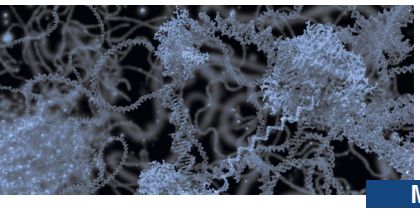
charles river



MICROBIAL SOLUTIONS

# Accelerating Development and Release of mRNA-based Therapeutics to Market Using Rapid Methods

## Key Points:

- mRNA-based therapies allow for ultra-short development times and unprecedented market responsivity
- mRNA developers are in a constant race between competitors to bring therapies to market faster and produce safe product quickly to meet market demand
- Traditional growth-based methods are still being employed by mRNA therapeutic developers
- Rapid methods are often overlooked yet provide distinct benefits to support being first to market and market responsiveness

## Overview

Biotech firms specializing in messenger RNA (mRNA)-based therapeutics are reshaping the face of medicine and industry development timelines. With the rising need for personalized medicine and responsivity to emerging pandemic diseases, such as COVID-19, this new development method allows for adaptability and efficiency, shortening the lead time for candidates. While much of the focus is on accelerating for approval, many companies overlook how to ensure speed to market safely after approval and during full production. Rapid microbial detection technology and rapid bacterial endotoxins tests can be effectively used for mRNA-based therapeutics, matching the speed of development with the speed of product quality testing.

mRNA therapies represent a new frontier in medicine, which has the potential to revolutionize the way we treat many previously untreatable conditions. They have gained recent awareness and global attention as the front-runners in potential vaccines for SARS-CoV-2, more commonly known as COVID-19. With dramatically shortened development timelines, cost-effective production techniques, and well-funded project plans, mRNA firms all have one critical driver to contend with: race to market.

## Situation

The mRNA Vaccines and Therapeutics Market was estimated at $3.43 billion in 2018 and is set to grow to $5.5 billion by 2024, with a CAGR of 9.77% in the next ten years.[1] In terms of drug discovery and development, mRNA therapeutics remains one of the least explored and populated fields in medicine. Using mRNA, a molecule used by all living organisms to make the proteins that are used to guide and build the entire organism's physiology, an emerging class of biologics is set to transform medicine in the next decade. Increasingly, there are many biotech organizations that are utilizing mRNA to create effective therapies for many diseases, including cancer, novel viruses such as influenza and COVID-19, as well as genetic diseases.

Currently, Charles River market research analysts determined there are approximately 92 mRNA therapeutic candidates in development, with 16 in phase I clinical trials and 10 in phase II. Of these candidates, the front-runners in the field are startup firms: Moderna Therapeutics (42 candidates), BioNTech (20), CureVAC (15), TranslateBio (11), and Arcturus Therapeutics (9).[2]

While many of the biotechs focusing on mRNA therapeutics are well-funded and staffed, the race to market is an ever-present burden for each firm's long-term success. Speed to market is a well-known driver in the pharma industry; however, in contrast to traditional small molecule development or monoclonal antibody development with costly and lengthy development cycles, mRNA therapies can be created, modified, customized, and scaled quickly and cost-effectively.

## Challenge

Many biotechs have also pioneered new ways to reduce their development time through the use of machine-learning algorithms to speed discovery; yet, they continue to use outdated microbiological methods for testing incoming raw materials, quality control, and product sterility. Continuing to use traditional, antiquated methods that require visual

analyses and produce subjective, analyst-dependent results lead to hours and potentially days of wasted time during each assay. These days can quickly add up to weeks, which can attribute unnecessary delays to market in an emerging industry that measures development cycles in mere months, rather than years, as does conventional pharma.

While the industry is racing to create effective therapies, such as pandemic response vaccines, through development, clinical trials, and approvals, is there a strategy to minimize the lead time and optimize release when in full production? We know the first vaccine that obtains regulatory approval will be in high demand, especially when addressing an immediate need relating to an epidemic or life-threatening illness. It might gain approval at a critical phase when even delaying release by a few days will mean putting populations at risk unnecessarily.

With all parenteral medicines requiring testing for the presence of endotoxins and viable microorganisms before being released to market, these quality control tests must comply with global regulatory requirements. Traditional methods of the Bacterial Endotoxins Test (BET) necessitate skilled analysts and manipulation of cumbersome reagents. The steps required to prepare standards and samples alone can often exceed the assay time, as the typical kinetic test can take up to one and a half hours, increasing the pressure for turnaround on potential samples and raw materials held in quarantine.

With traditional sterility testing, by testing the final product using membrane filtration or by direct-inoculation of pre-filled syringes (the typical vehicle for dispensing vaccines *en masse*), this method can take 14 days to obtain a visual, subjective result. Even prior to final product sterility testing, relying on traditional bioburden plate counts requires several unnecessary days of incubation to allow colony forming units (CFU) to be visible to the human eye. Often, as a product's manufacturing process matures, samples are typically clean, or functionally aseptic. Many samples ultimately result in zero counts at the end of several wasted days of incubation. Reducing test time means reducing overall response time.

## Solution

As a CGMP, FDA-approved, and licensed therapy manufacturer, the organization a company partners with for solutions should be held to those same standards. Charles River offers comprehensive QC testing solutions to vaccine manufacturers to help improve the safety and quality of the treatments delivered to their patients. Patients trust therapy to be administered safely; their lives depend on precision and sensitivity in all testing procedures.

Using Celsis® ATP-bioluminescence, vaccine producers can use the current traditional preparation method for final sterility, reduce the incubation period by 8 days (14 days down to 6), and have a confident presence/absence of contamination result through an automated detection instrument. Charles River has already partnered with other industry leaders to create optimized testing consumables, including sterility test canisters and TSB/FTM growth media pre-qualified for background ATP.

Additionally, Charles River has prepared a method equivalency report to fast-track validation. It's a ready-for-submission data package that demonstrates equivalency of Celsis to the traditional membrane filtration method, according to USP <71> and USP <1223>. It was created and used by another pharma industry leader and has already obtained first approvals by two regulatory agencies to help reduce the validation timeline by six months.

While final product sterility is a self-evident application for Celsis, it is not the only one. Celsis ATP bioluminescence instruments and reagents have industry-leading compatibility with other sample types and test methods. Sample matrix and composition does not have as great an impact on Celsis assays as they do with other competitors. It is compatible with filterable and non-filterable samples, high or low pH products, or products containing high debris or fluorescent particulates. This, in turn, allows Celsis technology to be applied to traditional assays upstream in the development chain. As such, other biotech and pharmaceutical companies utilize this to test column chromatography matrix samples, cell culture growth media,

and sterile water for injection. The net result of saving multiple days of incubation along many development and quality test assays has a cumulative effect for both speed to approval and speed to market.

The ability to detect all environmental Gram-negative bacterial endotoxins is an important safeguard for vaccine production. As the most sensitive and robust assay available, the Limulus amebocyte lysate (LAL) test has transformed from a qualitative gel-clot assay to a 15-minute quantitative assay available right on the production floor. Charles River's portfolio of Endosafe® FDA-licensed LAL products for rapid bacterial endotoxin testing was purposely built to deliver robust, consistent, and confident results. Using revolutionary cartridge technology, companies can obtain the advantages of improving sample management, decreasing testing time, eliminating bottlenecks, and accelerating production. Flexible and easy to use, the Endosafe® rapid bacterial endotoxins test platforms allow clients to perform real-time endotoxin testing, from in-process to final lot release testing, in conventional quality control settings or as a point-of use test to support the drug development process.

## Conclusion

Currently, the world's attention is focused on the biotech industry and the race to create an effective vaccine for COVID-19 from development to clinical trials and finally approvals. However, once in full production companies must ensure they have a plan to reduce the lead time and optimize release. The first vaccines to be approved will likely be in the highest demand we've seen for a therapy in recent history. This means any delay in release, even by just a day or two, could put populations at risk.

## References


1. mRNA Vaccines and Therapeutics Market Forecast 2019-2029 https://www.visiongain.com/report/mrna-vaccines-and-therapeutics-market-forecast-2019-2029/
2. Citeline (Source: Pharmaprojects March, 2020)
3. mRNA Will Revolutionise the Biopharmaceutical Industry, Dr Ingmar Hoerr https://www.ddw-online.com/therapeutics/p304798-mrna-will-revolutionise-the-biopharmaceutical-industry.html
4. Can mRNA disrupt the drug industry? https://cen.acs.org/business/start-ups/mRNA-disrupt-drug-industry/96/i35