

# Urgency of rapid *Legionella* detection post-COVID-19 lockdowns: an interview with Elizabeth Minogue

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## Please introduce BioProbe Diagnostics

BioProbe Diagnostics, a spinout company from the National University of Ireland, Galway, develops innovative PCR tests for the detection of microbial pathogens associated with water contamination in environmental and industrial processes. Our strong team of scientists, innovators and business experts develops and markets these PCR test kits worldwide. Using patented technologies, our goal is to transform the global marketplace with rapid, accurate, cost-effective and user-friendly PCR test kits. Our first product, Bio Lp-1, is the world's first open platform rapid nucleic acid diagnostic kit for simultaneously detecting and identifying *Legionella* genus, *Legionella pneumophila* and *Legionella pneumophila* serogroup 1 from water in a single test. It received the prestigious EU Fast Track to Innovation Award in 2020 and will be launched in early 2022 in collaboration with renowned international partners.

## Please describe BioProbe Diagnostics research background & current research interests

BioProbe Diagnostics has a strong team of scientists, innovators and business experts. This team has more than 20 years of research experience in the development of rapid nucleic acid-based diagnostic solutions for application in the clinical and environmental sectors.

Our current research interests focus on the design, optimization and validation of rapid nucleic acid diagnostic technologies for the detection and identification of microorganisms associated with contamination of water.

## What is Legionnaires' disease & why is it so important that we monitor the spread of the disease?

Legionnaires' disease is a severe and potentially fatal pneumonia caused by *Legionella* spp. usually found in contaminated natural and artificial water systems. Some cases can be mild to moderate; however, others result in respiratory and multiorgan failure. The associated mortality rate of Legionnaires' disease in the general population is 10%, but this rises to 25% when infection is associated with healthcare-associated infections (HCAIs). *Legionella* spreads mainly through contaminated aerosols, usually restricted to water systems. Infections acquired in buildings and healthcare institutions affect approximately 2 million people each year, resulting in 90,000 deaths and an estimated \$4.5–5.7 billion per year in additional costs for patient care. The most effective way to limit the spread of *Legionella* bacteria in water systems and to limit the subsequent spread of Legionnaires' disease is to implement a safe water management system with appropriate testing and preventative contamination measures in place. The water we use travels through vast, complex water systems before reaching our homes, schools, hospitals, offices, buildings, heating systems, air conditioning units, swimming pools, spas and fountains in our parks, among others. Wherever *Legionella* is present in water, there is risk for human exposure. The reported prevalence of Legionnaires' disease is estimated at 180–360 cases per million inhabitants, with the rate of incidence increasing in many parts of the world. For example, the US incidence rate has quadrupled in recent years. This increase in cases has largely arisen due to increased awareness of the disease, an emerging older population who are more susceptible to disease, deteriorating infrastructure, increased travel and climate change.

Recently, COVID-19-related lockdowns around the world have resulted in empty buildings and associated reduced water usage. This has provided ideal breeding grounds for *Legionella* bacteria, resulting in a worrying rise in Legionnaires' disease cases.

## What traditional testing methods are used to detect Legionnaires' disease?

The traditional method for *Legionella* detection is based on cell culture technology. It will detect most *Legionella* bacteria but not those that are stressed and viable but nonculturable. Another significant downside is that this test will take up to 14 days for completion. Additionally, multiple culture plates may be required to specifically identify species most commonly associated with human disease.

Other *Legionella* detection systems are based on biochemical and immune detection methods, but these tests do not always give a full *Legionella* profile and may only detect a select number of species. Furthermore, they lack sensitivity and are not truly quantitative.

In more recent years, there has been a growing acceptance within the water testing industry that rapid tests provide a better solution for this area.

## Please explain how your new test, Bio Lp-1, works & why it improves on traditional testing methods.

The Bio Lp-1 test kit is designed for use on water samples. The DNA purification component of the kit allows for the extraction and purification of DNA from water samples. The DNA is then used as a template in a real-time PCR assay. The Bio Lp-1 PCR assay is designed to target specific and unique DNA sequences within the *Legionella* genome. The PCR products from four different reactions can be detected by specific DNA probes labeled with four different fluorophores. This allows the simultaneous detection of, and differentiation between, all *Legionella* species associated with infection, all the *L. pneumophila* serogroups (1–16) and specifically identifies *L. pneumophila* sg-1, responsible for ~95% of human infections. An internal amplification control is also included in the master mix as an indicator that the PCR is functioning correctly. This real-time PCR assay can be performed qualitatively or quantitatively. Designed to work on the leading real-time PCR platforms, Bio Lp-1 gives a complete and accurate *Legionella* profile in a single water sample. In less than 5 h, water quality and safety can be assured. Simple and convenient to use, delivered in a freeze-dried format, the test contains all necessary components to process a water sample directly. Traditional testing for *Legionella* has been via culture methods, where a time lag of 14 days often is needed before results are able to determine whether *Legionella* is present in water samples.

## What inspired you to develop this new method?

Current European estimates attribute in excess of 16 million additional days spent in hospital by patients per year due to HCAs. Within these settings, water, water distribution and premise plumbing systems have been identified as a significant source of many HCAs and pose a significant threat to human health.

In the last number of years, outbreaks of Legionnaires' disease associated with contamination of water are rising. Appropriate testing, maintenance and contamination preventions methods are all required to limit the spread of *Legionella* bacteria in water and reduce the number of Legionnaires' disease outbreaks. Current *Legionella* testing methodologies including bacterial culture, biochemical and immune detection methods can be limited in their ability to provide a complete, quantitative *Legionella* profile in a timely manner. Effective water management systems, including *Legionella* water testing, must be capable of detecting all *Legionella* species. Furthermore, as between 80 and 95% of infections are caused by *L. pneumophila* serogroup 1, an effective test should also specifically identify this microorganism.

Bio Lp-1 detects and identifies *Legionella* species, *L. pneumophila* sg1-16 and *L. pneumophila* sg1 directly from water samples without a requirement to culture the microorganisms on traditional microbiological plates. By utilizing this approach, it is possible to reduce testing time from up to 14 days to <2.5 h.

## Why is Bio Lp-1 beneficial to the public?

Timely identification and reporting of *Legionella* is critical in reducing infection rates, especially where large groups of people are present – hospitals, schools, hotels and cruise liners, among others and particularly in hospital settings, where vulnerable patients, such as older people or those with pre-existing health conditions, are most susceptible. With the certainty of a complete, accurate and timely *Legionella* profile, public health officials can act quickly to identify and stop potential clusters and outbreaks by drawing links between new and previously reported cases. Additionally, large testing laboratories providing water testing services to customers will be in a position to provide the results of their *Legionella* testing more promptly and with confidence. Bio Lp-1 has been designed to work on the leading real-time PCR platforms available on the market (an open platform test), which means testing laboratories will not need to invest in costly specialized equipment to use this test.

## Do you have any tips for best practice for researchers looking to use this method?

The Bio Lp-1 test is designed to be user-friendly and easy to perform. DNA isolation and purification reagents are provided as part of the Bio Lp-1 kit. DNA is extracted from a membrane after water filtration.

The multiplex real-time PCR assay component of Bio Lp-1 is provided in 8 × 12-well strips. The PCR reagents are freeze-dried. The DNA sample, controls or DNA standards are the only components to be added to the real-time PCR reaction. The freeze-dried mix is rehydrated within seconds with aqueous solutions, which makes the reaction setup very simple.

### What are you hoping to develop next in this area?

Our team of scientists is currently working on the development and commercialization of additional culture-independent, rapid diagnostic technologies for the specific detection of a number of other pathogens associated with water contamination. Our aim is to produce a suite of rapid tests for the detection and identification of common contaminants in environmental and industrial processes.

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### Disclosure

The opinions expressed in this interview are those of Elizabeth Minogue and do not necessarily reflect the views of Future Science Ltd.

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