**Roundtable Session 1 – Table 4 - Speed to Clinic - Phase-Appropriate Strategies to Accelerate CMC Development Timelines**

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**Abstract**

Speed to clinic for pharmaceuticals requires phase-appropriate strategies that streamline Chemistry, Manufacturing, and Controls (CMC) development without compromising patient safety. Recent case studies and reviews published after the COVID-19 pandemic highlight the adoption of agile development approaches, tailored risk-based CMC strategies, and early regulatory engagement as pivotal accelerators for clinical entry. By leveraging adaptive manufacturing methodologies—such as concurrent process development/validation, stability data extrapolation, and proactive tech transfer—biopharma organizations have demonstrated that accelerated, phase-based planning and cross-functional collaboration can significantly reduce CMC timelines. Harmonizing regulatory frameworks and codifying these accelerated practices as industry standards are essential for sustaining these gains beyond emergency authorization, enabling faster responses to unmet medical needs in both pandemic and non-pandemic contexts.

**Questions:**

What acceleration levers have you considered employing for early or late development?

What acceleration levers have been most impactful?

For Ph1 IND submissions what push back did you get from the health authorities on trying to accelerate non-COVID programs? Any comments on use of stable pool for tox?

For speed to FIH what product quality is checked in expedited vs. non-expedited processes? Do you have any metrics for acceptable genetic mutations or AA misincorporations?

**Notes:**

The roundtable discussion centered on strategies for accelerating CMC timelines in early phase development, with particular focus on cell line development approaches, phase-appropriate practices, and emerging technologies.

A significant portion of the discussion focused on pool-to-clinic strategies as a means of compressing development timelines. The use of pooled clones for GLP toxicology studies is becoming increasingly common across the industry, with several participants sharing successful experiences. For well-understood modalities such as IgG1, regulatory agencies have generally accepted this approach when supported by appropriate comparability data. One company shared their experience using a mix of top clones for toxicology material, transitioning to a single clone for first-in-human studies without regulatory pushback. Aggressive timelines of six months from cell line to clinic were discussed, with site-specific integration technologies and improved promoters enabling faster generation of toxicology material—as quickly as 2.5 months for low-concentration monoclonal antibodies. However, some participants noted receiving questions about stability data when submitting less than three months of data, particularly regarding initial shelf-life assignments.

The group extensively discussed phase-appropriate GMP (PAGMP) practices, which are widely adopted across the industry. Participants agreed that GMP requirements appropriately increase over time, providing flexibility in early development. For raw materials, a risk-based approach was recommended: ensuring supplier certificates of analysis and identity testing for most materials, with additional bioburden and endotoxin testing reserved for excipients. The distinction between excipients and bioreactor process reagents was highlighted as an important consideration for compliance strategy.

An innovative approach to IND filing was discussed wherein companies file the IND with engineering batch data and subsequently add GMP batch results via an IND update, waiting the standard 30 days before initiating clinical trials. This strategy can provide significant timeline advantages, with one company noting they gained six additional months of stability data by using engineering batches primarily for shelf-life establishment.

The adoption of AI for IND writing is beginning across the industry, though implementation varies. Companies are starting with simple sections and evolving toward integrated module

generation. Key challenges include interfacing AI tools with existing LIMS systems and managing multiple CDMOs with different data systems. Participants noted that the real power of AI may lie in future applications such as investigations and extracting insights from development runs. There was also discussion about leveraging AI for lifecycle management and enabling continuity from discovery through CMC development, particularly for complex modalities.

Regarding characterization requirements, the consensus was that sequence variant analysis is generally not required in early phase development and is rarely requested by regulatory agencies, though pharmaceutical partners sometimes request it. The group discussed the challenge of determining appropriate thresholds and agreed that sequence confirmation is typically sufficient for early submissions. A phase-appropriate content strategy was recommended: submitting only evaluated parameters in Phase 1, adding parameters in Phase 2, and including full results in Phase 3. For FDA submissions specifically, full validation descriptions are only needed for non-compendial methods.

For ADC development specifically, the fastest reported timeline was 14 months, with the biggest hurdles being GLP toxicology initiation and obtaining toxicology data. Manufacturing drug linkers was identified as a significant challenge due to the heterogeneity of linker types and suppliers. Having a Drug Master File for specific linkers can substantially accelerate timelines. One company shared their experience going directly to clinic without animal toxicology studies for an ADC where no suitable animal model existed, relying instead on modeling for a second-time oncology indication.

The discussion also touched on regulatory strategy, with participants recommending the use of global IND templates for consistency and noting that FDA does not require shelf-life information in INDs. Type D meetings were suggested as a mechanism for discussing challenging scenarios, such as impurities present in GMP material but not in toxicology material. Regional considerations were also discussed, with some participants advising caution regarding certain jurisdictions in early development.