Validation & Regulatory Fit - How do we ensure NAMs meet regulatory confidence for specific decision contexts?

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Discussion Questions:

Context-of-Use Definition: What minimum evidence package (performance metrics, reproducibility, uncertainty quantification) satisfies regulators for early-stage versus pivotal decisions?

Qualification Pathways: How should multi-stakeholder consortia design prospective qualification studies to balance rigor, timelines, and resource constraints?

Decision Authority: For which specific contexts (screening, lead selection, safety signal triage) should regulators permit NAM-only decision making?

Main Takeaways

- Use case determines the regulatory pathway. Early-stage decisions using NAMs require less stringent validation than later-stage regulatory decisions, though both can share a common foundational framework that may support future regulatory pathways
- NAMs are unlikely to replace all animal models, but they have strong potential for early-stage screening, particularly when validated against in-vivo data with high predictive accuracy
- Certain development areas already rely heavily on in-vitro systems, such as ASO) development, which could serve as practical starting points for demonstrating NAM effectiveness.
- Back-testing failed drugs in advanced in-vitro models could help validate these systems, but industry currently has limited incentives to share compounds or data for this purpose.
- Progress requires multi-stakeholder collaboration and data sharing, including access to compounds and associated clinical data from industry.
- Companies rarely share failed results, making it difficult to understand the limitations of in-vitro systems and slowing adoption.
- Scalability, automation, and reproducibility are essential for NAMS adoption