Application note

Avoiding contamination in your SARS-CoV-2 diagnostic testing

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Prior to 2020, public health officials feared that serious disease outbreaks such as Ebola, severe acute respiratory syndrome coronavirus (SARS-CoV), bird flu (H5N1 influenza) and Middle East respiratory syndrome coronavirus (MERS-CoV) would evolve into a genuine pandemic. Most of these outbreaks had devastatingly high mortality rates: Ebola 40.4%[1], SARS 9.6%[2], MERS 35%[2] and bird flu 60%[3]. However, most had lower transmission rates and fewer deaths compared either to the 1918-1919 influenza pandemic or the current SARS-CoV-2 pandemic. The emergence of this far more infectious strain, SARS-CoV-2, has demonstrated the devastating potential of a modern viral pandemic.

While academic models predicted the 2020 pandemic, this unique event has dominated the global stage and affected all our lives, sometimes tragically. SARS-CoV-2 has also strained the resources of diagnostic kit developers and clinical testing laboratories as they scramble to meet unprecedented testing needs, and it is well documented that accelerated development of any test can result in missteps that may have serious consequences to the efficacy of a test and the reputation of a supplier or laboratory.

For PCR-based testing, one common and particularly painful pitfall is a contamination event. The negative effects on PCR results such as high background, low sensitivity and low specificity are particularly acute in regulated fields such as molecular diagnostic testing and therapeutics. As a result, one of the linchpins of the development and routine operation of any diagnostic PCR, qPCR or RT-qPCR assay is the precise design and incorporation of controls.

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With over 35 years' experience manufacturing consistently high-quality oligos, LGC, Biosearch Technologies protects the integrity of your PCR workflows with a rigorous screening policy to mitigate risk of cross contamination.

Biosearch Technologies' extensive PCR contamination risk mitigation plan includes:

Mitigation step	What it does	Why it is important
Longmer screening	100% screening of all oligos >45 bases produced at all manufacturing sites.	Our strict no template policy prevents false positive results by ensuring that template oligos are not part of our manufacturing environment.
Routine production floor testing of high-volume assays	Swab and test equipment, high-touch surfaces and aerosols in all manufacturing facilities to detect problematic concentration of high-volume oligos.	Maintains specificity and sensitivity of diagnostic assays by ensuring the manufacturing environment does not contain contaminants which will interfere with your desired test.
Quality control testing of all SARS-CoV-2 assay kits prior to release	100% screening for no template control (NTC) amplification of all lots .	Maintain high-quality standards by detecting contamination before test kits are shipped.
Contamination testing	R&D scientists perform tests to understand the magnitude of manufacturing contamination including production choices such as the amount of oligo produced, purification and formulation.	Data enables informed decisions about contamination risks, where to manufacture the request and offers a baseline to determine the efficacy of decontamination efforts.
Partnership with customer to identify potential contamination sources outside Biosearch Technologies' manufacturing	Since most contamination occurs outside of oligo manufacturing, we closely work with you to identify all other common contamination sources that may exist in your laboratory; for example, extraction kit buffers, master mixes and others. In these cases, contamination can be unintentionally introduced through your own workflow.	Avoid potential contamination sources that are commonly introduced from reagents that may be present in your laboratory.
Continuous process improvement to avoid all possible contamination	Manufacturing risks are continuously evolving. Biosearch Technologies has a dedicated team to engineer meticulous controls to safeguard your oligos and accessory reagents from contamination - following proven quality assurance policies.	Ensures that the manufacturing process provides oligos and accessory reagents that are of the highest quality and free from contamination throughout your test development process.
Exclude high-risk sequences from production	Bioinformatic, strategy and operations teams regularly update a list of high-volume or strategic targets that could introduce contamination; for example, a qualifying SARS-CoV-2 recombinase polymerase amplification (RPA) probe.	Ensures the reliability of your future assays by avoiding the manufacture of oligos with high-risk of cross-contamination.

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For more detailed technical information regarding PCR contamination risk mitigation, please refer to the white paper: Ensuring qPCR data reliability – controlling for contamination.

Reference

1. Ebola: Two Years and 11,300 Deaths Later: Global Health Lessons From an Epidemic; Adelaida Sarukhan; Barcelona Institute for Public Health; 17 March 2016; https://www.isglobal.org/en/ebola. Accessed 28 Jan 2021.

2. Comparison of the COVID-2019 (SARS-CoV-2) pathogenesis with SARS-CoV and MERS-CoV infections; Fani, M., Teimoori, A., and Ghafari, S. (2020) Future Virol. 2020 May doi:10.2217/fvl-2020-0050; Epub 20 May 2020; accessed 28 Jan 2021.

3. FAQs: H5N1 influenza; World Health Organization website; https://www.who.int/influenza/human_animal_interface/avian_influenza/h5n1_research/faqs/en/#:~:text=Human%20cases%20of%20H5N1%20avian,mortality%20rate%20is%20about%2060%25. Accessed 28 Jan 2021.

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