Roundtable Session 1 – Table 2 – How Has AI Changed the Way We Work? What Role Will AI and ML Play in Personalized Cell/Gene Therapies?

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Abstract:

Artificial intelligence (AI) is no longer a future-facing concept in biologics development; it is already changing how teams generate, interpret, and apply scientific knowledge. Across discovery, process development, analytical development, manufacturing, quality, and regulatory CMC, AI and machine learning (ML) tools are being used to analyze large and complex datasets, support predictive modeling, optimize process parameters, accelerate method development, identify product quality trends, and improve documentation and knowledge management. These applications offer opportunities to improve efficiency, consistency, and decision-making across the product lifecycle. However, broader adoption will require careful attention to data integrity, data architecture, model robustness, validation, lifecycle maintenance, regulatory expectations, and the continued role of human scientific judgment. Recent CASSS roundtable discussions have similarly emphasized that AI can enhance efficiency and quality in process and analytical development, while adoption still depends on overcoming technical, cultural, and regulatory hurdles.

The potential impact of AI/ML may be especially significant for personalized cell and gene therapies, where patient-specific variability, complex mechanisms of action, limited batch sizes, compressed manufacturing timelines, and evolving analytical strategies challenge traditional development models. AI/ML approaches may help connect patient, donor, raw material, process, analytical, and clinical data to support donor and patient stratification, process monitoring, potency assay development, comparability assessments, release decision support, and prediction of critical quality attributes. For these tools to be meaningful in personalized therapies, developers must define where AI/ML can support decisions, how model outputs should be qualified and explained, and what evidence is needed to establish confidence with regulators, manufacturers, clinicians, and patients. This roundtable will explore where AI/ML is already changing daily work in biologics development, where it may provide the greatest value in personalized cell and gene therapies, and how the field can responsibly advance these technologies while ensuring quality, safety, and patient access—consistent with the CASSS CGTP focus on scientific dialogue among industry, regulators, and academia.

Discussion Questions:

1. Where is AI/ML currently providing the most practical value in biologics development: process development, analytical development, manufacturing, quality, regulatory CMC, knowledge management, or another area?
2. What data quality, data architecture, governance, and validation expectations are needed before AI/ML outputs can be confidently used to support CMC decisions?

3. For personalized cell and gene therapies, which use cases are most promising for AI/ML: patient or donor stratification, raw material assessment, process control, potency prediction, comparability, release testing, or lifecycle management?
4. How should industry and regulators define the appropriate role of human oversight when AI/ML tools are used to support development, manufacturing, or regulatory decision-making?

Notes:

Overview

- Roundtable with **11 participants**, focused on applying AI/ML in **CMC**, cell and gene therapy development.
- Consensus that AI is already useful for **document drafting**, **data summarization** and **process monitoring**, while full automation of critical decisions requires strong human oversight (human-in-loop / **QP** responsibility).
- Key enablers: **structured data**, metadata standards (ICH **M16** / M4Q, FHIR-like approaches) and continuous model lifecycle management (drift detection / rolling models).

Human oversight & responsibility

- Participants agreed a human must remain in the loop for critical GMP decisions (see EU **Annex 22** for human in the loop concept). QP must be comfortable and able to justify decisions informed by AI.
- Use of AI as an additional data stream or advisor was framed as staged: AI outputs can inform reviewers, who then inspect flagged parameters before final sign-off.
- For batch release / locked disposition scenarios, speakers recommended presenting any AI-flagged exceptions to the QP with underlying data so the QP can verify and take responsibility.
- Outlook: regulators will accept AI-assisted workflows if **explainability, validation, and ongoing performance monitoring** are demonstrable.

Practical applications reported

- Common, low-risk uses included **drafting regulatory text (Module 3, BLAs)**, decoding guidance, summarizing gap assessments, generating draft stability/assessment reports — often reducing a task from **hours/days to minutes**.
- Analytical / process uses discussed:
    - Multivariate, real-time process analytics and PCA for variable selection (from ~22 variables in one example).

    - Pattern recognition / image-based analysis (cell morphology) and higher-dimensional deep learning for process characterization.
- Outlook: many companies already apply local ML models for data aggregation, report generation and deviation monitoring; adoption for higher-risk decisions will be staged and validated.

Data, standards & engineering challenges

- Major barrier: fragmented, poorly structured data and inconsistent metadata across instruments, ELNs and LIMS. Speakers emphasized the need for **data governance**, metadata standards, and structured capture to enable AI value.
- Standards & initiatives referenced: **ICH M16**, M4Q, GAMP concepts (Annex11/22) and FHIR-like structuring for manufacturing and submission-ready data.
- Sampling and dimensionality: handling high-dimensional datasets requires PCA / feature selection to avoid curse of dimensionality; realistic sample sets discussed for local models were on the order of **tens–hundreds** of samples for focused variables, larger runs for production monitoring.
- Outlook: structured-data initiatives (M16, standardized metadata) are enablers that make downstream AI tools practical and easier to submit to regulators.

Model validation, lifecycle & explainability

- Validation expectations differ between pharma validation and ML model validation; regulators expect demonstrable predictive performance across the relevant design space and ongoing validation over time.
- Suggested approach:
    - Start with interpretable methods (PCA / explainable ML) to identify top contributing parameters.
    - Validate models across design space and demonstrate performance/robustness; use staged deployment (advisor -> assist -> control).
    - Maintain lifecycle management: drift detection, periodic revalidation or rolling-model updates.
- Explainability vs performance trade-off: regulators comfortable with performance-based approaches if accompanied by sufficient validation and the ability to interrogate outputs (e.g., top contributing features, outputs to review).

Risks & failure modes (operational and trust)

- Hallucinated / incorrect citations and sourcing from LLMs were reported as a real problem — users must spot-check and provide references or train models on validated internal corpora before relying on outputs.

- Data provenance and reproducibility are critical: participants stressed feeding AI curated internal documents improves reliability; public-domain sourcing without traceable citations is risky.
- Operational risk: insufficient testing of model outputs (especially for predictive tasks with many components) can leave untestable or unvalidated blind spots; testing strategies should prioritize highest-impact outputs and use spot-checks.

Use-cases where AI added immediate value

- Drafting and summarizing regulatory content (Module 3 drafts, stability assessments).
- Regulatory gap assessments and guidance decoding with targeted prompts and iterative layering to refine outputs.
- Process monitoring dashboards: automated aggregation, drift detection, and report generation accelerated workflows that previously took months.
- Outlook: immediate ROI is highest for repetitive, structured tasks; higher-risk predictive and control use-cases require more data and staged validation.

Outstanding challenges & next steps discussed

- Data standardization and metadata capture across instruments and ELNs is a prerequisite for broad AI deployment in CMC.
- Need for clear validation frameworks and regulatory expectations for AI-assisted tools (explainability, test datasets, lifecycle management, QP oversight).
- Practical testing strategies proposed: rank outputs (top-N features) and spot-checks, ensemble or multi-model voting, and staged operationalization (advisor -> verifier -> controller).
- Outlook: regulators and industry are moving quickly; pragmatic adoption will lean on local, validated models and structured-data initiatives to scale up safely.