From Pipeline to Product: FDA's Approach to Accelerating Gene and Cell Therapy Development and Commercialization

CASSS CMC Strategy Forum Latin America 2026

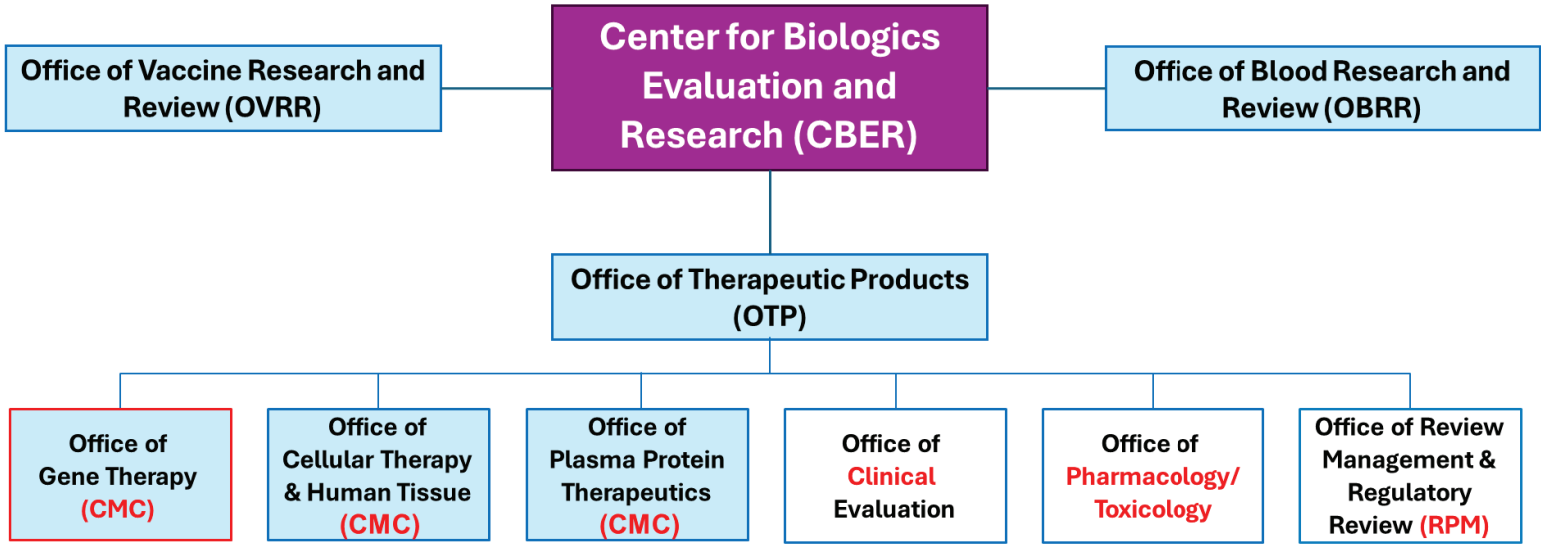
Timothy Kamaldinov, PhD
Office of Gene Therapy
Office of Therapeutic Products
Center for Biologics Evaluation and Research, US FDA

Outline

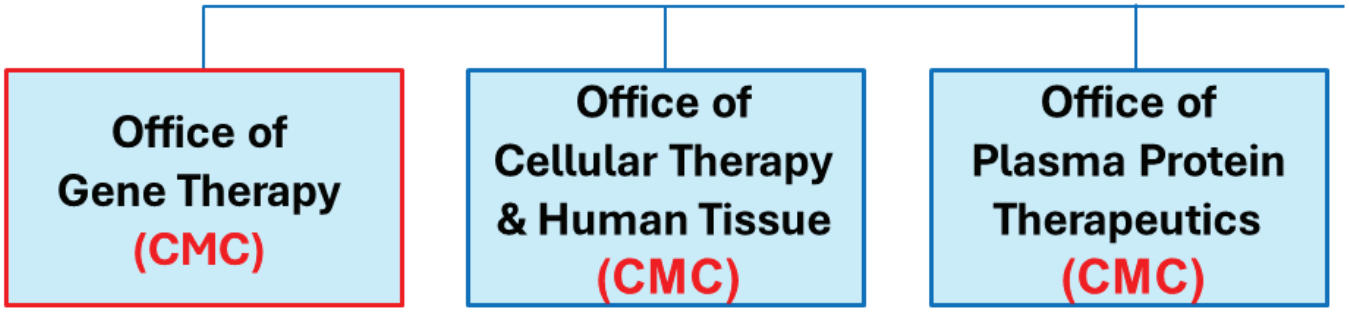
- CBER/OTP Overview and Product Jurisdiction
- IND/BLA Review Process
- Recent CMC Guidance for Gene Therapy Products
- 2026 CMC Flexibilities Guidance
- 2026 Leveraging of Prior Knowledge in the Development of Gene Therapy Products Guidance
- Final Thoughts

CBER Product Review Offices

CBER regulates a variety of biological product types including *blood and blood products, cellular and gene therapies, tissue and tissue-based products, vaccines, live biotherapeutic products, and xenotransplantation products*



OTP CMC Review Offices and Product Types



Gene Therapy (GT) Products

- Ex vivo modified genetically engineered and genome-edited cells: immune and stem cells, including CAR-T, TCR-T, and CD34 cell products
- Viral Vectors: e.g., AAV, Ad, HSV
- mRNA, LNPs, plasmids
- Oncolytic viruses and bacteria
- Active immunotherapy
- Genetically modified microbial vectors

Cell Therapy (CT) Products

- Stem cells: HSCs, MSCs, cord blood-derived, etc.
- Cell products derived from pluripotent stem cells
- Pancreatic Islets
- Chondrocytes, keratinocytes, hepatocytes
- Xenotransplantation products
- Tissue-engineered and acellular products

Plasma Protein Therapeutics

- Immunoglobulins
- Enzyme inhibitors
- Coagulation Factors

Office of Gene Therapy: Clinical and Commercial Products

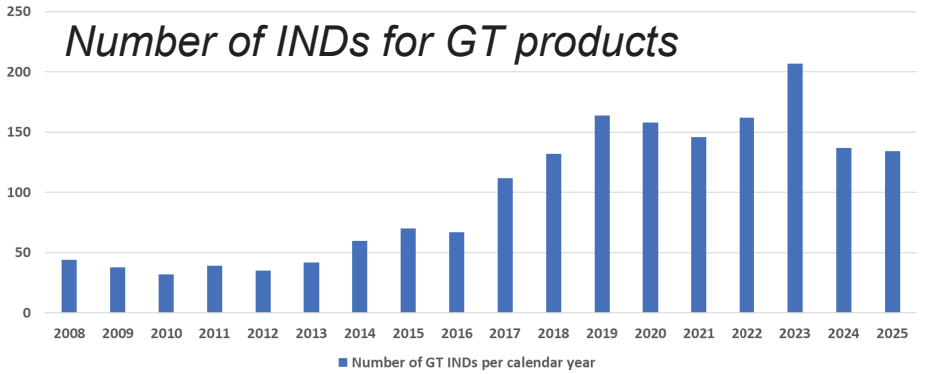
Gene Therapy Products

- **Ex vivo modified genetically engineered and genome-edited cells: immune and stem cells, including CAR-T, TCR-T, and CD34 cell products**
- **Viral Vectors: e.g., AAV, Ad, HSV**
- **mRNA, LNPs**, plasmids
- Oncolytic viruses and bacteria
- Active immunotherapy
- Genetically modified microbial vectors

Commercial: Over two dozen licensed GT products since 2017

9 AAV products
7 CAR-T and 1 TCR-T
7 genetically modified CD34 products
3 HSV products
2 adenovirus products

Clinical: over 1800 authorized investigational studies using GT products



** Excluding expanded access*

Emerging Trends in Immune Cell-Based Gene Therapies

CAR-T for Autoimmune Indications

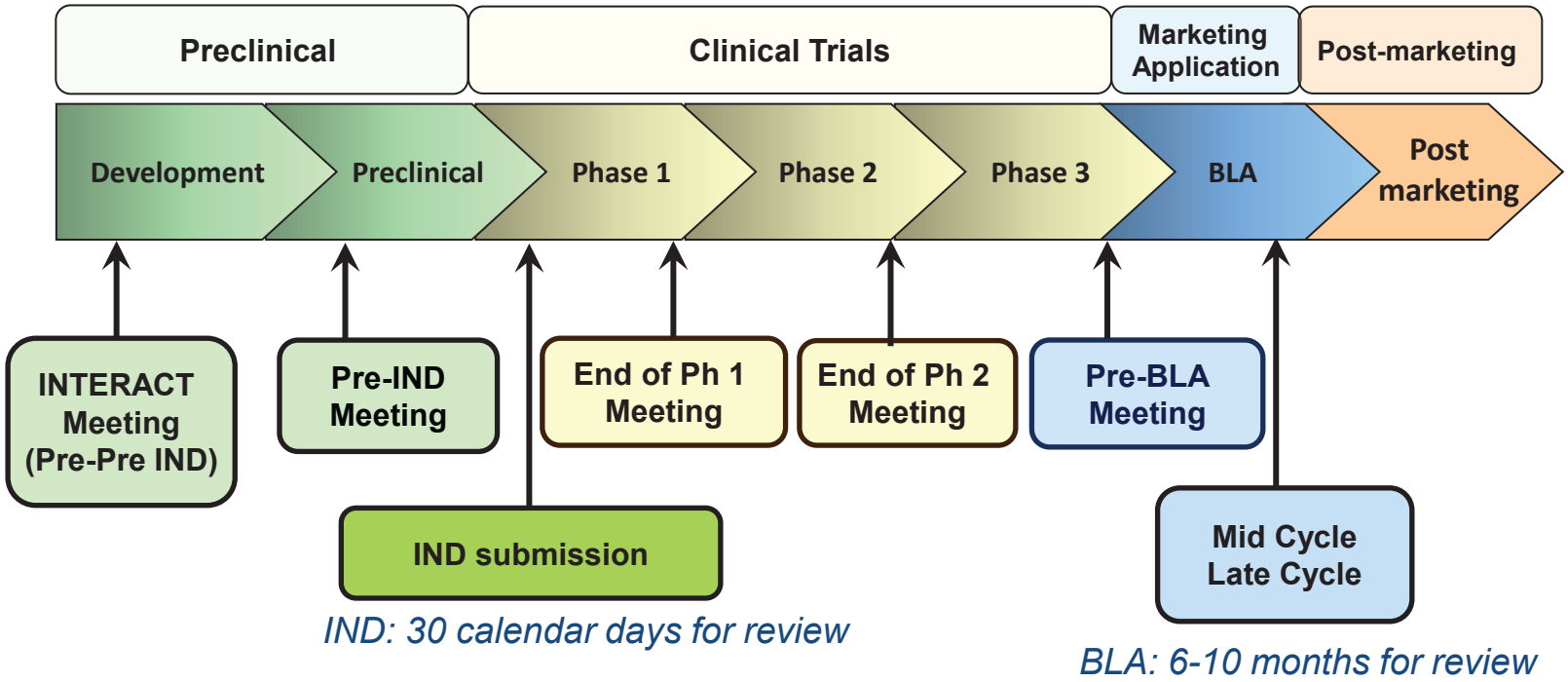
TCR-T/CAR-T/TILs for Solid Tumor Indications

Allogeneic CAR-T and TCR-T products

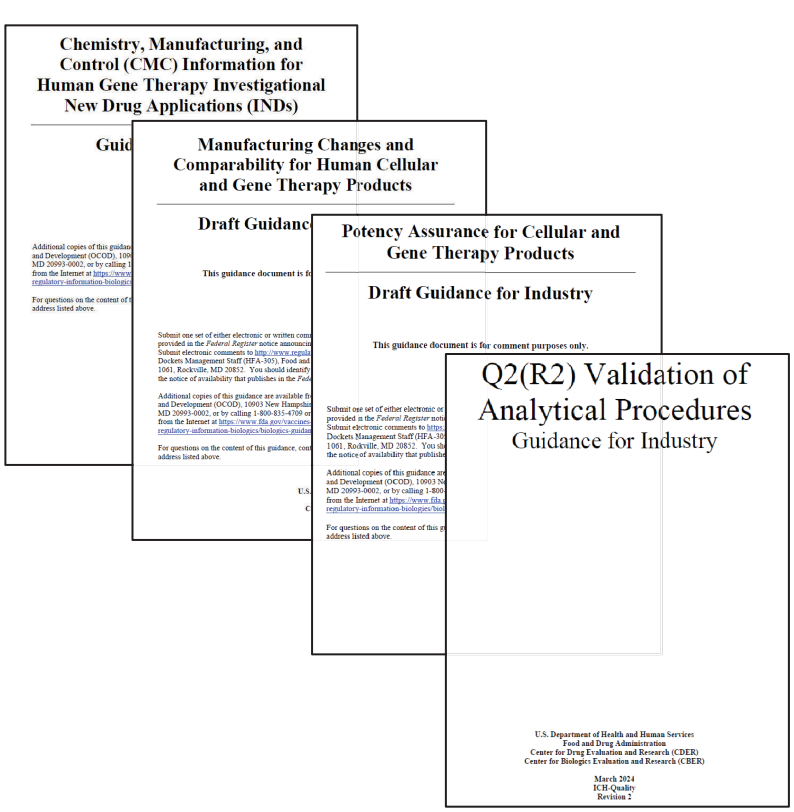
In vivo CAR-T generation (mRNA-LNP and LVV)

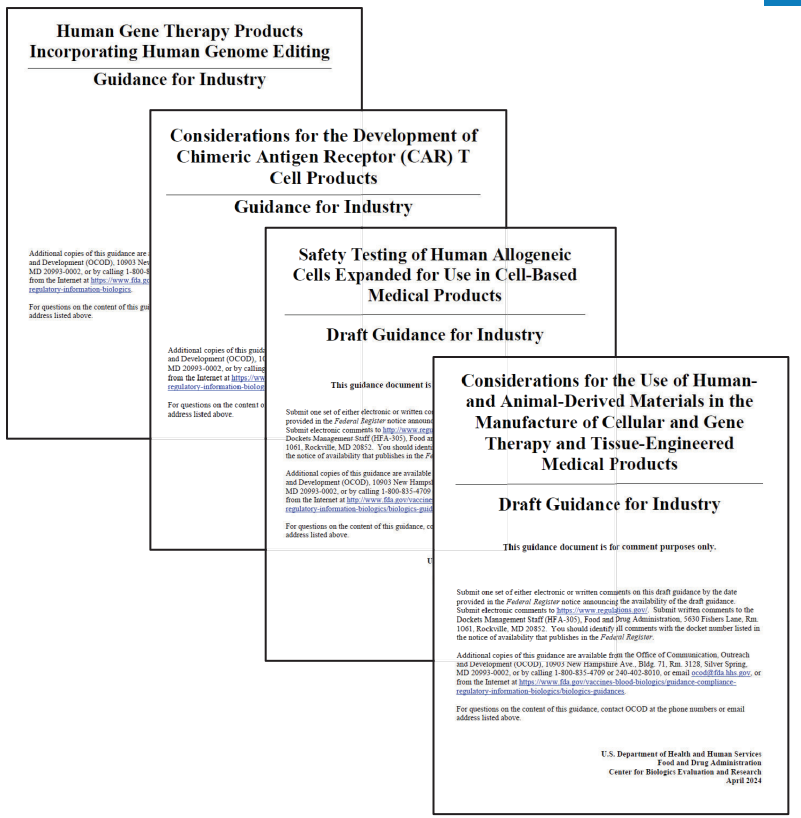
Allogeneic CAR-NK products

GT Product Development Regulatory Milestones

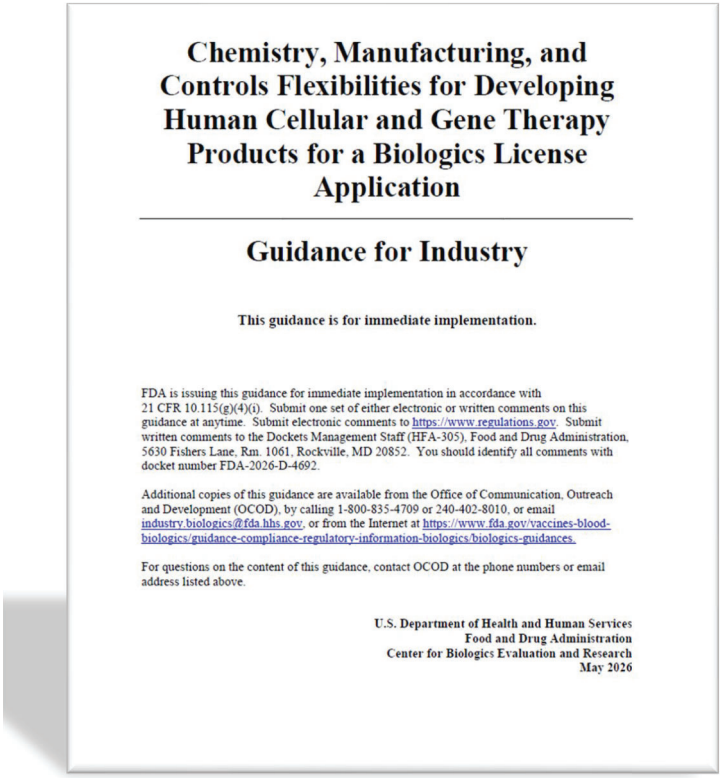


Recent CMC Guidance for GT Products





2026 Guidance: CMC Flexibilities for CGT products



Chemistry, Manufacturing, and Controls Flexibilities for Developing Human Cellular and Gene Therapy Products for a Biologics License Application

Guidance for Industry

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(4)(i). Submit one set of either electronic or written comments on this guidance at anytime. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with docket number FDA-2026-D-4692.

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), by calling 1-800-835-4709 or 240-402-8010, or email industry.biologics@fda.hhs.gov, or from the Internet at https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
May 2026

CONTEXT: Cell and gene therapy (CGT) products have unique characteristics that may necessitate nontraditional approaches to satisfy regulatory requirements

GOAL: Clarify, consolidate, and communicate existing CMC flexibilities rooted in risk-based approaches for CMC requirements for CGT products.

DISCLAIMER: This guidance does not lower the applicable regulatory standards for product quality and safety

CMC Flexibilities: Clinical Development

Phase-appropriate cGMP

- Phase 1 studies to assess product safety are exempt from full cGMP requirements
- Full cGMP requirements apply to investigational products used in Phase 2 and Phase 3 clinical studies

Lot Release Criteria

Wide acceptance criteria are acceptable for early-stage studies, unless overly permissive criteria compromise product safety, e.g., VCN for CAR-T cells

Analytical Comparability

- Risk-based approach to manufacturing and analytical changes
- Some changes may not require comparability studies if introduced early in clinical development and pose low risk to product quality

CMC Flexibilities: Process and Method Validation

Number of PPQ runs

- No minimum number of Process Performance Qualification (PPQ) runs
- PPQ strategy should be based on overall process understanding, complexity, and controls in place

Concurrent release of PPQ batches

PPQ batches can become commercial batches if supported by process validation study outcomes, commercial acceptance criteria (AC), and stability data

Number of lots used in analytical method validation

- No minimum number of lots to be used in the validation study
- One lot may be acceptable when scientifically justified

Additional CMC flexibilities

Commercial Release Specifications

- Limited data may be acceptable
- Wider AC can be established for initial commercial manufacturing and re-evaluated after approval, if justified

Stability Data

- Limited data may be acceptable
- Leverage all relevant stability data: similar products, clinical lots, accelerated and thermal stress stability studies

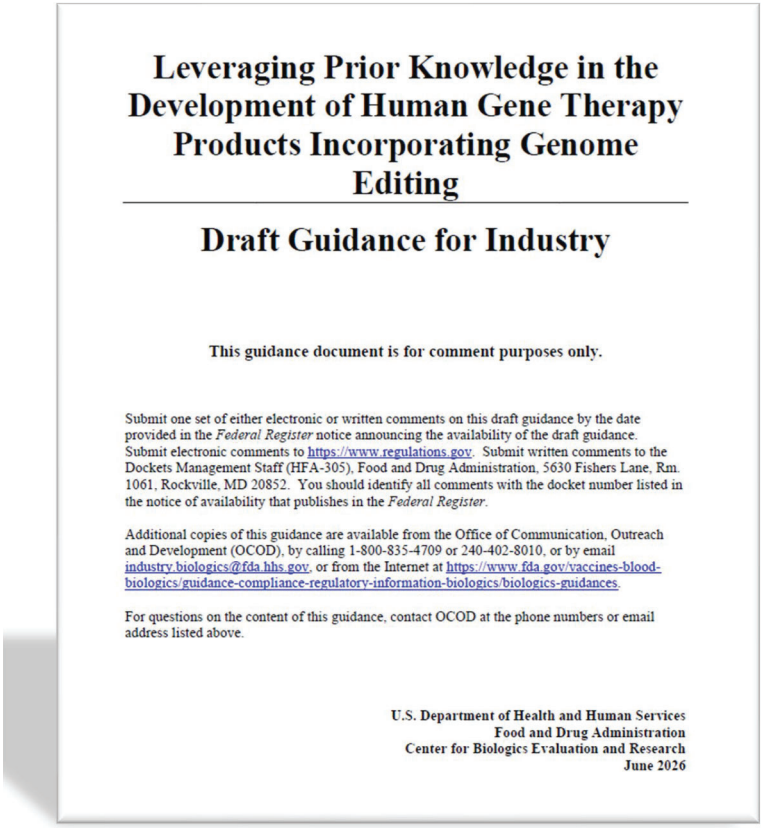
Alternative microbiological methods

Allowed to enable expedited release of CGT products and reduced sampling volume, provided the methods are validated

Reserve sample requirements

If needed, the Applicant can discuss alternative plans to meet regulatory requirement, or request an exception

2026 Guidance: Leveraging Prior Knowledge



Leveraging Prior Knowledge in the Development of Human Gene Therapy Products Incorporating Genome Editing

Draft Guidance for Industry

This guidance document is for comment purposes only.

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
June 2026

CONTEXT: The amount of product development data for similar CGT products (i.e., *prior knowledge*) across multiple product classes continually increases

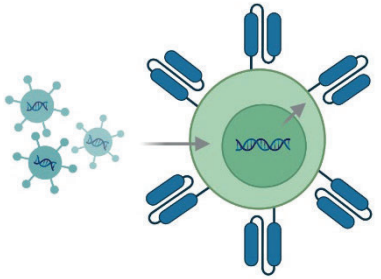
GOAL: Accelerate development of CGT products and streamline submissions by encouraging developers to use prior knowledge/data to support INDs and BLAs

ANTICIPATED OUTCOME:

- *Fewer required new CMC, PT and clinical studies*
- *Reduced cost of development*
- *Reduced product development timelines*

Leveraging CMC data

Hypothetical Product:
Autologous **CAR T product (CASSS-201)** manufactured using lentiviral vector transduction at a CDMO that manufactures a similar CAR T product (CASSS-101) from the same Sponsor using similar process, but with a **different vector transgene**



What CMC information can Sponsor leverage from CASSS-101 to accelerate the development of CASSS-201 product?

If the manufacturing processes and/or analytical methods are nearly identical ("platform process/methods") – a lot! And the best part is that this information may not have to come from an approved product!

Leveraging CMC data: Analytical Methods

Analytical Method Qualification/Validation

Analytical method validation packages can be leveraged from other products and components, including flow cytometry, VCN, and potency assays

- *Product- and vector-specific considerations still apply*
- *Limited product-specific verification may be necessary*

Lot Release Specifications

Critical Quality Attributes's (CQA) AC can be supported and justified by data from other well-characterized products and components

- *For example, cell phenotype, purity, product- and process-related impurities, etc.*
- *Depending on similarities between the products and vectors*

Leveraging CMC data: Process Validation

Process Characterization & Validation Data

Process characterization data from CASSS-101 can be used to inform CASSS-201 process parameter criticality and proven acceptable ranges of these parameters, i.e., Critical and Key Process Parameters (CPP/KPP), In-Process Controls (IPC)

PPQ data from CASSS-101 may be used to inform a PPQ study design and specifications for CASSS-201 (e.g., *number of PPQ runs needed*) and/or support process validation for CASSS-201.

Leveraging CMC data: Manufacturing Changes and Stability

Comparability Data

Comparability data obtained from one product or component may support changes in other similar products or components:

- *If the Sponsor previously switched the supplier of Human AB Serum in CASSS-101 with appropriate studies, these data may be used to support a similar change in CASSS-201.*

Stability Data

Stability data from CASSS-101 may be used to support long-term and in-use shelf-life, and potential commercial expiration for CASSS-201, *if both products are:*

- *Manufactured using sufficiently similar process and scale*
- *Formulated in the same formulation buffer using similar formulation parameters*
- *Stored in the same container and conditions*

Final thoughts

- FDA is actively looking for ways to accelerate CGT product development without compromising patient safety and product quality.

- CGT products and manufacturing processes are complex, diverse and evolving, thus, **CMC flexibilities and leveraging of prior CMC knowledge are applied on a case-by-case basis**, rather than universally.

- We encourage CGT developers to engage in **data sharing with other developers**, especially those that use the same manufacturing sites and platform technologies for manufacturing and testing.

Contact Information

Timothy Kamaldinov
Timothy.Kamaldinov@fda.hhs.gov

Regulatory Questions
OTP Main Line – 240-402-8190
Email: OTPRPMS@fda.hhs.gov

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