# Abstract

Testing for infectious diseases underpins diagnosis, treatment, surveillance, and epidemiology of disease as well as maintaining safe transplantation of blood and tissue. Over the past decades, infectious disease testing has changed from manual, qualitative functional biological methodologies such as haemagglutination inhibition and complement fixation, to highly automated immunoassay and molecular platforms. In developed countries, much of this testing has moved from specialised microbiology laboratories to high throughput "core" laboratories testing a range of clinical chemistry and other medical pathology analytes on the same test platforms. As these test systems are generally managed and controlled by clinical chemists, it is not surprising that methods used to standardise and control testing usually employed in clinical chemistry are being introduced for infectious disease testing. However, there are significant differences between inert, homogeneous clinical chemistry analytes, such as glucose, potassium and urea, and the highly variable and heterogeneous biological testing used for infectious diseases. These differences in testing have been identified as the reason why standardisation and control processes have been largely unsuccessful when applied to infectious disease testing.

This thesis details my original and significant body of work identifying the deficiencies of traditional approaches to standardisation and control when applied to infectious disease testing. Papers presented in the thesis demonstrate the lack of standardisation of rubella IgG tests across two decades and investigates the clinical impact caused by poor standardisation. A further publication demonstrates that the traditional standardisation approach is appropriate for molecular testing using the quantification of CMV DNA as the example. My work in developing a novel approach to understanding and interpreting external run control results has had significant impact, being the only scientifically validated method for controlling infectious disease testing and is now licensed of use by two large quality control manufacturers. One paper presented demonstrates the QConnect™ concept and associated software EDCNet™. Additional papers demonstrate that QConnect™ is more fit-for-purpose than traditional methods such as Westgard rules when applied to infectious disease serology. Finally, a significant paper investigated whether variation detected by quality control had an impact on the clinical sensitivity and specificity of a test system.

The concepts presented in this thesis have been developed over time in a systematic manner, building upon each study to develop an understanding of the standardisation of infectious disease testing. This concept remains relevant and topical today with the emergence of SARS-CoV-2 infections and the release of an international standard for anti-SARS-CoV-2. The thesis highlights the differences between clinical chemistry and infectious disease analytes; reviews the utility of traditional methods for standardisation and control of medical testing when applied to infectious disease testing and describes and validates novel, alternative approaches. The clinical impact of the proposed alternatives was investigated. Together, these peer-reviewed publications form a significant and on-going impact on knowledge in the areas of standardisation and controls of infectious disease testing and continue to inform scientific discussion and influence national and international policy in this area.