

## 1. PUBLISHABLE SUMMARY

### **Rapid, robust & scaleable**

platform technology for fully automated reference laboratory grade **Polymerase Chain Reaction (PCR)** based diagnostics **regardless of Global setting...**



### **SUMMARY**

The RANGER consortium has brought together a breadth of clinical, scientific, engineering and regulatory expertise to successfully deliver the Enigma Mini-Lab (Enigma@ML) system; a revolutionary system providing accurate diagnosis of human seasonal influenza. Capable of providing a laboratory standard result from raw sample in less than 60 minutes, the Enigma@ML will enable clinicians, healthcare professionals and outbreak specialists to make timely, informed decisions critical to effective patient management.

Production-ready prototype Enigma@ML instruments, cartridges and test assays have been developed during the RANGER project and extensively tested in preparation for future validation as human *in-vitro* diagnostic test for influenza diagnosis. Without the need for specialist operator knowledge or ancillary equipment, the Enigma@ML provides rapid diagnosis of influenza in the point-of-care environment, enabling faster and better informed medical intervention to reduce suffering and save lives. The system will allow a more co-ordinated surveillance effort, enabling rapid deployment of resources to control disease spread and assist in cost-effective patient management.

### **PROBLEM BEING ADDRESSED**

Seasonal, or epidemic influenza, has a global incidence of 10-20%, is responsible for between 3 and 5 million cases of severe illness every year and causes 500,000 deaths annually. Total direct and indirect costs of a severe epidemic are estimated at over \$12 billion in the US alone. A global pandemic has been projected to infect 25-35% of the global population and conservative estimates from the World Health Organisation (WHO) have placed the likely death toll at 2-7.4 million people and the cost at over \$800 billion. As a consequence, Seasonal Influenza is one of today's biggest threats to the world's socio-economic health.

Although vaccination is effective in minimizing the health impacts of Seasonal Influenza in 'at-risk groups' such as the elderly, current global vaccination coverage is less than 5% and viral mutation requires constant review of vaccine efficacy. Consequently, the most effective means of controlling the spread of influenza is early diagnosis followed by containment and where appropriate, antiviral therapy. However, currently available diagnostics technologies are not suitable for widespread use in developed & developing countries. Rapid antigen-based tests are insensitive, whilst existing PCR based techniques and microarrays are slow, expensive and require specific laboratory equipment and expertise. Consequently there is an immediate need for a rapid, robust, sensitive and cost effective point-of-care diagnostic for the identification of

influenza strains and subtypes which requires minimal expertise to operate & no specialist laboratory equipment.

## **OBJECTIVES**

The RANGER consortium brings together expertise in a diverse range of fields, including: influenza diagnosis and surveillance; sample preparation; molecular diagnostics; in vitro diagnostic system development; software, engineering, materials science, freeze drying and surveillance monitoring.

The RANGER consortium aimed to deliver a system capable of diagnosing influenza accurately and quickly, enabling healthcare professionals and outbreak specialists to make timely and informed decisions. The Enigma@ML system is the culmination of 3 years of focussed development effort to deliver a fully automated platform capable of providing a laboratory standard result from a raw sample. It will be validated for use in both developed and developing territories, with evaluations led by world renowned clinical investigators in Thailand and the UK.

### **Expected results:**

The RANGER programme was intended to deliver pre-production prototype instruments, cartridges and an assay suitable for eventual commercialisation and qualification as a human *in-vitro* diagnostic tool for influenza diagnosis and surveillance.

### **Potential applications:**

Rapid diagnosis of influenza in the point-of-care environment, enabling faster and better informed medical care to reduce suffering and save lives.

Co-ordinated surveillance of influenza incidents and outbreaks, enabling rapid deployment of resources to control disease spread and treat patients.

## **PROGRESS & ACHIEVEMENTS**

During the third reporting period, work has been focussed on the finalization of the ML instrument, Seasonal Influenza test assay cartridge and integration of the entire automated system. Specifically, the following development activities have taken place:

- Final integration of the Instrument, software and RANGER assay consumable cartridge
- Characterisation and validation of the integrated system
- Proof-of-principal clinical testing activities in the UK
- Finalisation of the instrument and cartridge supply-chains and GMP manufacturing capability for the final RANGER product

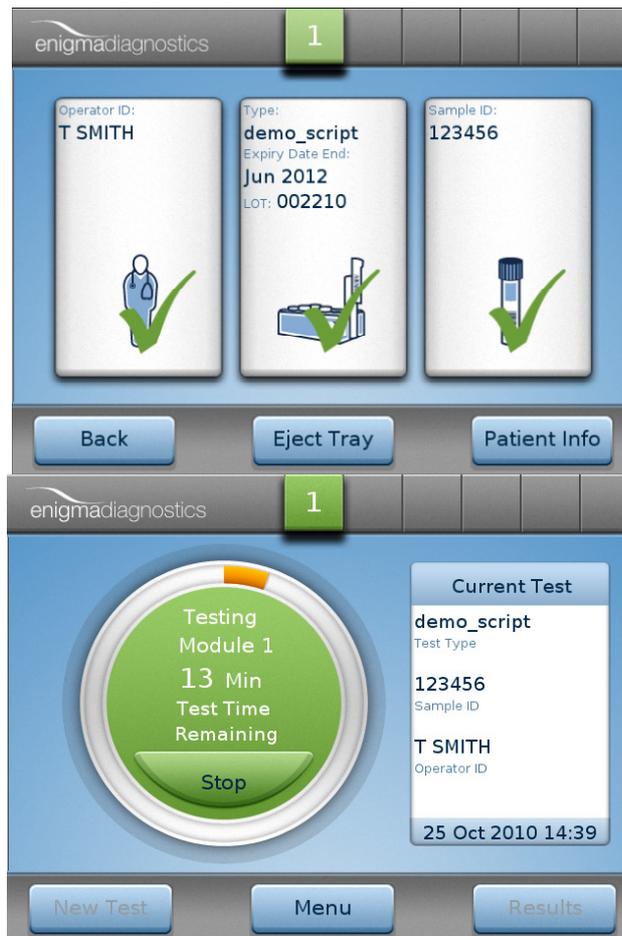
During the third and final RANGER reporting period, the consortium has focussed on the primarily on finalisation of the prototype Enigma@ML instrument and the accompanying

Seasonal influenza test assay for subsequent process validation and clinical sample testing. By expending significant effort early in the programme, the user requirements were rapidly established and continually reviewed by engaging with global experts in the field of influenza research, surveillance and disease treatment. The outputs of this consultation enabled the system development teams to generate a comprehensive system specification (instrument, software, cartridge, assay). All the system specifications have been met during the development programme, successfully delivering a production-ready system suitable for commercialization and clinical validation.

Reporting period three has seen successful delivery of the fully-integrated 'A3.1' prototype instrument with its final operating software and graphical user interfaces embedded. A comprehensive package of rigorous testing, refinement and process validation has taken place to ensure the system is robust, reliable and ultimately fit-for-purpose in point-of-care scenarios. The RANGER consumable cartridge design specifications have also been fully realised as a production-ready, ambient storage consumable containing all plastic components, sample extraction reagents and lyophilised RT-PCR required for fully-automated diagnostic testing. Completion of these major integration activities has enabled the consortium to successfully report completion of RANGER Work Package 7 (WP7) - System Integration activities.



*Three-module Enigma@ML production-ready prototype instrument and consumable*



*Enigma@ML interactive touch-screen Graphical User Interface (GUI)*

Having demonstrated reliability of the integrated Enigma@ML system and successfully established the full-automated test routine for influenza diagnostic testing, Work Package 8 (WP8) - Validation was undertaken to establish the proof-of-principal clinical performance of the system. WP8 generated significant experience in the diagnostic performance of the system and its suitability for volume manufacture and future commercialisation as a next-generation molecular diagnostic platform. Completion of the RANGER deliverables in period 3 involved updating progress against WP9 - Dissemination and Exploitation and WP10 - Project Management activities. These have included profiling the Enigma@ML and RANGER project at a number of global clinical and lifescience expos such as Medica, AACC and ArabHealth, press releases and commercialisation activities to support future product launch.

## **EXPECTED IMPACT OF THE PROJECT**

The Enigma@ML system will make a significant contribution to the protection of public health by enabling very rapid diagnosis of influenza, guiding both international control measures as well as individual patient management. It will help to reduce the overall societal disruption, economic impact and public health consequences of influenza, whilst aiding healthcare professionals to reduce the morbidity and mortality associated with seasonal influenza cases, particularly in children and elderly patients. Face-to-face meetings with both the World Health Organisation

(WHO, Geneva) and Centres for Disease Prevention and Control (CDC, USA) have indicated significant unmet need for rapid, accurate diagnostics and positive support for project RANGER.

The RANGER project also supports the assertion that Small-Medium Enterprises (SMEs), academia and government agencies can successfully combine to deliver cost-effective, innovative and commercially viable diagnostic solutions to the European healthcare industry through focussed, collaborative research programmes such as RANGER.

## **WEBSITE**

The project has a public website which can be found at: [www.rangerfp7.com](http://www.rangerfp7.com)