Publishable JRP Summary Report for JRP HLT08 (INFECT- MET) Metrology for monitoring infectious diseases, antimicrobial resistance, and harmful micro-organisms

Background - Infectious diseases account for over 20% of human deaths globally and 25% of all morbidity. Respiratory tract infections (RTI) including pneumonia, influenza and tuberculosis account for almost 50% of all pathogen associated deaths. Accurate and rapid diagnosis alongside methods for monitoring transmission and spread in the community and resistance to therapeutic agents are vital for public health protection. Molecular approaches, such as qPCR and sequence analysis, offer the potential to improve management of infectious diseases through increased speed, accuracy, sensitivity and information when compared to conventional microbiological methods. Consequently, the infectious disease testing market is one of the most rapidly growing segments of the in vitro diagnostics industry and is expected to reach €38 billion by 2013 with advances in molecular diagnostic technologies the main driving force behind the expected growth. However, measurement support for molecular approaches is lacking, with issues concerning quality, comparability and traceability of measurements widely highlighted.

Pathogens may be present in clinical samples at very low levels making accurate detection and measurement challenging. In many instances tests are being used in non-commercial 'home-brew' formats of variable and undefined quality, and even commercially available tests cannot always be directly compared. Clinical reference materials which are traceable to SI or equivalent are currently lacking. Full confidence in molecular measurements can only be achieved if the appropriate metrology framework, standards and higher order reference measurement procedures are developed. Without this support healthcare providers and the biotechnology/diagnostics industry will not be able to demonstrate the reliability of their assays in a traceable and comparable manner. This is critical for implementation of assays deployed in a wide range of healthcare settings.

Scientific Objectives - This project aims to develop novel measurement procedures and validation frameworks to support current and emerging molecular approaches for efficient, harmonised and rapid diagnosis, surveillance and monitoring of infectious diseases, with a particular focus on RTIs. The project's ultimate aim is to establish routes for improving the accuracy, robustness, comparability and traceability of measurements within the metrology and diagnostics/epidemiological communities across Europe linked in to international standardisation initiatives in the area through CDC, JCTLM and WHO.

INFECT-MET addresses the following scientific and technical objectives:

- To develop quantitative, validated and highly accurate methodologies for the measurement of infectious agents, such as viruses and bacteria
- To develop methodologies for accurately quantifying the performance of commercially available diagnostic assays, 'in-house' clinical assays and novel emerging approaches
- To quantitatively and comparatively evaluate new and emerging molecular approaches for the surveillance and monitoring of infectious disease load and detection of antimicrobial resistance mutations
- To quantitatively and comparatively evaluate new and emerging diagnostic technologies for the rapid detection of infectious agents

EMRP European Metrology Research Programme Programme of EURAMET

The EMRP is jointly funded by the EMRP participating countries within EURAMET and the European Union

Overview - The work of JRP HLT08 INFECT-MET is broken down into the following areas:

- Development and evaluation of higher order methods based on enumeration (for example, digital PCR and single molecule counting in flow) for accurate measurement of infectious agents with known uncertainties
- Investigation of the measurement challenges associated with emerging methodologies such as next generation sequencing and high throughput PCR for surveillance, epidemiology and antibiotic resistance screening
- Investigation of the measurement challenges associated with emerging methodologies for rapid, near-patient testing, including DNA/microfluidic surface interactions and isothermal nucleic acid amplification evaluations
- Development of a reference measurement framework using higher order measurement approaches in collaboration with end-user communities to improve calibration and quality assurance of current clinical PCR approaches

INFECT-MET will investigate the development of higher order reference measurement methods and procedures. It will consider the process as a whole incorporating sample extraction from different matrices (e.g. blood and saliva) and highly accurate and sensitive methods for enumerating single molecules and infectious particles and define the measurement capability of current and emerging molecular approaches. Identification of major sources of uncertainty, data interpretation and integration will assure an integral approach of the work. A measurement framework will be developed in a multidisciplinary team in close co-operation with key stakeholders including healthcare providers, public health laboratories, academics, standards bodies, biotechnology/diagnostics industries.

Impact – The methodology proposed in this project will provide proof of concept and create a reference measurement framework to enable National Metrology Institutes (NMIs) to perform traceable and accurate measurement of infectious agents. The stakeholders and collaborators will work with the NMIs to support and validate the reference measurement procedures developed during the lifetime of the project and demonstrate utility through clinical evaluation for assessing/validating end-user assays. Outputs from this project will be used to directly inform standards/guidance/development by appropriate bodies with links to the consortium (e.g. ISO TC212, IFCC Molecular Standards WG, JCTLM, and CCQM). A stakeholder workshop is planned to disseminate outputs to the target stakeholder community and a series of publications and conference presentations will disseminate the findings to the wider stakeholder community. Cooperation of funded partners and stakeholders from different countries will improve the efficiency of use of available resources and will increase the metrology capacity of Member states.

JRP start date and duration:	1 June 2012, 36 months
JRP-Coordinator: Dr Carole Foy, LGC, UK Tel: +44 (0) 208 943 7000 E-mail:carole.foy@lgcgroup.com JRP website address:	
JRP-Partners: JRP-Partner 1 LGC, UK JRP-Partner 2 BAM, Germany JRP-Partner 3 JRC, EU JRP-Partner 4 NIB, Slovenia JRP-Partner 5 PTB, Germany JRP-Partner 6 TUBITAK, Turkey	
REG-Researcher (associated Home Organisation):	Isabella Honeyborne, UK UCL, UK

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