ICH CGT DG

Cell and Gene Therapy Discussion Group

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Atsushi Nishikawa, PMDA, TL
Satoshi Yasuda, NIHS, DTL

Yuki Miyatake, JPMA, TL
Hiroaki Miida, JPMA, DTL
Yoko Watanabe, JPMA
Masato Komuro, JPMA

Outline

- Overview of topic
- Status before the meeting
- Progress made at the meeting
- Status at the end of the meeting
- Work Plan: Key Milestones and Activities
- Conclusions

Overview: Scope

- **Initial focus on more mature product classes**
  - *Ex vivo* genetically modified cells (e.g. chimeric antigen receptor T-cell products (e.g., CAR T-cells)) including both autologous and allogeneic
  - *In vivo* viral vector-based gene therapies (e.g., AAV vector-based gene therapy products)
- **Challenges:**
  - There are often challenges in scope of product classes given rapid evolution in genetic modification technologies
  - Advanced Therapy Medicinal Product (ATMP) terminology
  - Disciplines: Clinical, Nonclinical, and Quality
    - Intent to address interdependencies
  - Other EWGs are asked to address *all ATMP* product classes

ICH CGT DG Members

Regulatory/Administrative Authorities

- EU commission, Europe
- FDA, USA
- MHLW/PMDA, Japan
- ANVISA, Brazil
- EDA, Egypt
- HSA, Singapore
- MFDS, Republic of Korea
- MHRA, UK
- NMPA, China
- SFDA, Saudi Arabia
- TFDA, Chinese Taipei
- Health Canada, Canada
- Swissmedic, Switzerland
- ANMAT, Argentina
- ANPP, Algeria

Industry Associations

- EFPIA
- JPMA
- PhRMA
- BIO
- IFPMA
- IGBA

Other/International Associations

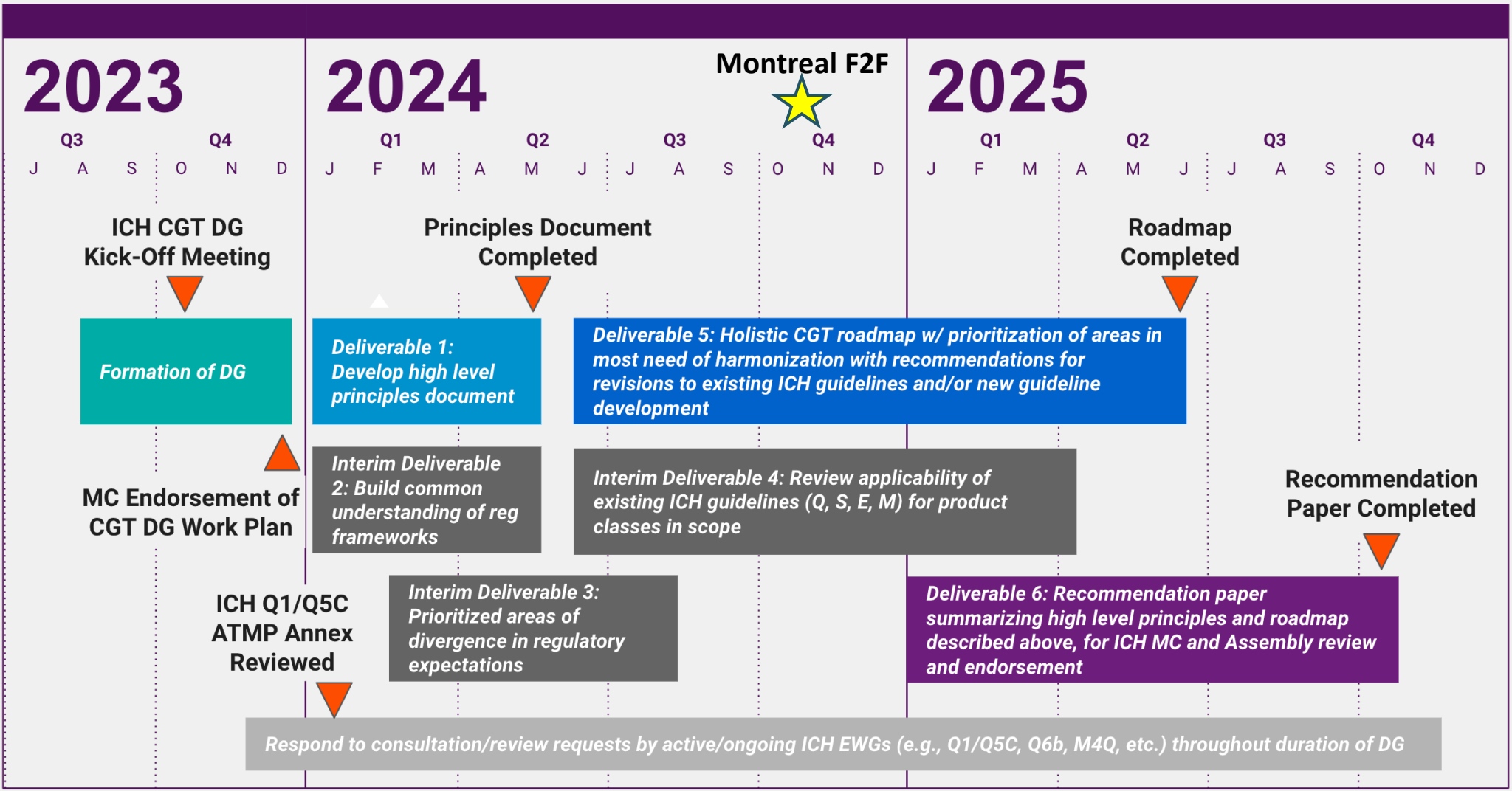
- EDQM
- USP
- IPRP
- WHO

Status before the ICH meeting

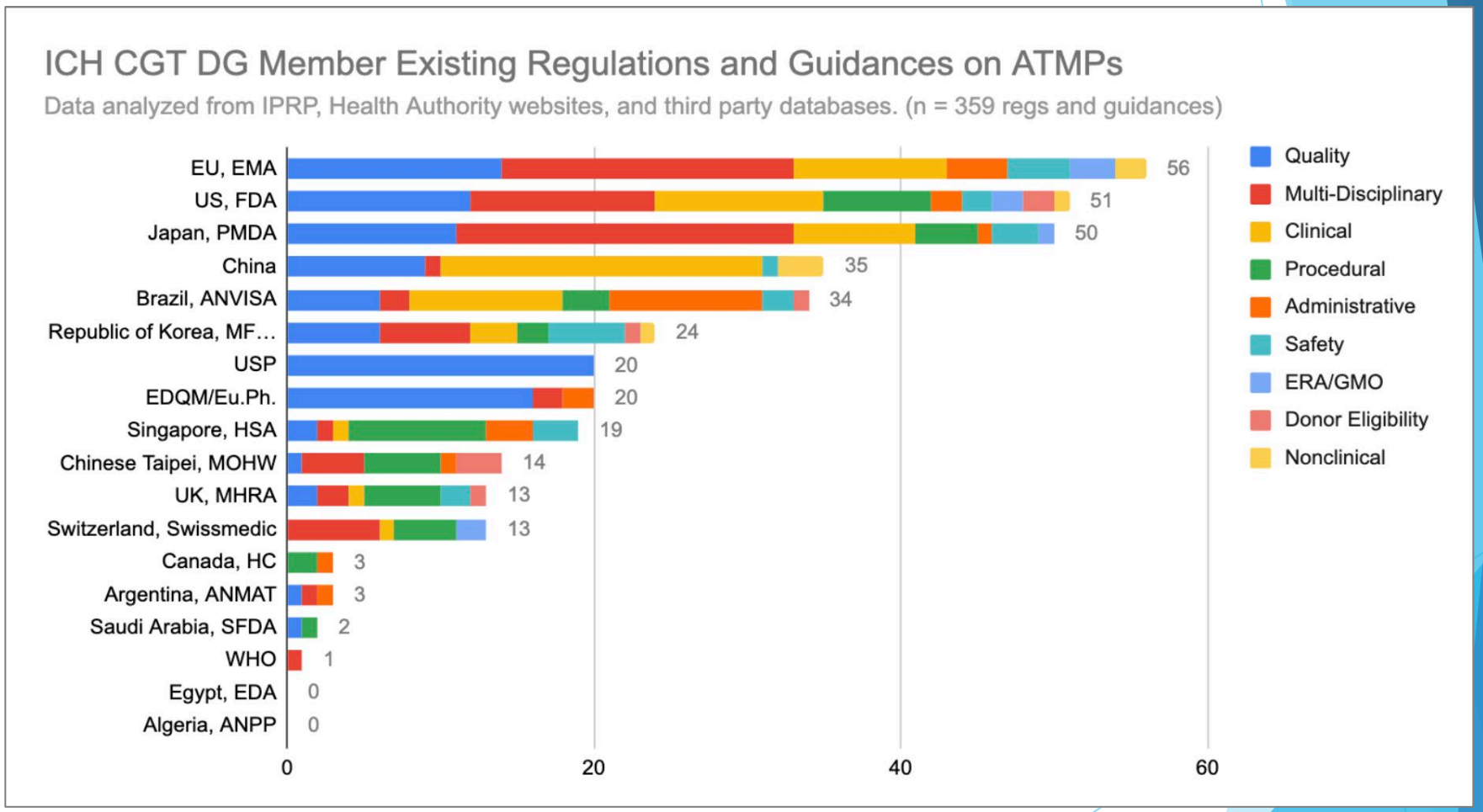
Deliverables:

1. High level principles document – draft done (current working draft with additional updates planned)
2. Overview of global regulatory framework – draft done
3. Areas of divergence and harmonization in regulatory expectations – draft done
4. Stepwise review of existing ICH guidelines for applicability to ATMPs – in progress
5. Holistic ATMP strategic roadmap – in progress
6. Recommendation paper – final deliverable due Oct 2025

Work Plan Milestones Timeline



ATMP Global Regulatory Framework



- Nearly 400 ATMP-specific guidelines and regulations across regulatory agencies participating in CGT DG (Feb 2024).

Areas of divergence in regulatory expectations

- Divergence that developers encountered while trying to conduct global clinical trials and/or commercialize ATMPs in multiple regions globally.
- Surveys conducted to gather info (Feb 2024); Compiled information gathered by trade groups (Feb - May 2024). Ranked according to priority (high-medium-low)
- Key challenges identified by regulators – ranked according to priority (high-medium-low)
- Issues/topics identified and prioritized by regulators and industry/trade associations – largely aligned perspectives from trades and regulators

Mapping priority issues/topics to existing ICH guidelines

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Efficacy Guidelines

Multidisciplinary Guidelines

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Quality Guidelines

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Safety Guidelines

ICH Consideration Documents General Principles to Address the Risk of Inadvertent Germline Integration of Gene Therapy Vectors.....2743

Oncolytic Viruses.....2746

General Principles to Address Virus and Vector Shedding.....2751

Sex-Related Considerations in the conduct of Clinical Trials.....2757

- A large PDF consolidation activity created keyword-searchable files, aiding in the topic mapping process. Includes: All Guidelines, Q&As, consideration documents, and drafts available as of September 2024. (2,765 total pages)
- Assess applicability of ICH guidelines to ATMPs

Topic Mapping Template

1. Please review the preliminary **keyword results** above to ensure better accuracy. Update the table (delete/add guidelines as needed). Add any additional keywords used (synonyms, related concepts etc.) Explain the revisions here: -
2. Which ICH Guideline(s) **primarily define ICH's current position on this topic,** including considerations for both ATMPs (if specified) and general (i.e. traditional) drug development? -
3. Please copy/paste the **relevant text** (or refer to the Guideline's sections/entirety if too long to copy/paste) demonstrating ICH's thinking on this topic, including considerations for both ATMPs (if specified) and general (i.e. traditional) drug development: -
4. Consider the identified text for its **applicability** to the identified topic in the context of *in-vivo* viral-vector based gene therapies (e.g., AAVs) and *ex vivo* genetically modified cells (e.g., CAR-Ts). Does the current text apply, partially apply, or not apply, and why? Highlight potential challenges or gaps. -
5. Please provide your **recommendation(s) about how ICH could address this topic** as it relates to the two modalities (e.g., New Guideline, Revised Guideline, Annex, no action needed, etc.) -
6. Please list the primary **national or regional guidance(s)** that addresses this topic specifically for ATMPs: -

- This activity is ongoing and conducted uniformly across subgroups.

Advise other EWG

- "The CGTDG is not tasked with the development or revisions of specific ICH Guidelines but may act as an advisor group to existing ICH Expert Working Group (EWG) undergoing new or revised guideline development where CGT products are in scope."

  - ✓ Completed: Review ATMP Annex for ICH Q1/Q5c Stability Revision EWG (January, 2024).
  - ✓ Advise: ICH Q6 Specifications Revision EWG

Progress made at the meeting

- Met with Q6 Specification EWG and with Q1 Stability EWG – shared relevant sections HLP document; global map of ATMP regulations; searchable PDFs of all ICH guidelines; prioritized issues/topics
- Mapping issues/topics to ICH guidelines as subgroups and DG: Quality, Non-clinical and Clinical
- For ICH Topic Proposal, narrowed from 20+ topics to 5 suggestions to top 2:
  - ✓ Multidisciplinary guideline on unique ATMP development considerations w/ first annex on Comparability
  - ✓ Comparability (Annex to ICH Q5E)

Topic Proposal by 22 Nov 2024

- ICH Multidisciplinary (M) guideline on Unique ATMP Development Considerations with first annex on Comparability
- Proposing members:
  - **BIO (lead)**
- Vote among CGT DG members supported topic proposal by majority

Work Plan:
Expected Future Key Milestones

Expected Completion date	Deliverable
Apr 2025	(“Interim Deliverable 4”) Review existing ICH guidelines (Q, S, E, M) in terms of their applicability to CGT product classes in scope and identify areas where harmonisation already exists and areas for improvement in harmonisation
Jun 2025	(“Deliverable 5”) Holistic CGT roadmap w/ prioritization of areas in most need of harmonization with recommendations for revisions to existing ICH guidelines and/or possibly new guideline development
Oct 2025	(“Deliverable 6”) Recommendation paper summarizing high level principles and roadmap described above, for ICH MC and Assembly review and endorsement

Conclusions

- CGT DG has completed several interim deliverables and is on track to fulfill remit on ATMP modalities in the initial focus by October 2025

Thank you!