Agilent Case Study: Fragment Analyzer system

Testing Integrity of In Vitro Transcribed RNA Vaccines

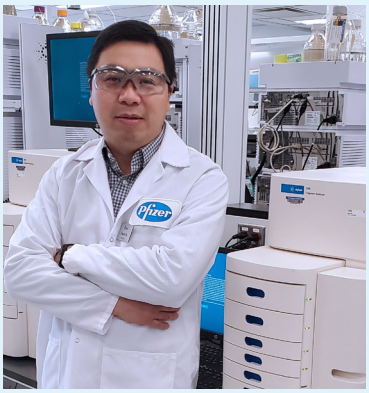
Focusing on RNA-Based Vaccines

In the early days of the COVID-19 pandemic, hundreds of scientists had to quickly pivot their ongoing work to address the urgent need for a vaccine that could help protect our communities. Experienced researchers in laboratory sciences, analytics, pharmaceuticals, and biotechnology could not anticipate how their backgrounds would prepare them for leading the way in testing one of the most important vaccines of our time. Ultimately, in vitro transcribed (IVT) RNA-based vaccines for COVID-19 would be on the forefront of changing the course of the global crisis.

Pfizer researchers, including Principal Scientists Gaofei He, Ph.D., and David Ripley, B.Sc., had the necessary experience and were asked to optimize and implement good manufacturing procedures (GMP) for the IVT RNA vaccine candidate molecule. Better known as the Pfizer-BioNTech COVID-19 vaccine, it was developed together with German-based biopharmaceutical company, BioNTech.

Implementing RNA Integrity Methods

From the beginning of this fast-moving project, Dr. He and Mr. Ripley recognized they would need instrumentation that could analyze RNA quality and generate reliable data. Ensuring sample quality control (QC) across development workflows is of paramount importance at Pfizer, but because of the urgent community need to move as quickly as possible, sample QC was more important than ever. "We knew RNA integrity had to be one of the cornerstones to our understanding of the molecule and to our control strategy. RNA integrity is a critical component of knowing that we are providing a safe and efficacious dose of the vaccine that we were developing for the patient," Mr. Ripley noted.



Gaofei He, Ph.D.

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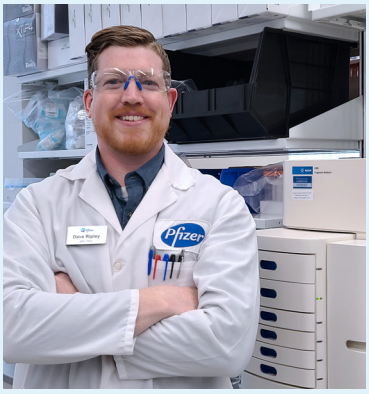

David Ripley, B.Sc.

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Although the team had some knowledge about the Agilent Fragment Analyzer system from their colleagues, the instrument's reliability, establishment in the market, and the maturity of the consumables contributed to their ultimate decision. Dr. He said, "The Fragment Analyzer rose really quickly as a frontrunner during our initial evaluations." Using automated parallel capillary electrophoresis, Agilent Fragment Analyzer systems deliver nucleic acid QC with efficient sample processing and accurate measurement. Fragment Analyzer systems help researchers analyze DNA and RNA fragments for a range of applications such as next-generation sequencing (NGS) libraries, restriction digest analysis, cell-free DNA (cfDNA), and IVT RNA.

During the Pfizer-BioNTech COVID-19 vaccine development, Pfizer researchers assessed the Fragment Analyzer systems using the quantitative Agilent HS RNA kit (15 nt) and RNA kit (15 nt). To track bioprocess development, the researchers used the system in their design of experiment (DOE) studies to analyze samples and provide feedback about RNA integrity throughout the IVT process. The Fragment Analyzer systems were also used to monitor vaccine stability throughout the entire production workflow.

Finally, the Fragment Analyzer system was validated so that it could be used as part of the QC process. The multiplexing capability of the system enabled Pfizer to quickly generate a lot of data, but they needed to demonstrate that the data from each of the 48 capillaries in the array was robust, reproducible, and reliable. To do this, the researchers ran the same sample through each of the capillaries. The outcome produced negligible bias and variability. These results passed the established acceptance criteria and enabled the method to become an essential part of the GMP release procedure.

Throughout the project, Dr. He and Mr. Ripley appreciated the productive, collaborative interactions fostered with their suppliers in the life science industry. They noted that even though supply chains and distribution channels were substantially disrupted through the pandemic, Agilent was able to deliver the important sample QC resources used in Pfizer's efforts for vaccine development and production. Instruments were quickly installed, qualified, and training was rapidly completed. This enabled the team to analyze critical samples within 24 hours of installation and qualification. Dr. He said, "Agilent was fantastic to support us by getting the consumables and critical kits we needed."

Promising Future of IVT RNA

There is surely much more to come from RNA-based technology. The diverse applications of IVT RNA innovations may include helping to prevent other infectious diseases or possibly treat rare diseases, cancer, and other pathologies. The potential future impact of the next generation of vaccines and therapeutics is enormous thanks in part to scientists like Dr. He and Mr. Ripley.

Learn more about Agilent solutions for sample quality control in vaccine development at **www.agilent.com/genomics/sample-qc**

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