new acceptance criteria based on better understanding the relationship between quality attribute and safety and efficacy.

-Challenges in Setting Specifications Using Modelling and Statistical Methods: What are the challenges involved in setting specifications using modelling and statistical approaches, if applicable?

Session Speakers:

ICH Efforts Towards Developing a Unified ICH Q6 Guideline and Modernizing Global Standards for Specifications Setting
Ingrid Markovic, *CBER, FDA*

Establishment of Specifications for Monoclonal Antibodies
Chuanfei Yu, *National Institutes for Food and Drug Control (NIFDC)*

Expectation for ICH Q6 Revision: Case Study of Commercial Specification Setting
Kumi Mizuguchi, *Chugai Pharmaceutical Co., Ltd.*

Industry Expectations for ICH Q6 Revision: Reflecting Advancements in Biopharmaceutical Manufacturing and Analytical Technologies
Takahiro Yamaguchi, *Japan Pharmaceuticals Manufacturing Association (JPMA), Asahi Kasei Pharm*

Role of ICH Q14 Analytical Procedure Development on
Establishment of Control Strategy and Its Relation to ICH Q6B Specifications
Hiroko Shibata, *National Institute of Health Sciences (NIHS)*

10:55-11:15 South Ballroom Foyer

Morning Networking Break

11:15-12:30 Ballroom North AB

Session III - Panel Discussion: Questions & Answers

Andrew Chang, Akiko Ishii

Session Chair: Akiko Ishii, National Institute of Health Sciences (NIHS) and Andrew Chang, Novo Nordisk Inc.

Additional Panelists:

Kathleen Francissen, *Genentech, A Member of the Roche Group*
Akiko Ishii, National Institute of Health Sciences (*NIHS)*
Yukiko Shirahata, *Pharmaceuticals and Medical Devices Agency (PMDA)*
Daisuke Tsuchida, *Kyowa Kirin Co., Ltd.*

12:30-13:30 Ballroom South CD

Buffet Lunch

13:30-15:15 Ballroom North AB

Session IV - Key Strategies and Harmonization Efforts on Raw Material Managements of Cell Therapies – What for CAR-T

Kathleen Francissen, Satoshi Yasuda

Session Chairs: Satoshi Yasuda, *National Institute of Health Sciences (NIHS),* and Kathleen Francissen, *Genentech, A Member of the Roche Group*

As cell and gene therapy products have become prevalent, there is a developing need for the international harmonization on regulatory framework based on scientific consideration, to address regulatory divergences among areas and to make clear the requirements and expectations for global developments and global commercialization of the cell and gene therapy products. To address the future harmonization needs for this emerging field, the ICH Cell and Gene Therapy Discussion Group (ICH CGT DG) has been formed as a technical discussion forum for issues related to advanced therapy medicinal products' development whereby technical consensus can be achieved with specific recommendations for new guideline development or revision to existing ICH Guidelines. The scope of the Discussion Group activity includes both autologous and allogenic CAR-T cells, and in-vivo viral vector-based gene therapy.
Meanwhile, the US-FDA has issued guidance on CMC, non-clinical and clinical developments for both autologous and allogenic CAR-T cell products in January 2024 (Considerations for the Development of CAR-T Cell Products). The guidance provides specific expectations and recommendations for respective autologous and allogenic CAR-T, including recommendations on comparability assessments during product lifecycle. The assessment of comparability is one of the technically challenging issues and donor-to-donor variability of the leukapheresis starting material could be a source of variability of CAR-T lots.
In this session, we will focus on CAR-T to hear about ICH CGT DG activities and their progress toward targeted deliverables, and the recommendations for CMC development of CAR-T in the US-FDA guideline. In addition, the approaches to address the divergences in regulatory requirements among areas, especially regarding raw materials and leukapheresis starting materials, such as donor eligibility determination including screening and testing and recommendation to minimize variability and promote consistency between CAR-T lots, will be discussed, from global clinical development perspectives of CAR-T.

Preliminary Key Questions:
- The requirements and expectations on the raw materials and cell starting materials in respective areas, from perspectives of attributes related to not only safety but also efficacy.

- The requirements of donor eligibility determination including screening and testing for relevant communicable disease agents and diseases, and rules or expectations of informed consent for leukapheresis.

- For allogeneic CAR T-cell production, the requirements and/or recommendations to manage the regulatory change control and the comparability study for changing leukapheresis starting material during product lifecycle. (It could be challenging to establish analytical methods or specific acceptance criteria of starting materials in early-phase. Meanwhile, the changing leukapheresis starting materials is expected in the product lifecycle and donor-to-donor variability of the leukapheresis starting material could be a source of variability of CAR-T lots.)

- The regulatory divergences regarding control or standard of biological raw material, such as selection reagents, activation reagents, cytokines, serum and growth factors.

Session Speakers:

ICH Cell & Gene Therapy Discussion Group: Progress Toward Delivering a Strategic Roadmap for ATMPs
Kathleen Francissen, *Genentech, A Member of the Roche Group*

Global Convergence Considerations to Accelerate Availability of Cell & Gene Therapies
Ingrid Markovic, *CBER, FDA*

Quality Control of the Raw Materials for Cell and Gene Therapy Products
Atsushi Nishikawa, *Pharmaceuticals and Medical Devices Agency* (*PMDA)*

Challenges in the Clinical Implementation of piggyBac Transposon Mediated CAR-T Cell Therapy
Shigeki Yagyu, *A-SEEDS*

15:15-15:45 Ballroom South CD

Afternoon Networking Break

15:45-17:00 Ballroom North AB

Session IV - Panel Discussion: Questions & Answers

Kathleen Francissen, Satoshi Yasuda

Session Chairs: Satoshi Yasuda, *National Institute of Health Sciences (NIHS)* and Kathleen Francissen, *Genentech, A Member of the Roche Group*

Additional Panelist:

Yuki Miyatake, *Bristol-Myers Squibb Company K.K.*

17:00-17:15 Ballroom North AB

Closing Remarks and Invitation to CMC Strategy Forum Japan 2025