ThermoFisher SCIENTIFIC

TheraPure GMP

Beyond GMP grade

How to ensure more robust development and manufacturing processes

At what point do you transition materials and processes to materials that follow **good manufacturing practice (GMP)**?

Small and medium-sized biotech companies often struggle with this decision.

It is important to understand how your processes and material usage strategy during the development phase could impact your manufacturing processes and regulatory approval downstream.

Here are some considerations to help you make **the right decisions to improve your downstream outcomes**.

What is GMP grade?

Products that are labeled as "GMP grade" are labeled this way as a marketing term. There is no concrete definition of what GMP grade actually is, or that it provides the quality attributes needed for manufacture of a therapeutic. This term can be used by suppliers to describe materials with a wide range of quality attributes. While sometimes manufactured to high standards, these materials may not fulfill certain quality-standard requirements for regulatory approval.

What is TheraPure GMP?

Thermo Scientific™ TheraPure™ GMP* materials have been specifically designed to be used in the GMP manufacture of therapeutics. These products are manufactured to relevant ICH Q7 guidelines and manufactured and tested to ICH Q2 standards. TheraPure GMP products possess a number of important quality attributes and are supported by a comprehensive quality documentation package.

TheraPure GMP product quality attributes

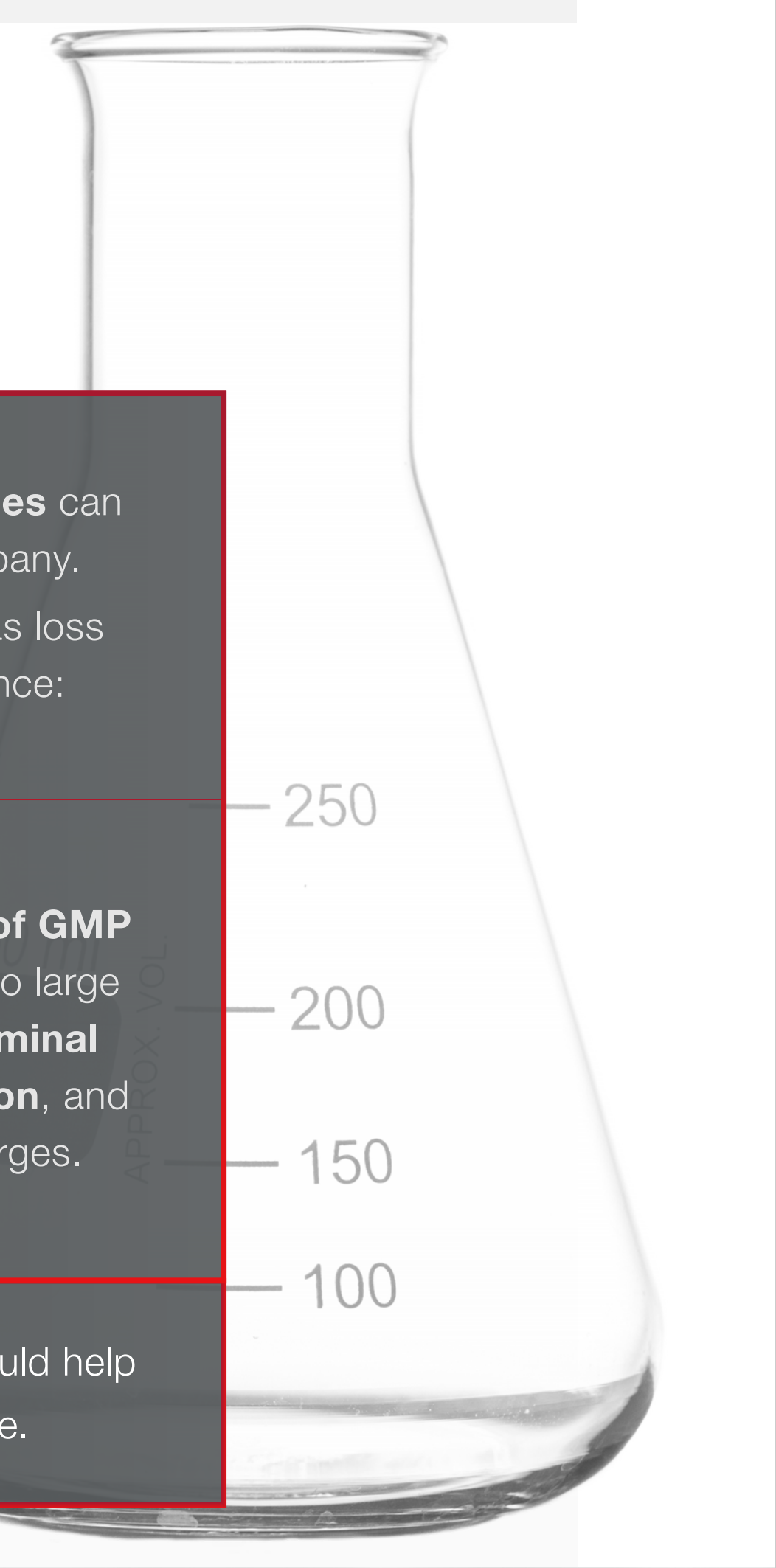
- Manufacture follows relevant ICH Q7 GMP principles
- Animal origin–free (AOF) manufacturing processes and raw materials
- Validated manufacturing processes and analytical methods
- Product-specific stability data
- Impurity profile
- Verified compendial test methods, where applicable
- Manufactured in β-lactam–free facilities

TheraPure GMP product quality documentation package

- Certificate of analysis (CoA)
- Certificate of origin (CoO)
- TSE/BSE statement
- Nitrosamine statement
- Melamine statement
- Compendial test results (e.g., bioburden, endotoxin, residual host cell material)
- Impurity profile, including heavy metals and residual solvents
- Stability test results
- Drug Master File

The importance of GMP

GMP guidelines help provide a robust quality management system to help ensure products are designed to meet product requirements such as identity, strength, purity, and quality, to be safe and effective.



Adulterated products are those not made in compliance with GMP guidelines.
The consequences could lead to severe health impairment or loss of life:

- In 1937, **cough medicine** with impure sulfanilamide led to **over 100 deaths** in the US.
- The **early polio vaccine** was insufficiently processed, which led to **several cases of polio** in children.

Failing to comply with GMP guidelines can have a devastating impact on a company.
The impact could be financial as well as loss of reputation and consumer confidence:

- **Deviations from GMP** during quality control can lead to a whole **product batch going to waste**, or even worse, if not caught early, **product recall**.
- **Violation of GMP** may lead to large fines, **criminal prosecution**, and civil charges.

Even though GMP guidelines can't completely prevent mistakes, following GMP recommendations could help reduce the frequency of such incidents, which demonstrates how important these guidelines are.

TheraPure GMP quality management system

The quality attributes of TheraPure GMP products are achieved through effective implementation of a robust quality management system that includes the following elements:

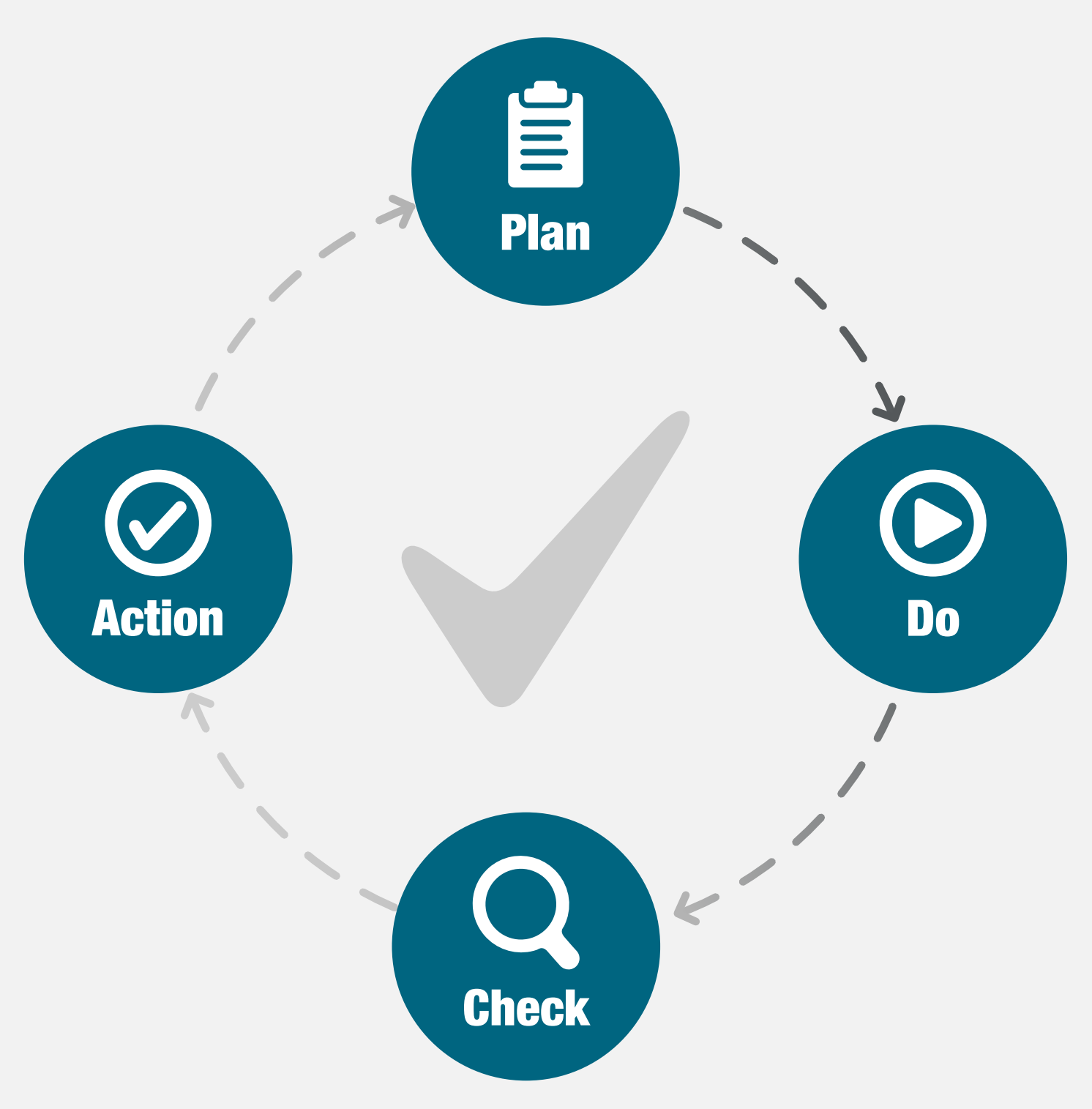
- Documentation requirements, including storage of information and Drug Master Files
- Qualification procedures for equipment and materials
- Validation of processes and test methods
- Standard operating procedures (SOPs)
- Qualification and training of people performing work
- Audits

GMP and ISO standards

ISO quality standards, such as ISO 9001 and ISO 13485, set the criteria for a quality management system. Manufacturers who are ISO certified could self-certify for GMP compliance, if they can meet the additional requirements between the two sets of guidelines.

Companies that are implementing a quality management system often implement the Plan-Do-Check-Action (PDCA) cycle:

- **Plan:** set goals, prepare, take precautions, and document them
- **Do:** implement validation plans for new products; small-scale testing minimizes potential damage
- **Check:** analyze implementation or testing data; make changes in case of unexpected outcomes
- **Action:** check that the system works as intended; update documentation



TheraPure GMP products

Acheiving TheraPure GMP status **takes time and expertise**—there are **numerous rules for GMP-compliant products**.

Raw materials and source (starting) materials

TheraPure GMP products are manufactured to relevant ICH Q7 GMP guidelines and are produced and tested following ICH Q2 standards. These stringent quality requirements include characterization of the following materials:

- **Raw materials** are components or reagents used in manufacturing therapeutic products. They require qualification and safety and performance risk assessment.
- **Source (starting) materials** are a part of the active biological substance of the final product. For them, guidelines focus on purity profiles and early biological activity characterization.

Animal-origin materials

Should you use **raw materials** containing **human- or animal-origin components**?

- When possible, it is preferable to not use them.
- Most suppliers of materials have an animal policy statement. TheraPure GMP products are documented animal origin–free products, so the viral safety risk is improved.

Working with mRNA?
Understanding starting material quality is crucial.

Producing mRNA for therapeutics involves the use of enzymes, nucleotides, and *in vitro* transcription reaction accessories. Using TheraPure GMP materials that meet the quality standards appropriate for GMP manufacture as early as possible, can accelerate process development and avoid costly, time-wasting issues with product quality or documentation.

Supplier reliability

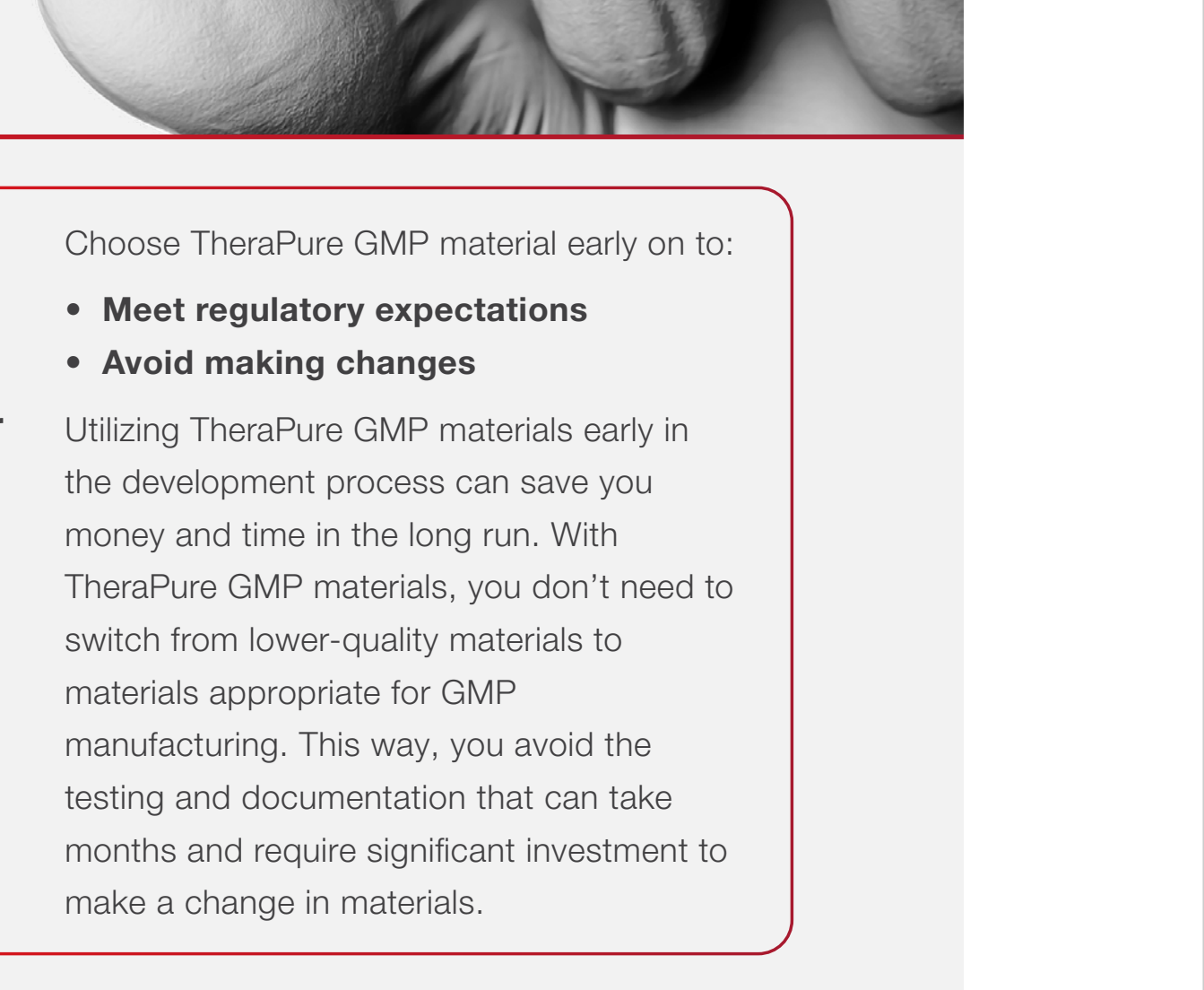
You need to ensure that your suppliers meet your needs. There are requirements for manufacturers to follow for the types of products they plan to manufacture for use in therapeutics.
The quality systems define the test methods and acceptance criteria for the products they manufacture.

TheraPure GMP products deliver a number of important quality attributes, including:

- **Key characterization tests** for identity, purity, content, biological activity, etc.
- **Traceability and documentation** with certificates of analysis, origin, compliance, safety data sheets, and regulatory support files
- **Drug Master Files,** for countries that support master file processes (e.g., US, Canada, Japan)
- **Robust supply chain** to ensure continuity

Downstream considerations: TheraPure GMP vs. GMP grade

GMP-grade materials may not meet all the quality requirements needed for GMP manufacture of a therapeutic. In contrast, TheraPure GMP products possess the quality attributes necessary for use in manufacture of a therapeutic. These materials are proven in the marketplace and have been used successfully in the manufacture of a number of mRNA-based therapeutics. While GMP-grade materials can go through validation and qualification to be used in GMP manufacturing of a therapeutic, the process can require significant additional time, resources, and costs. Because of their exceptional product quality attributes, TheraPure GMP materials are a great way to avoid expensive material changes and help ensure end-product compliance for GMP manufacturing.



Using TheraPure GMP products for development and manufacturing

Using **lower-quality materials** in the research phase can save you a little bit of money in the short term. However, switching to TheraPure GMP products early in the development phase can help **save you significant money and time** in the long run.

When to make the switch?

When you are evaluating **moving to GMP-compatible products**, consider:

- **Risk** for your specific project
- **Impact to your external partners** who may need to redevelop your processes to meet GMP guidelines
- **Type of process**, developed from a small-scale research process to a validated system (some are easier than others)

Choose the TheraPure GMP product portfolio as early as possible to enable seamless, efficient process development and manufacturing.

Sooner rather than later

Choose TheraPure GMP material early on to:

- **Meet regulatory expectations**
- **Avoid making changes**

Utilizing TheraPure GMP materials early in the development process can save you money and time in the long run. With TheraPure GMP materials, you don't need to switch from lower-quality materials to materials appropriate for GMP manufacturing. This way, you avoid the testing and documentation that can take months and require significant investment to make a change in materials.

Work with a trusted partner

If you're considering materials to utilize in process development and manufacturing of an mRNA therapeutic, focus on **step-by-step process implementation**.

Questions to consider are:

- What are the challenges for the raw materials?
- What kind of support will you need to use the materials in your process? Is that support readily available to you?
- Have these materials been used for a therapeutic before?
- How much risk are you willing to take on with your choice of materials?
- Are the raw materials sole-sourced?
- What is the country of origin?

At Thermo Fisher Scientific, we offer TheraPure GMP products to support development and manufacturing of therapeutics.

You **transform lives** by making better therapeutics more accessible.
The **safety and availability** of these treatments are crucial.

How do you **get it right the first time?**

As you move from preclinical stage to commercialization, **TheraPure GMP materials** and **proper documentation** are essential.

If you want to learn more about TheraPure GMP products and find out more about our product range and quality standards, go to **thermofisher.com/therapure**

* "TheraPure GMP" refers to the quality level of the raw, ancillary, or starting materials to be used for further manufacturing. TheraPure GMP products are manufactured in facilities with ISO 9001–certified quality management systems operating in accordance with relevant good manufacturing practice (GMP) principles as outlined in ICH Q7 or equivalent guidance documents or standards.

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