cytiva

New to mRNA manufacturing?

Here's what you need to know

DNA template

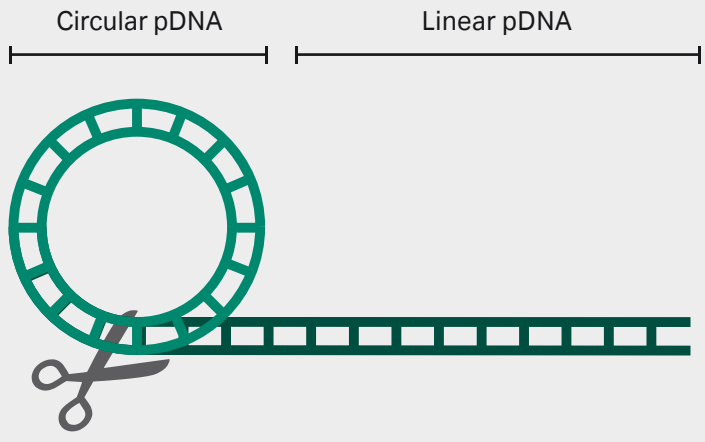
Objective: Synthesize DNA template

What to consider:

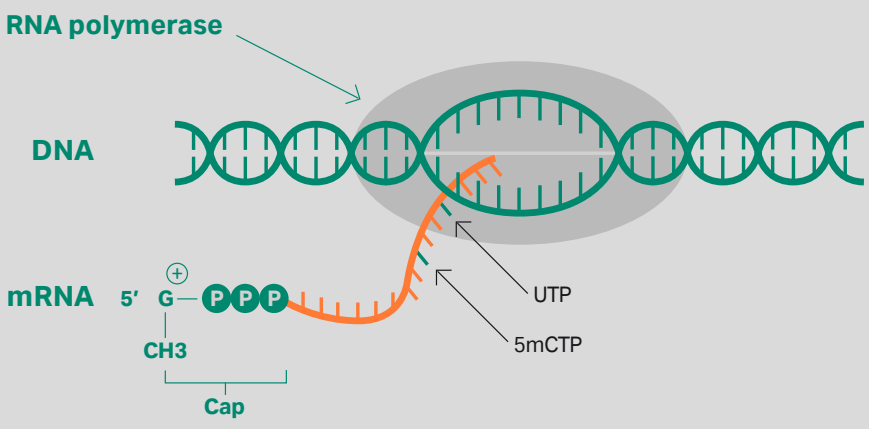
- Synthesis is labor intensive and time consuming
- Template quality affects yield and mRNA integrity
- Need organic solvents, but they denature *in vitro* transcription (IVT) enzymes
- Difficult to maintain a nuclease-free environment

Strategies:

- Use high-quality, standardized and linearized plasmid DNA (pDNA) from **Aldevron**
- Simplify pDNA extraction and purification with plasmidPrep Kit and GFX™ PCR DNA and Gel Band Purification Kit, both from **Cytiva**
- Use RNaseAlert® kit, Nuclease Decontamination Solution, nuclease-free water, and custom primers, all from **IDT**



mRNA product – IVT



Objective: Synthesize and cap mRNA

What to consider:

- Need high-quality enzymes, reagents, and filters
- Important to choose a capping method that's cost effective and scalable

Strategies:

- Use high-quality, customizable (from mg-to-g scale) IVT enzymes from **Aldevron**
- Choose nucleoside triphosphates (NTPs) from **Cytiva** – they're tested for RNase activity and purified to ≥ 98%

mRNA product – purification

Objective: Purify mRNA

What to consider:

- Need to optimize removal of impurities, especially aberrant mRNA
- Difficult to choose the analysis method for aberrant RNA

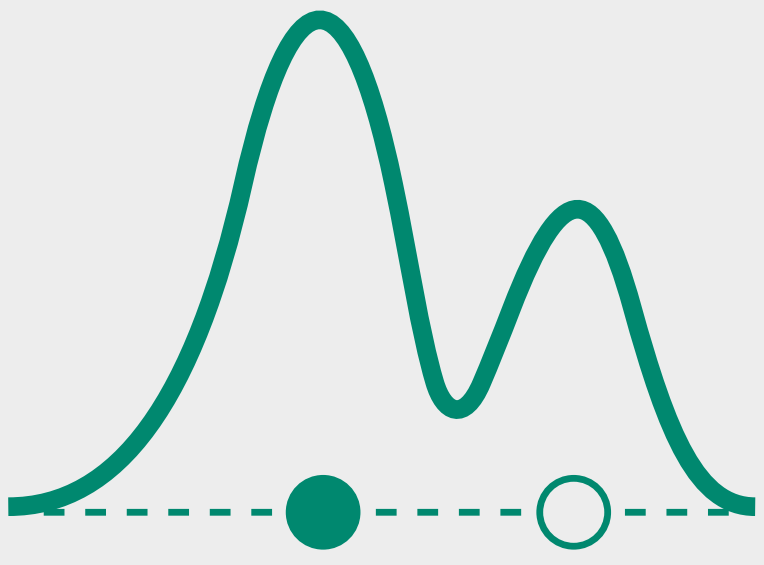
Strategies:

Choose mRNA capture, polishing, and analysis products from **Cytiva**:

- Capture mRNA using Sera-Mag™ Oligo(dT) magnetic particles
- Perform microscale purification by converting ÄKTA pure™ 25 chromatography system using a Micro kit
- Simplify the workflow with HPLC-certified regenerated cellulose (RC) filters, as they're compatible with many solvents to minimize extractables
- Perform dot blotting with Nytran™ SuPerCharge (SPC) nylon membrane and Cy™3/Cy™5 secondary antibodies

Choose filtration products from **Pall Corporation**:

- Prior to encapsulation, perform a sterile filtration step with 0.2 µm pre-sterilized Acrodisc® syringe filters



LNP encapsulation

Objective: Form lipid nanoparticles (LNPs) for mRNA drug delivery

What to consider:

- Require targeted, optimized reagent formulations for precise, effective, and safer mRNA delivery
- Need scalable instruments to create high-quality nanoparticles at increased volumes
- Must use high-quality centrifugal ultrafiltration devices with wide range of molecular weight cutoffs (MWCOs)

Strategies:

- Accelerate drug programs with **Precision Nanosystems**, which offers a range of systems, reagents, and services with deep expertise in LNP formulations
- Speed up timelines from research to clinic with scalable microfluidic mixing technology that results in uniform and reproducible high-quality LNPs
- Screen and optimize LNP reagent formulations using off-the-shelf lipid reagent kits, and access a custom library of formulations designed and optimized for established use cases
- Use appropriate analytics to determine appropriate particle size, polydispersity index, and encapsulation efficiency
- Polish LNPs with centrifugal ultrafiltration units from **Pall Corporation**

Fill-finish

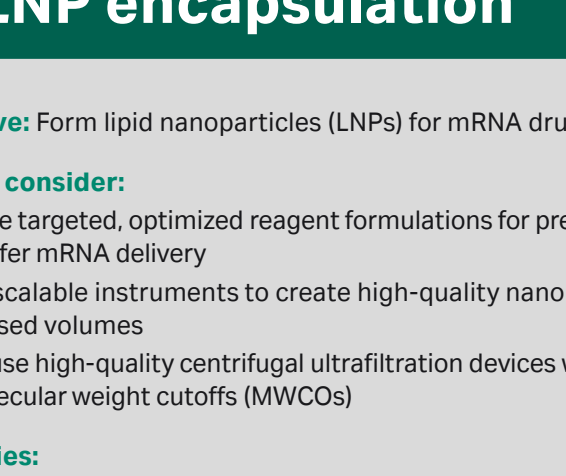
Objective: Finish drug product for delivery to patient

What to consider:

- Need to choose a path: personalized or platform mRNA drug product
- Long-term storage conditions are important
- Must perform visual inspection of translucent drug product

Strategies:

- Scale out to add capacity quickly, especially for personalized products
- Streamline production and reduce supply chain risk by co-locating drug product with drug substance
- Think about options to transition from vial to syringe for launch



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Learn more about mRNA manufacturing