Cell & Gene Therapy Discussion Group (CGT DG)

ICH Regional Meeting FDA-Health Canada

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

Overview

- Describe the Cell & Gene Therapy Discussion Group (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

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 globally

- 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)

Global Development

- Increasingly global development and commercialization

~104 CGT products approved globally.

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 of CGT DG is to 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 CGTDG to work in close coordination with IPRP and WHO to ensure a holistic approach to harmonization efforts, and minimize duplicative efforts

CGT DG to advise existing ICH EWG

- CGT DG is expected to advise and/or provide expertise to existing ICH EWG undergoing new guideline development or revision to guidelines where ATMPs are in scope

- Completed: Review ATMP Annex for ICH Q1/Q5c Stability Revision EWG– Jan, 2024

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

Deliverables Progressing in Parallel

- Work Plan reflects milestones outlined in remit paper

- Deliverables:

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

High Level Principles for ATMPs

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

- **High level principles document**: Feb-May
  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-Apr

- ✓ Review global map of ATMP-specific regulations

- Inter-agency meeting among regulators (Feb-May)
  -Discuss areas that are harmonized
  -Identify areas of divergence or gaps

Identify Areas of Divergence: Industry

- Identify areas of divergence in regulatory expectations – industry perspective

- Inter-association meeting to align on approach to gather info: Feb, 2024
  BIO, EFPIA, IFPMA, JPMA, and PhRMA

- Compile information gathered by trade groups: Feb-May 2024

Divergence that developers encountered while trying to conduct global clinical trials and/or commercialize globally.

Bring Perspectives Together

- CGT DG collectively discuss topics for harmonization
  – identified and prioritized by regulators and 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

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

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 medical terminology (MedDRA), th Common Technical Document (CT development of Electronic Standa Transfer of Regulatory Informatior

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

Ambitions for ATMP regulatory harmonization

- **Complete the CGT DG remit by October, 2025**
- **Details on ICH website**

Happy to take any questions!