

# mRNA manufacturing workflow

# MADE WITH PURPOSE & PRECISION

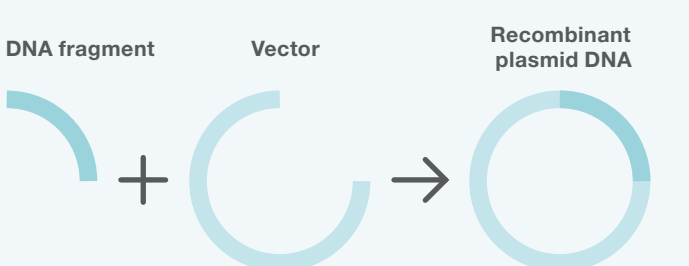
Like many therapeutic manufacturing workflows, every step in the mRNA process builds upon the prior step. Plasmids are critical starting materials used for mRNA synthesis, after which the resulting purified mRNA is encapsulated for more efficient stability and delivery. The encapsulated final drug product must then be sterile-filled, packaged, labeled, and shipped to its final clinical destination. Additionally, in-process and final release testing are critical to ensure robust Chemistry, Manufacturing, and Controls (CMC). As the manufacturing process progresses, every step adds complexity and cost, so it's important to ensure steps are compatible and integrated into each other. This infographic explores each intertwined step in the mRNA manufacturing process and outlines how Thermo Fisher Scientific's flexible approach can get your mRNA product to clinic and market faster.



## Plasmid production

### Target discovery

Sequence, analyze, and validate therapeutic gene target



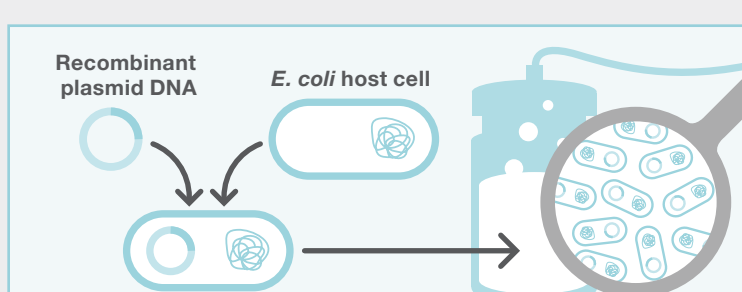
### Template generation

Create plasmid template of your therapeutic gene target



### Plasmid production

Transform plasmid into *E. coli* and replicate via fermentation



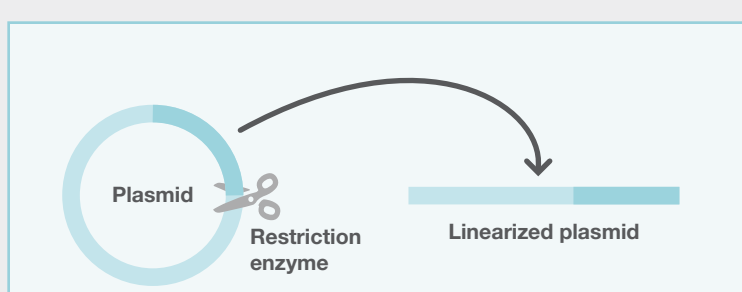
### Plasmid purification

Harvest, lysis, and purification of resulting plasmids



### Plasmid linearization

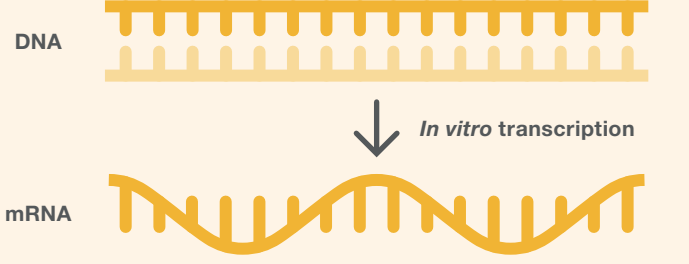
Linearize plasmid with restriction enzymes to provide IVT template



## mRNA synthesis

### mRNA production

*In vitro* transcription (IVT) creates mRNA from linearized DNA plasmid



### Modifications

Addition of 5' cap, poly(A) tail, and other modifications can be done either **co-** or **post-IVT**



### mRNA purification

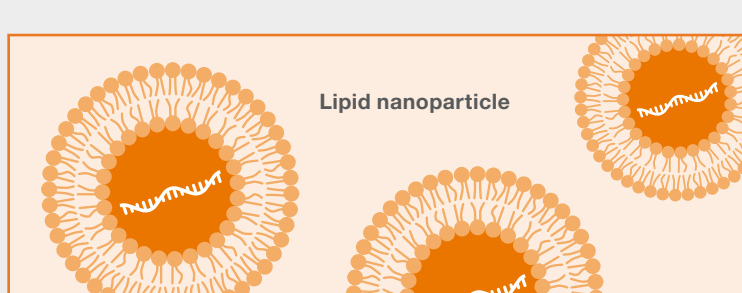
Resulting mRNA transcripts undergo tangential flow filtration (TFF), precipitation, and/or chromatography to remove residual process contaminants



## Encapsulation

### Formulate and encapsulate mRNA

Purified mRNA is combined with **lipids and/or polymers** to encapsulate the mRNA for efficient delivery and stability



### LNP purification

Resulting lipid nanoparticles (LNPs) undergo TFF and diafiltration to remove any residual process contaminants and ensure sterility of the final product



## Sterile fill-finish

### Fill, cap, and seal

Purified drug product is filled into primary product containers, capped, sealed, and lyophilized (if appropriate), all while maintaining sterility



### Primary labeling

Primary product packages are labeled to ensure product traceability and compliance



## Cold chain logistics

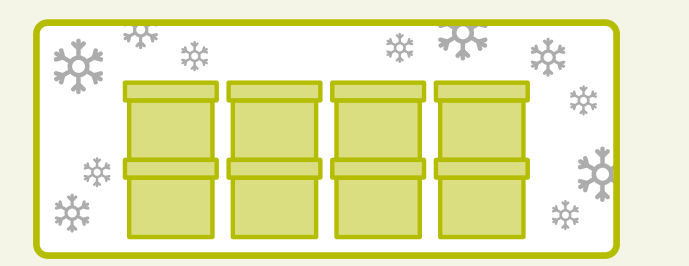
### Secondary packaging and labeling

Labeled product is placed into secondary packaging containers to ensure quality and integrity throughout storage and distribution



### Temperature-controlled storage

It is critical to properly maintain chain of custody and temperature requirements of the drug product during storage



### Temperature-controlled distribution

Maintenance of chain of custody and temperature requirements during distribution is equally important to ensure that the drug product arrives on time, in full, and at temperature



## Flexibility of à la carte options within an integrated mRNA service offering can get you to clinic faster

Flexibility brings speed. Quickly filling capability or capacity gaps can help you bring your therapeutic to clinic and to market faster. That's why we offer choices of à la carte options within our integrated mRNA service offering. From process development to cGMP manufacturing, you can choose within the core mRNA therapeutic service options and add upstream and downstream services where needed. Analytical methods and regulatory support are also offered for all services.



### Flexibility means choice:

- 1. End-to-end integrated mRNA service offering:** We take care of everything from plasmid production to mRNA manufacturing to cold chain logistics
- 2. Core mRNA service offering:** Have us do all your mRNA work—including synthesis, encapsulation, and fill-finish—while you do the upstream and downstream work
- 3. Mix and match to fill gaps:** Choose from among our core mRNA service options, and add any upstream and/or downstream services where needed

Learn how **Thermo Fisher Scientific** can help you fill mRNA gaps quickly to get to clinic and to market with speed.