From Development to Bedside: Overcoming Challenges in Regulatory and Manufacturing Process for mRNA-LNP Vaccines

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Personalized mRNA LNP therapy is transforming the concept of precision medicine, but its translation is limited by a drug product challenge that remains underrecognized. For each patient, the final therapeutic dose is an individualized batch that must be formulated, tested, released, stored, and administered within clinically meaningful timelines. This creates constraints that are fundamentally different from conventional biologic manufacturing, including construct to construct variability, limited retained material, compressed quality control, variable LNP formation behavior, uncertain stability windows, raw material limitations, and evolving regulatory expectations. These limitations directly affect feasibility, reproducibility, and access to care, particularly for academic or hospital-based programs attempting to move personalized RNA products beyond exceptional use. From a drug product perspective, the solution is not to simplify personalization, but to control it through a defined platform. Critical quality attributes, process parameters, mRNA drug substance input specifications, LNP formulation ranges, downstream processing steps, release assays, stability assumptions, and material risk assessments must be prospectively organized into a phase appropriate control strategy. Representative construct bracketing, fit for purpose analytics, real time release logic, auditable documentation, and early regulatory dialogue can allow patient specific batches to remain individualized while being manufactured under a common scientific framework. This approach reframes personalized mRNA LNP therapy as a repeatable drug product model rather than a series of isolated custom preparations. By integrating formulation science, manufacturing readiness, regulatory strategy, and clinical delivery, personalized RNA therapy can move toward more reproducible translation and broader patient access.