Charles River and PathoQuest Announce Publication of a Head-to-Head Study Validating Proprietary Next Generation Sequencing Viral Safety Assay as a Reliable In Vitro Alternative to Animal Testing Methods

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NGS assay demonstrated a broader detection range than standard in vivo tests with comparable or higher analytical sensitivity

WILMINGTON, Mass. & PARIS--(BUSINESS WIRE)--Sep. 6, 2023-- Charles River Laboratories International, Inc. (NYSE: CRL) and PathoQuest SAS, a leader in the development and provision of next-generation sequencing (NGS) testing services for biopharmaceuticals, today announced the publication of the results of a seminal study in Vaccine. This unique study demonstrated that PathoQuest's proprietary, good manufacturing practice (GMP) grade NGS-based assay had a greater capability of detecting viral contaminants when compared to *in vivo* assays.

While the classical approach to testing for viral contaminants in biologics includes animal- and egg- based methods, the long turnaround time, limits in the ability of current methods to detect viruses, and increased demand for in vitro testing are major concerns for the pharmaceutical industry.

The results presented in this publication document that PathoQuest's proprietary NGS approach is an effective and more robust replacement to *in vivo* adventitious virus testing of cell substrates used in the production of biologics, including monoclonal antibodies, vaccines, cell and gene therapies.

What was the Study?
The objective of the study was to compare classical *in vivo* testing methods used to screen cell lines for adventitious viruses with a GMP-compliant viral transcriptome NGS assay. The study was conducted as a head-to-head comparison of standard *in vivo* testing and NGS-based testing of cell substrates. Charles River's leading Biologics experts prepared the test materials and ran the *in vivo* assays, while PathoQuest's team tested the material using their proprietary NGS-based assay.

Cells were infected with a wide variety of viruses which are reflective of the diversity and various patterns of virus-cell interactions in a real world setting for biologics to determine the range of detection. The infected cells were increasingly mixed with uninfected cells to assess the analytical sensitivity and analyzed across several conventional *in vivo* tests and with the NGS-based transcriptomic assay. Non-infected cell lines were used as controls for the study. The PathoQuest transcriptomic assay demonstrated a higher capability to detect cell infection including infection by viruses not detectable with standard *in vivo* tests.

What are the Implications of the Study?
The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) has released a draft version of ICH Q5A(R2) which provides proposed updated guidelines on the testing and evaluation of the viral safety of biotechnology products derived from cell lines of human or animal origin.

This update is a result of advances in scientific knowledge and biotechnologies since the release of the original ICH Q5A(R1) guideline in 1999. Examples of advances include the development of new types of products like genetically engineered viral vectors, and the availability of new and more robust viral safety technologies, like NGS.

Another important aspect of the proposed revised guidelines is their support for the use of new testing methodologies that align with the 3Rs (the Replacement, Reduction and Refinement of animals used in research). The results of the present study support the use of the evaluated NGS-based transcriptomic assay as a superior alternative to current *in vivo* testing methods and aligns with the proposed ICH Q5A(R2) guidelines which are anticipated to be finalized and implemented by the end of 2023. The data are suitable to justify *in vivo* assay replacement by using the "Prior Knowledge" principles also outlined in the ICH Q5A(R2) draft.

This project was funded by Charles River and PathoQuest, understanding the importance of the results for future viral safety testing strategies.

Approved Quotes

- "The use of NGS addresses the limitations of current testing approaches for viral contaminants and enables clients to follow the 3Rs principles of replacement, reduction, and refinement of animal-use methods. Additionally, unlike current general virus screening testing methods, the agnostic transcriptomic NGS approach combines both the detection and identification of known and unknown viruses and has the capacity to replace additional virus testing methods, like the cell based *in vitro* assays or even single PCR assays." –Horst Ruppach, PhD, Executive Director Scientific and Portfolio for Global Biologics at Charles River
- "Our study demonstrates that PathoQuest's unique NGS assay significantly increases the capability of detecting viral contaminations in cell substrates like cell banks, the starting material for biologics production, and in bioreactors during biologics production. The test has been validated to GMP standards and provides the pharmaceutical industry a faster, more efficient, and reliable testing option compared to animal-based testing." – Professor Marc Eloit, DVM, PhD, Head of the Pathogen Discovery Laboratory at the Institut Pasteur and Founder of PathoQuest

About Charles River
Charles River provides essential products and services to help pharmaceutical and biotechnology companies, government agencies and leading academic institutions around the globe accelerate their research and drug development efforts. Our dedicated employees are focused on providing

clients with exactly what they need to improve and expedite the discovery, early-stage development and safe manufacture of new therapies for the patients who need them. To learn more about our unique portfolio and breadth of services, visit www.criver.com.

About PathoQuest
With over 20 peer reviewed publications on NGS applications, PathoQuest is a leading expert in the application of Good Manufacturing Practices (GMP)-compliant Next Generation Sequencing (NGS)-based biosafety testing. PathoQuest offers biopharmaceutical companies a game-changing genomic approach to ensuring the safety of biologics such as cell and gene therapy products, vaccines, and recombinant proteins, ultimately enabling a reduction in the time to market for these innovative treatments. PathoQuest's technology combines NGS platforms with proprietary sample preparation and data analysis processes to bring novel solutions to the industry. PathoQuest, headquartered in Paris, France, with a US based site in Wayne (PA) has worked with over 100 of the leading biopharmaceutical companies globally. To learn more about our service offerings and how we can help you to transition to animal free testing, visit pathoquest.com.

To learn more about PathoQuest's GMP validated transcriptomic assay for adventitious virus detection and testing strategies to enable the transition to animal free testing, visit www.pathoquest.com/adventitious-virus-testing

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