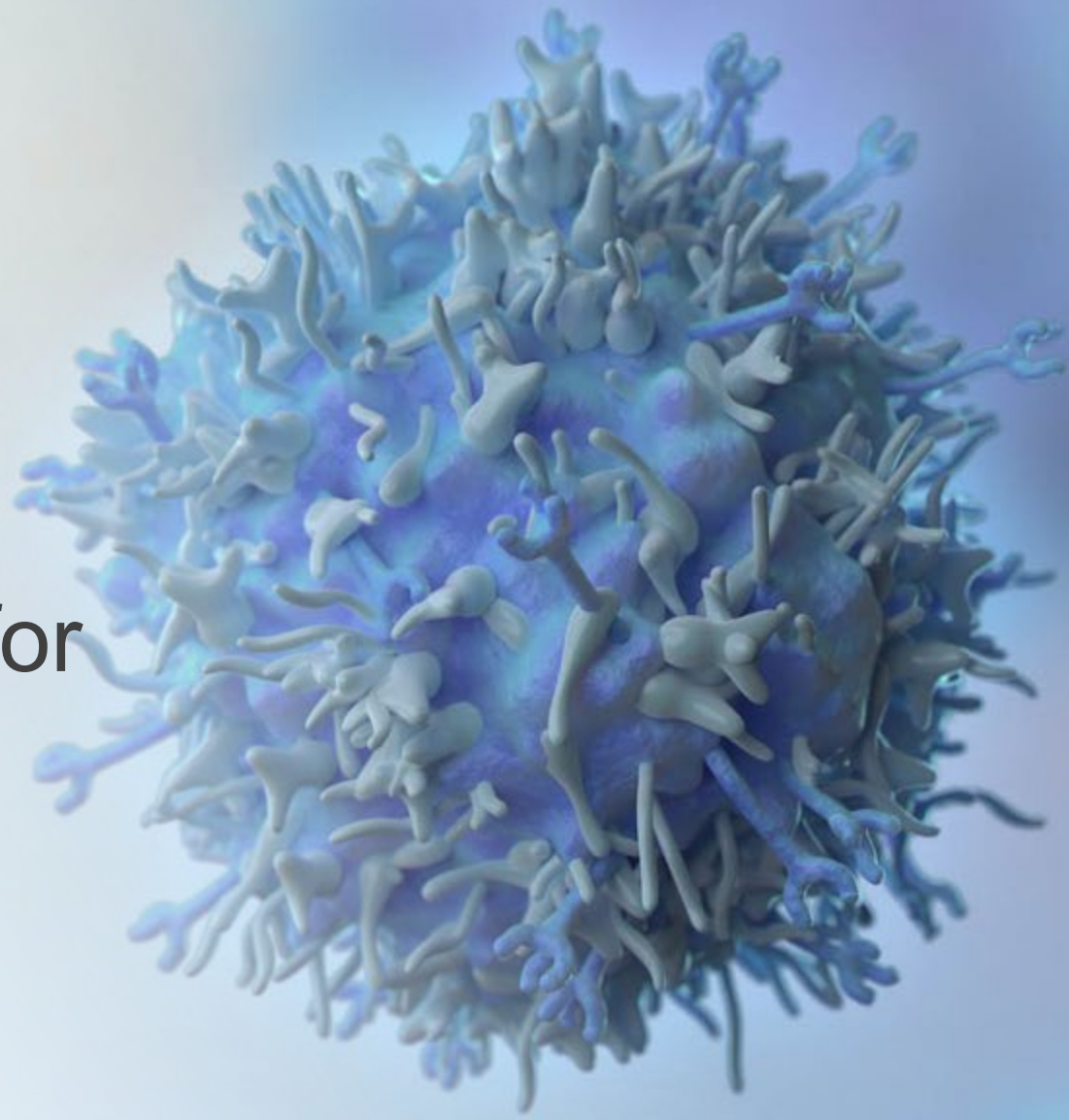

Global Regulatory Strategy for Cell Therapy Development and Manufacturing

Jingying Xu, PhD

June 22, 2026

Agenda

- Kite Global Presence
- ICH Framework
- Strategic Principles of Global Development
- Lifecyle Management with FDA, EMA and PMDA

Kite's Strong Global Presence

Kite by the Numbers…

33,500+
Patients Treated
(Clinical & Commercial Patients)

2
Global Commercial
Products on Market

5
Approved Indications
in CAR T-cell Therapy*

4,000+
Employees

1 million+
Square Feet of Cell Therapy
Manufacturing and R&D Space

29
Countries
with Reimbursed Product

(Data on File as of 10//2025)
*Approved indication number varies per market

Kite
A GILEAD Company

ICH Framework

- As of 2026, ICH has 25 members and 43 observers worldwide

Category	Description
Founding Regulatory Members	European Commission (EU), FDA (US), MHLW/PMDA (Japan)
Standing Regulatory Members	Health Canada, Swissmedic
Additional Regulatory Members	Include agencies from China, UK, Brazil, Mexico, Singapore, South Korea, Saudi Arabia, South Africa, Egypt, Argentina, Türkiye, Jordan, Nigeria, and others.

- What began as a collaboration among the EU, US, and Japan has evolved into a global network of 25 ICH members representing most major pharmaceutical markets worldwide.

ICH Quality Guidelines

ICH Guideline	Topic	Simplified Scope
Q1	Stability	Establishes requirements for stability studies, storage conditions, shelf life assignment, and stability data evaluation.
Q2	Analytical Validation	Defines how analytical methods are validated to demonstrate suitability for their intended use.
Q3	Impurities	Provides approaches for identification, qualification, and control of process-, product-, solvent-, elemental-, and leachable-related impurities.
Q4	Pharmacopoeias	Promotes harmonization and regulatory acceptance of pharmacopoeial methods across ICH regions.
Q5	Quality of Biotechnological Products	Addresses quality considerations unique to biologics, including viral safety, cell substrates, expression constructs, stability, and comparability.
Q6	Specifications	Establishes principles for setting release and shelf-life specifications, test procedures, and acceptance criteria.
Q7	GMP	Defines GMP requirements for manufacturing and control of active pharmaceutical ingredients (APIs).
Q8	**Pharmaceutical Development**	**Describes a science- and risk-based approach to product and process development and design.**
Q9	**Quality Risk Management**	**Provides a systematic framework for identifying, assessing, controlling, and reviewing quality risks.**
Q10	**Pharmaceutical Quality System**	**Describes an integrated quality system supporting product realization, process control, and continual improvement throughout the lifecycle.**
Q11	**Development & Manufacture of Drug Substances**	**Provides guidance on drug substance development, manufacturing processes, control strategies, and starting material selection.**
Q12	**Lifecycle Management**	**Facilitates efficient post-approval change management through enhanced product and process knowledge and risk-based regulatory approaches.**
Q13	Continuous Manufacturing	Establishes principles for development, implementation, control, and regulatory submission of continuous manufacturing processes.
Q14	Analytical Procedure Development	Provides a structured approach to analytical method development and complements Q2 analytical validation.

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Strategic Principles of Global Development

Market Prioritization

- Which countries?
- Commercial objective?
- Reimbursement environment?
- Regulatory hurdles?

Assumptions:
- Alignment with clinical regulatory plan
- CMC facts including manufacturing sites
- Supply chain and logistics implications

Filing Sequence

- Where first approval?
- Parallel vs sequential strategy?
- Timeline considerations
- Team bandwidth

Regulatory Pathway

- RMAT? PRIME? Orphan?
- Accelerated pathways?
- Reliance vs standard submission?

Strategic Principles of Global Development

Core vs Regional Package

- Local requirement
- Global CMC Package
- Local adaptions
- GMO/environment requirements

Agency Engagement Strategy

- Key Meetings
- Scientific advice
- Critical regulatory questions

Lifecycle Management

- Comparability
- Process evolution
- Post-approval changes

CMC Expectations

Comparison of FDA, EMA, PMDA

Aspect	FDA	EMA	PMDA
Process Description	Risk-based Quality by Design	Detailed control strategy	Granular process details
Raw Material Control	Source & viral safety	Traceability & TSE/BSE	Strict traceability and more scrutiny, safety review for GCTP compliance
Validation (PPQ)	3 runs typical	Similar to FDA	Extra runs often required
Analytical Assays	Expect multi-assay potency (e.g. molecular, functional, phenotypic)	Functional assays, genomic integrity	Granular method details
Stability	Accelerated + real-time; extension to next timepoint	Similar to FDA	Prefers longer real-time data
Comparability	Risk-based, deep comparability package	Similar to FDA, but greater regulatory flexibility	More stringent, generally requires more data and justification

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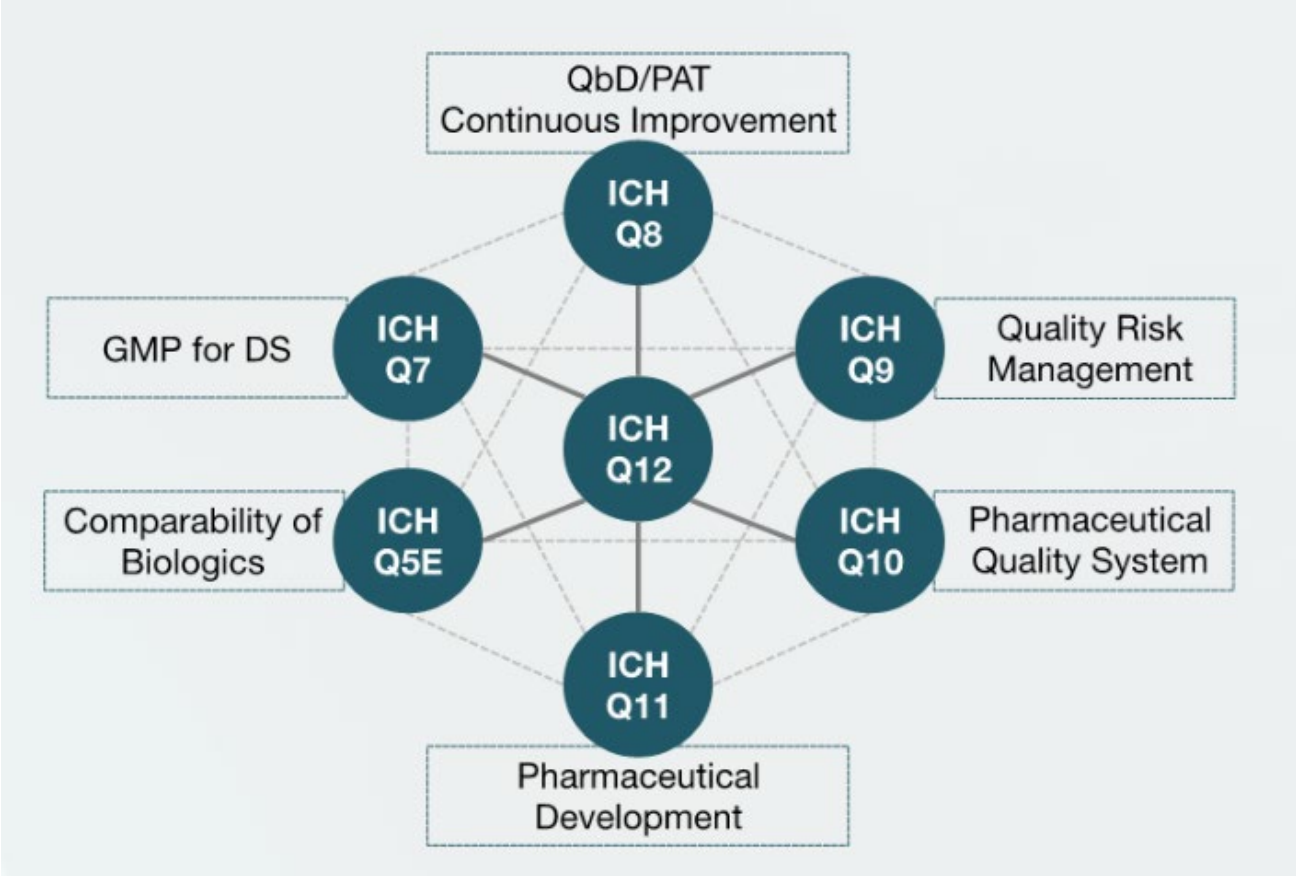
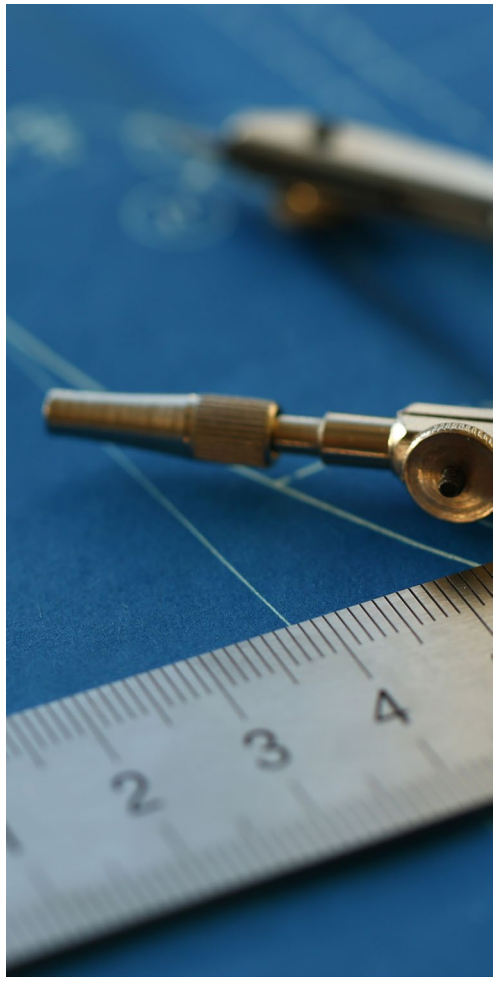
ICH Q12 Toolkit

- ICH Q12 integrates key concepts from other ICH guidelines.



Reference: https://www.valgenesis.com/blog/ich-q12-implementation-enhancing-pacm-agility

ICH Q12: Pharmaceutical Product Lifecycle Management



Risk-Based Change Management

Changes require formal evaluation and approval based on risk to ensure quality and compliance under Q10 guidelines.

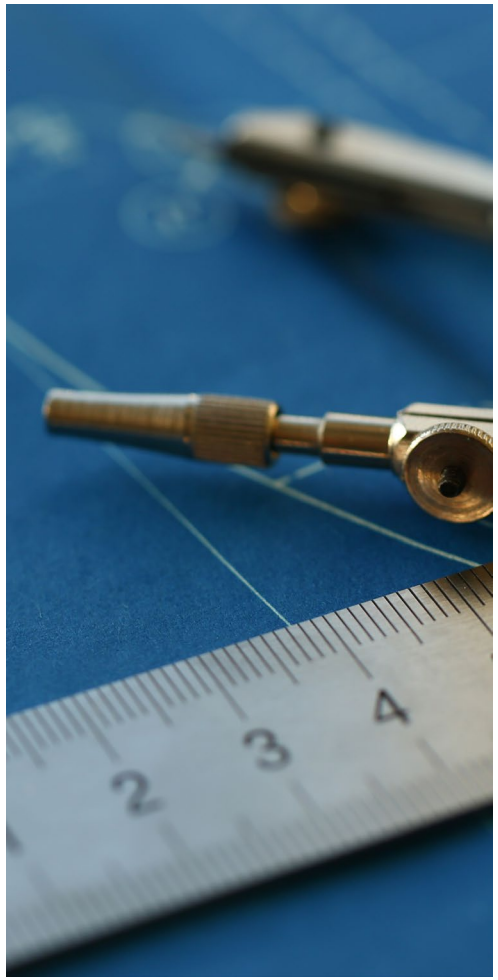
Driving Continual Improvement

Continual improvement relies on monitoring, CAPA, and effective knowledge management to enhance processes.

Structured Approach to CMC Changes

Require an effective and compliant change management system that captures and assesses full scope of change, implications, risk mitigation, planned implementation, and effectiveness

ICH Q12: Pharmaceutical Product Lifecycle Management



Key Elements

- Established Conditions (ECs): Define critical elements requiring regulatory reporting when changed
- Post-Approval Change Management Protocols (PACMPs): Pre-agreed plans with authorities to streamline changes
- Product Lifecycle Management (PLCM) Document: Central repository summarizing product and change control strategy
- Benefits: Transparency, predictability, reduced regulatory burden across FDA, EMA, PMDA

Effective PQS necessary to support these tools

FDA Post-Approval Change Framework

Change Categorization

FDA classifies post-approval changes into PAS, CBE-30, CBE-0, or Annual Report based on their impact on potential product quality and safety.

High-Impact Viral Vector Changes

High-impact changes involving viral vectors generally require Pre-Approval Supplements to ensure safety and efficacy.

Comparability Protocols Encouragement

FDA encourages use of Comparability Protocols to manage predictable post-approval manufacturing changes efficiently.

Components of Comparability Protocols

CPs include change descriptions, QRM-based impact analyses, validation protocols, and analytical comparability assessments.

FDA Expectations

FDA requires a strong scientific rationale with predefined acceptance criteria for CP submissions.

Submission and Change Management

Initial CP submissions are via PAS and subsequent changes under CP may quality for CBE-30; step-wise approach applied

EMA Post-Approval Change Framework

Change Categorization

EMA categorizes changes into Type IA, IB, and II to organize regulatory variations effectively.

High-Impact Viral Vector Changes

High-impact changes involving viral vector require Pre-Approval (Type II)

PLCM Compatibility

Lifecycle documentation aligning ECs with reporting categories

Purpose of PACMP

PACMPs outline planned changes with supporting studies and proposed reporting categories for regulatory review.

Components of PACMP

PACMPs include change descriptions, QRM-based impact analyses, validation protocols, and analytical comparability assessments, timelines (when will change be implemented), linkage to PLCM

Submission and Change Management

Initial PACMP submissions are usually via Type II; subsequent changes under may qualify for Type 1B or Type 1A submissions

PMDA Post-Approval Change Framework

Change Categorization

PMDA categorizes changes into Partial Change Application (require pre-approval, 1 year standard review) and Minor Change Notification (notification within 30 days of implementation)

Concurrent submission while one is under review not recommended if the same sections are impacted

Viral Vector as Intermediate

Manufacturing process described in the marketing authorization, specifications and detailed test methods in attachments. High impact changes involving viral vector require pre-approval (PCA)

PACMP Submission

PACMP procedure can be leveraged by submitting a change plan and obtaining confirmation, if confirmed the change can be shifted from “approval” to “notification”

Components of PACMP

PACMPs include change descriptions, QRM-based impact analyses, validation protocols, and analytical comparability assessments, timelines (when will change be implemented), with focus on patient and environmental safety

Summary of Reporting Categories

Comparison of FDA, EMA, PMDA

Change Type	FDA	EMA	PMDA
Minor	Annual Report	Type IA/IA(IN)	Minor Change
Moderate	CBE-30/CBE-0	Type IB	N/A
Major	PAS	Type II	Partial Change
PACMP / Protocol	PACMP	Post-Approval Protocol	Change Plan

Harmonized Global Regulatory Strategy

Design a unified control strategy anchored in Q9/Q10 principles.

Define ECs where feasible and map to the most stringent expectations.

Maintain a global PLCM to track region-specific commitments, reporting categories, and EC implementation status.

Develop a global PACMP for planned changes

Thank You