Cell & Gene Therapy Discussion Group (CGT DG)

CaSSS CGTP Symposium

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International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

Overview

- Describe the Cell & Gene Therapy Discussion Group (ICH CGT DG)
- Provide rationale for CGT DG formation
- Outline the scope
- Describe deliverables in the Work Plan

Cell & Gene Therapy Discussion Group

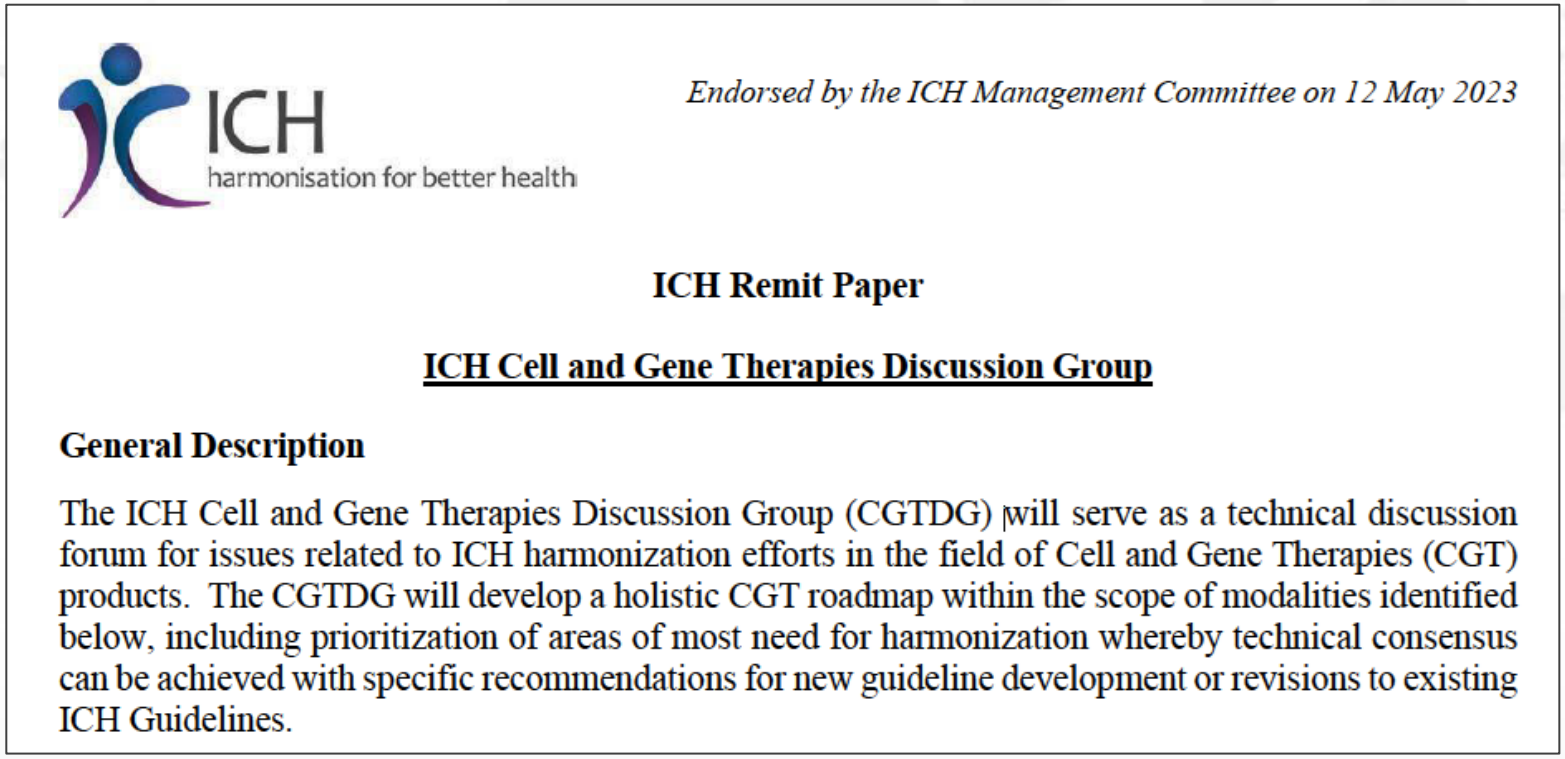
- Topic adoption date: August, 2023
- Rapporteur: Dr. Kathleen Francissen, BIO
- Regulatory Chair: Dr. Melanie Eacho, FDA, United States
- CGT DG Kick-off Meeting: October, 2023
- Work Plan endorsement: December, 2023

ICH Website

Cell & Gene Therapy Discussion Group

- CGT DG Remit Paper
- CGT DG Work Plan
- CGT DG Roster

Remit Paper



Endorsed by the ICH Management Committee on 12 May 2023

ICH Remit Paper

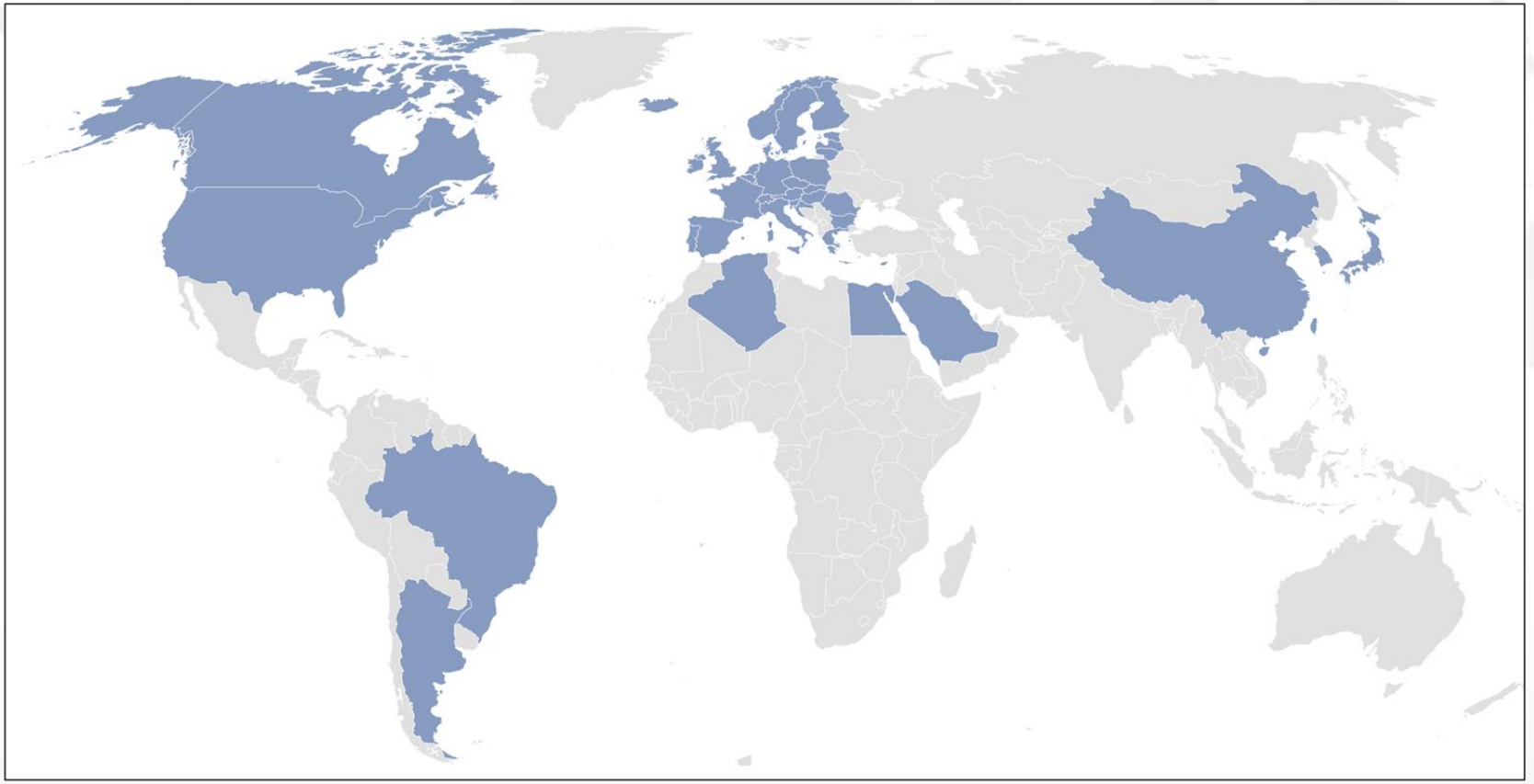
ICH Cell and Gene Therapies Discussion Group

General Description

The ICH Cell and Gene Therapies Discussion Group (CGTDG) will serve as a technical discussion forum for issues related to ICH harmonization efforts in the field of Cell and Gene Therapies (CGT) products. The CGTDG will develop a holistic CGT roadmap within the scope of modalities identified below, including prioritization of areas of most need for harmonization whereby technical consensus can be achieved with specific recommendations for new guideline development or revisions to existing ICH Guidelines.

- Remit paper describes scope and timelines
- Final deliverable by October, 2025

ICH CGT DG Members



25 member organizations representing 45 countries

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

Rapporteur Supporter: Elaine Shults (BIO)

Cell & Gene Therapy *Discussion* Group

- Technical discussion forum

- Ultimate deliverable: Strategic Roadmap

Rationale for forming CGT DG

- Numerous studies: estimate ~1400 active ATMP clinical trials worldwide.*

- Largest numbers are:
  - CAR T-cell products and
  - Adeno-associated viral (AAV) vector-based gene therapy products

- Estimate ~5,800 patients dosed with AAV-based GT and ~38,000 with CAR T-cell products (including clinical + commercial setting).

* This figure refers to Advanced Therapy Medicinal Products (ATMPs) as defined by WHO. Therefore, it does not include prophylactic vaccines against infectious disease or synthetic oligonucleotide products. Excludes preclinical programs. Includes active/open trials only. Verified number of trials (vs clinical trial sites).

Global Development

- Increasingly global development and commercialization.

~104 CGT products approved worldwide*

* This estimate refers to Advanced Therapy Medicinal Products (ATMPs) as defined by WHO, which are approved in at least one country worldwide.

Rationale for forming CGT DG

- Application of current ICH guidelines for traditional biologics does not fully address the unique characteristics of ATMPs and may even cause additional challenges.

- Nonclinical, clinical, and manufacturing development of ATMPs can be uniquely complex.

- Important to advance and converge on a science-based regulatory framework across all regions to make clear the development requirements.

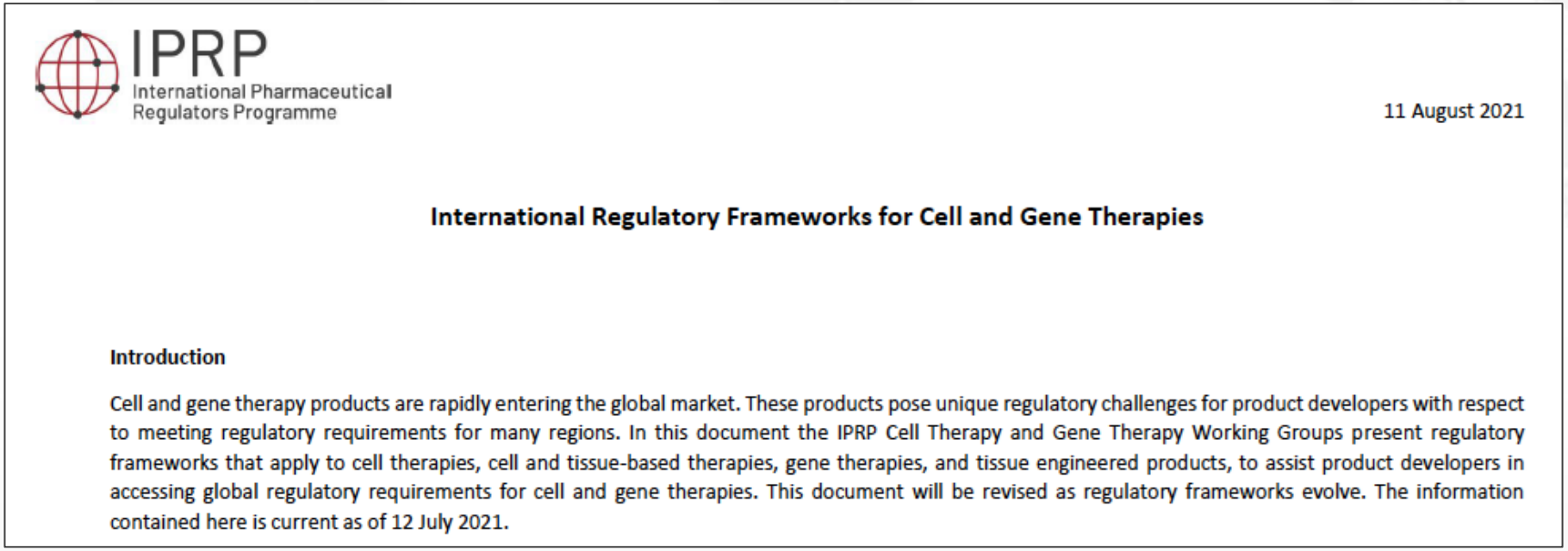
ICH MC Endorsed Formation of CGT DG

- Overall aim: Develop a strategic framework to address future harmonization needs for ATMPs.

- Roadmap: Prioritized areas of most need for harmonization where technical consensus can be achieved with specific recommendations for new guideline development or revisions to existing ICH Guidelines.

- ICH CGT DG to work in close coordination with IPRP and WHO to ensure a holistic approach to harmonization efforts, and minimize duplicative efforts.

International Pharmaceutical Regulators Programme



IPRP
International Pharmaceutical Regulators Programme

11 August 2021

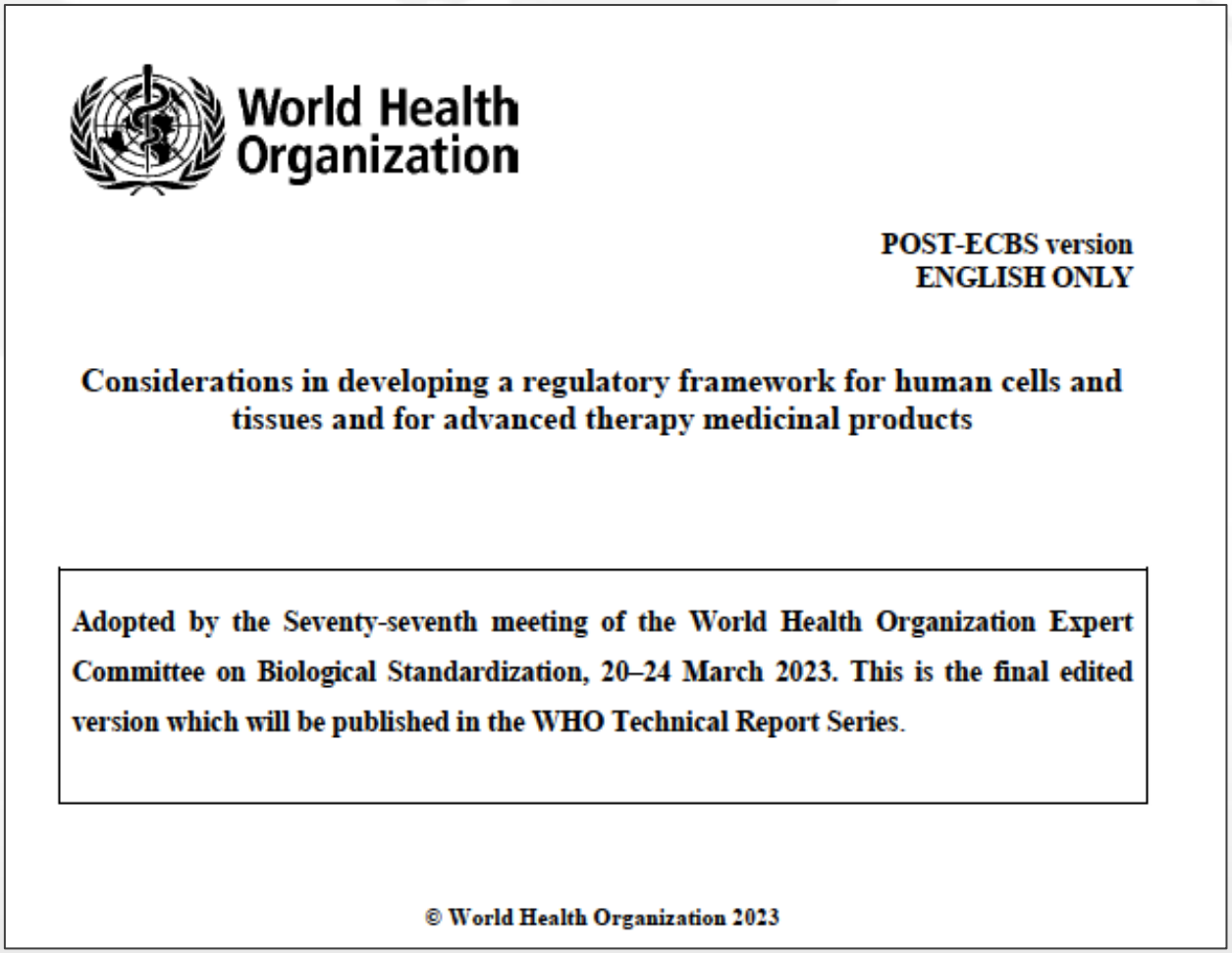
International Regulatory Frameworks for Cell and Gene Therapies

Introduction

Cell and gene therapy products are rapidly entering the global market. These products pose unique regulatory challenges for product developers with respect to meeting regulatory requirements for many regions. In this document the IPRP Cell Therapy and Gene Therapy Working Groups present regulatory frameworks that apply to cell therapies, cell and tissue-based therapies, gene therapies, and tissue engineered products, to assist product developers in accessing global regulatory requirements for cell and gene therapies. This document will be revised as regulatory frameworks evolve. The information contained here is current as of 12 July 2021.

IPRP Working Groups for cell therapies and gene therapies

WHO paper on HCT and ATMPs, adopted in 2023 (Annex 3, TRS 1048)



World Health Organization

POST-ECBS version
ENGLISH ONLY

Considerations in developing a regulatory framework for human cells and tissues and for advanced therapy medicinal products

Adopted by the Seventy-seventh meeting of the World Health Organization Expert Committee on Biological Standardization, 20–24 March 2023. This is the final edited version which will be published in the WHO Technical Report Series.

CGT DG to Advise Existing ICH WGs

- CGT DG is expected to provide expertise to existing ICH working groups (WGs) undergoing new guideline development or revisions where ATMPs are in scope.

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

- CGT DG agreed to use the term Advanced Therapy Medicinal Product (ATMP).

Initial Scope of CGT DG

- Initial focus on CGT modalities of relatively high maturity.

- Classes of products with global marketing authorization or prominent in global clinical development programs.

  - *In vivo* viral vector-based gene therapy products (e.g. AAV vector-based gene therapies)

  - *Ex vivo* genetically modified cells (e.g. CAR T-cell products), both autologous and allogeneic

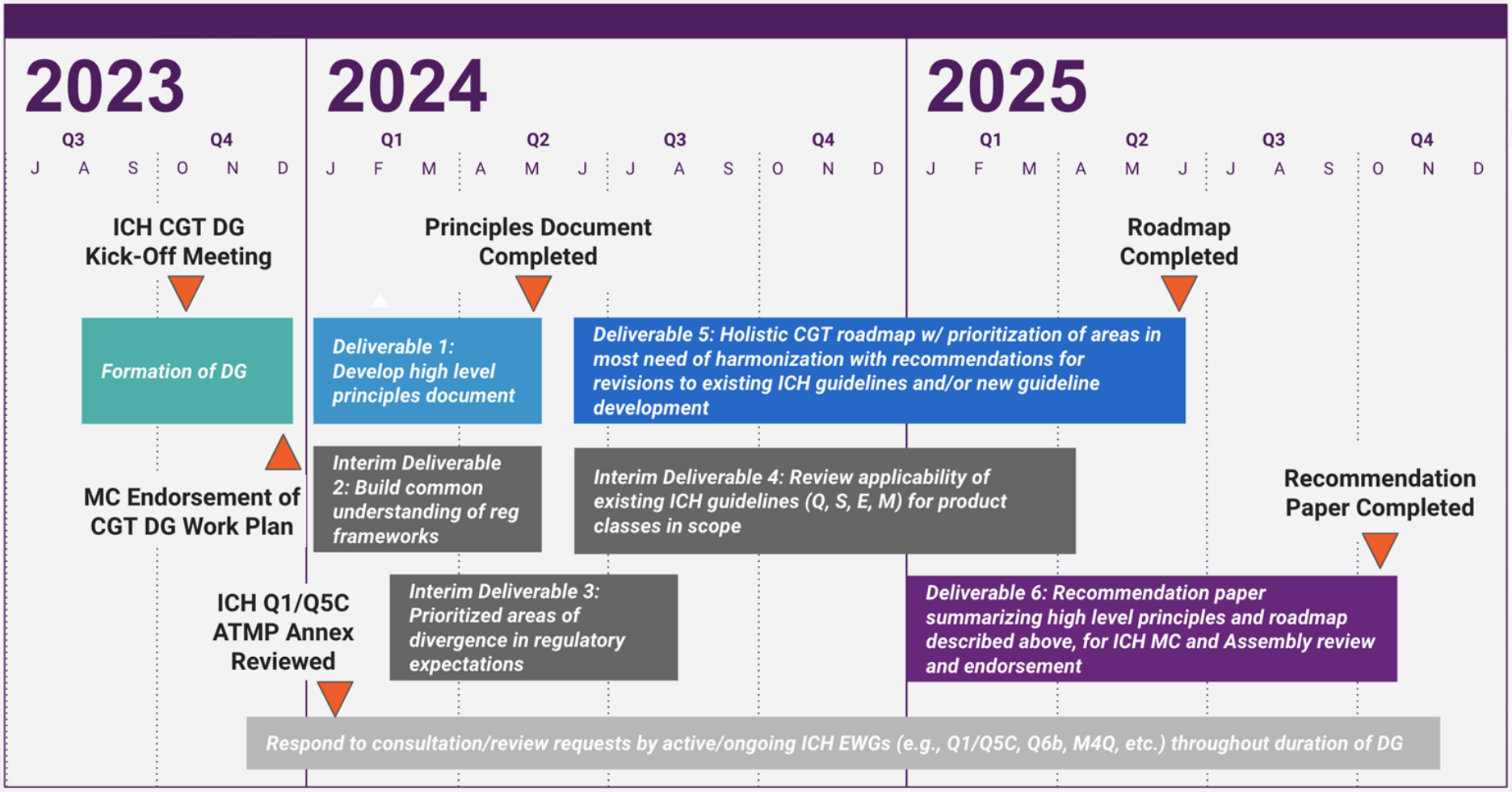
CGT DG Work Plan

1.a. Current status of key milestones

Past completion date	Milestone
October, 2023	*ICH CGT DG Kick-Off Meeting*
December, 2023	*DG endorsement of Work Plan, shared with MC*
December, 2023	*Provide review to EWG of ICH Q1/Q5C Revision (Annex on ATMPs)*
January, 2024	*Acknowledge/discuss current level of maturity of both modalities*
February, 2024	*Review high level map of global CGT regulatory frameworks for CGT products*
February, 2024	*Reached consensus on use of "ATMP" and associated terminology put forth by WHO for ICH CGT DG business*
February, 2024	*Agreed upon two subteam formations for drafting of High Level Principles document(s), divided by (1) Clinical/Non-Clinical and (2) Quality*
February, 2024	*Inter-association meeting to align on approach for gathering trade association input on areas of divergence*
March, 2024	*Inter-agency meeting to discuss approach to gathering and prioritizing areas of harmonization and/or gaps in current ATMP regulatory guidance*

As of April, 2024

Work Plan Milestones Timeline



Deliverables Progressing in Parallel

- Work Plan reflects milestones outlined in remit paper.

- Deliverables:
  1. High level principles document
  2. Overview of global regulatory framework
  3. Areas of divergence and harmonization in regulatory expectations
  4. Stepwise review of existing ICH guidelines for applicability to ATMPs
  5. Holistic ATMP roadmap
  6. Recommendation paper

High Level Principles for ATMPs

- Discuss current maturity levels: (Jan 2024 - Mar 2024)
  These product classes are generally not well characterized but are considered sufficiently mature for harmonization.

- High level principles document: (Feb 2024 -May 2024)
  Align on high level principles in key areas where baseline consensus can be achieved.

What makes ATMPs different from other pharmaceutical and biotech products?

Global ATMP Regulatory Framework

- ❖ Build common understanding of existing regulatory frameworks across regions (Feb 2024 – Apr 2024).

- ✓ Review and verify global map of ATMP-specific regulations.

- ❖ Inter-agency meeting among regulators (Feb 2024 – May 2024)
  - Identify areas of divergence or gaps.

Identify Areas of Divergence: Industry

- Identify areas of divergence in regulatory expectations – industry perspective (BIO, EFPIA, IFPMA, IGBA, JPMA, and PhRMA).
- Inter-association meeting to align on approach to gather info (Feb 2024).
- Compile information gathered by trade groups (Feb - May 2024).
- Divergence that developers encountered while trying to conduct global clinical trials and/or commercialize ATMPs in multiple globally.

Bring Perspectives Together

- CGT DG collectively discuss topics for harmonization: identified and prioritized by regulators and industry/trade associations.

- This is key step in identifying topics for harmonization and their readiness and priority, based on collective experience of DG members.

- Consolidate and prioritize areas for harmonization.

Creating a lens for examining existing ICH guidelines…

Review all ICH Guidelines

Quality Guidelines

Harmonisation achievements in the Quality area include pivotal milestones such as the conduct of stability studies, defining relevant thresholds for impurities testing and a more flexible approach to pharmaceutical quality based on Good Manufacturing Practice (GMP) risk management.

Safety Guidelines

ICH has produced a comprehensive set of safety Guidelines to uncover potential risks like carcinogenicity, genotoxicity and reprotoxicity. A recent breakthrough has been a non-clinical testing strategy for assessing the QT interval prolongation liability: the single most important cause of drug withdrawals in recent years.

Efficacy Guidelines

The work carried out by ICH under the Efficacy heading is concerned with the design, conduct, safety and reporting of clinical trials. It also covers novel types of medicines derived from biotechnological processes and the use of pharmacogenetics/genomics techniques to produce better targeted medicines.

Multidisciplinary Guidelines

Those are the cross-cutting topics which do not fit uniquely into one of the Quality, Safety and Efficacy categories. It includes the ICH medical terminology (MedDRA), the Common Technical Document (CTD) and the development of Electronic Standards for the Transfer of Regulatory Information (ESTRI).

- Evaluate all ICH guidelines: Quality, Safety, Efficacy, and Multi-disciplinary

Holistic Roadmap

- Generate holistic CGT roadmap with prioritized areas for harmonization: June, 2025.
- Recommend staggered approach to address these areas.
- Recommend revisions to existing ICH guidelines and/or new guideline development.

Recommendation Paper

- Summarize high level principles and strategic roadmap in Recommendation Paper: October, 2025.

- Submit to ICH MC for review and endorsement.

CGT Regulatory Harmonization

- Complete the CGT DG remit by October, 2025.
- Further details on ICH Website.

Happy to take any questions!