The Use of Novel Technologies for the Manufacture of Biosimilars

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General Requirements: 351(k) BLA

- A 351(k) application for a biosimilar must include information* that demonstrates biosimilarity to the reference product (RP)
  - Biosimilar is highly similar to and has no clinically meaningful differences from the FDA-approved RP
  - utilizes the same mechanism(s) of action, if known, as the RP
  - condition(s) of use in the labeling have been previously approved for the RP
  - has the same route of administration, dosage form, and strength as the RP
  - is manufactured, processed, packed, or held in a CGMP-compliant facility
- A robust comparative analytical assessment (CAA) can reduce or eliminate the need for comparative PK/clinical data

***Guidance for Industry**
Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations (September 2025); New and Revised Draft Q&As on Biosimilar Development and the BPCI Act, Revision 4 (Draft, March 2026)

Novel Technologies for Biologics

- Novel* technologies may be used for biosimilars; offer potential benefits
  - Support Quality by Design, improve manufacturing consistency or analytical sensitivity, strengthen CAA outcomes, streamline development
  - Novel technology examples
    - Continuous Manufacturing: improve efficiency, batch-to-batch consistency
    - Advanced Analytics (e.g., High-resolution mass spectrometry, NMR, and multi-attribute monitoring): Enhance characterization and comparability assessments
    - Process Analytical Technologies: Enable real-time in-process monitoring, support real-time release testing (RTRT)
    - Modeling/Digital Twins/AI/ML: Enable virtual process design, manufacturing optimization and scale-up, support process control, accelerate development and manage site activities
    - Aseptic & environmental monitoring technologies: Improvement from current
    - Novel dosage forms and drug delivery methods
  - Insufficient experience — requires early engagement with FDA

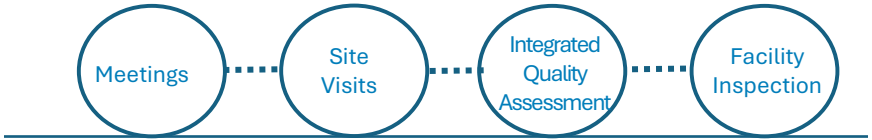
* In this presentation, the term ‘novel technology’ refers to emerging and advanced manufacturing technologies

Novel Technologies — CMC Programs

ETP Center for Drug Evaluation and Research (CDER)	CATT Center for Biologics Evaluation and Research (CBER)	AMTDP CDER and CBER
A cross-functional team from the Office of Pharmaceutical Quality, Office of Compliance, and Office of Inspections and Investigations	A cross-functional team composed of CBER leadership and members of the policy, review, and inspection programs	A cross-functional team consisting of members from ETP and CATT
Key Aspects: • Supports industry with development and implementation of novel technologies • Involves discussing, identifying, and resolving technical and regulatory issues early in development through application assessment • Focuses on novel product technologies, manufacturing processes, and control strategies	**Key Aspects:** • Facilitates pre-submission interactions with CBER • Involves discussing technical and regulatory issues • Focuses on novel technologies that impact product development, manufacturing processes, or control strategies	**Key Aspects:** • Supports industry with development and implementation of novel manufacturing technologies • Intended for more mature technologies - need data • Designates a technology within a specific context of use. • Allows a designation to be used by multiple products

ETP Collaborative Approach

The Emerging Technology Team may employ a combination of collaborative approaches



The same Emerging Technology Team representative(s) is involved throughout process



ETP Metric (as of Dec 2025)	Total Number
Accepted Meeting Requests	197
Site Visits	26
Approved Applications	25

Twelve Years of the ETP

Technologies accepted into ETP include process models, continuous biomanufacturing processes, novel unit operations, advanced analytics, and novel container-closure systems

Best Practices for ETT Meetings

- Focus only on CMC issues in CDER applications
- Submit the complete list of questions, proposals and information in the meeting package
- Provide specific proposals for ETT input – not issues for ETT to develop solutions
- Provide sufficient information and data to enable an informed response.
- Ability to provide input is limited when there without a specific product and data
- Final agreement is contingent on the review of the marketing application in its entirety

Using Novel Technologies for Biosimilars

- Technology is appropriately developed, controlled and validated prior to use in commercialization — demonstrate ‘fit-for-use’
  - Objective scientific risk assessment to identify potential risks
  - Develop robust control strategies; obtain supporting data
  - Update Pharmaceutical Quality System for novel technology implementation
- Regardless of the technology, CAA remains the foundation for biosimilarity
- When implementing a novel technology, several factors could impact CAA and bridging data requirements. E.g.,
  - Lifecycle stage when the ET is used — biosimilar development? post-approval?
  - Type and purpose of the technology:
    - Process development support? Manufacturing process?
    - Analytical method – used for IPC? CQA? CAA method?
  - Impact of technology on product quality
- Discussion and FDA prior agreement highly recommended

Key Takeaways & Path Forward

- Emerging and Advanced Manufacturing technologies offer significant opportunities to enhance biosimilar manufacturing quality, consistency, and efficiency
- CDER's ETP provides a proactive, collaborative pathway for sponsors to engage FDA early and navigate new technical and regulatory issues associated with novel manufacturing technologies
- Regardless of technology used, a robust Comparative Analytical Assessment remains central to demonstrating biosimilarity
- Engagement with FDA during novel technology development — control strategies, bridging, CAA, submission content — greatly facilitates first-cycle approval