Dr Joanne Macdonald, Chief Scientific Officer at Australian diagnostic start-up BioCifer, reviews the novel amplification process for a new rapid diagnostic technology that can produce results from raw samples within 20-40 minutes, without centrifuge. More information on this collaborative DMTC project involving BioCifer, University of Sunshine Coast (USC), UQ and CSIRO can be found on Page 26.

MEDICAL COUNTERMEASURES
Overview

The MCM Program has continued to deliver successful industry-research collaborations that enhance Australia's defence and national security capabilities. Over the past five years, the program has progressed more than 20 collaborative vaccine, therapeutic and diagnostic projects against a range of Chemical, Biological and Radiological (CBR) and infectious disease threats.

Currently, the program has 10 active projects, comprising two therapeutics, two vaccine candidates, four rapid diagnostics, and two manufacturing scale-up projects. This diversity in our project portfolio enables the program to contribute to addressing military and public health capability gaps as well as developing Australia's sovereign resilience.

The MCM program has benefited from strong engagement with its Stakeholder Group, a senior whole-of-government advisory group with representatives from the Department of Defence; Department of Health; Department of Industry, Science, Energy and Resources; the Department of Foreign Affairs and Trade and most recently the Department of Home Affairs. In light of the COVID-19 pandemic, this Stakeholder Group has had an even more significant role in directing and prioritising our collective response to the pandemic.

Furthermore, consistent with the aims of the MCM Program, Defence provided funding and support for DMTC to sponsor a clinical trial to determine the effectiveness of chloroquine as a pre-exposure prevention measure against COVID-19, in collaboration with ADF-MIDI.

The MCM program is an agile and adaptive mechanism which can pivot to provide direct investment into priority areas. It has also proven itself as a credible model for product development, backed by a strong national and international network. This year, two of DMTC's rapid diagnostic projects were able to quickly respond to SARS-CoV-2, one involved in detecting the virus and the other modifying a universal buffer to inactivate the virus. Furthermore, two of DMTC's flow chemistry manufacturing projects are involved in the scale-up of two therapeutics in high global demand. These projects contribute to supply chain security and building our in-country capacity, while also enhancing workforce skills in flow chemistry manufacturing.

This year has also seen the appointment of Dr Leigh Farrell as Head of Health Security Strategy at DMTC. Dr Farrell joins Dr Pradera as co-lead for the 2020-2021 **National Health Security Resilience Assessment**, which will revisit and expand on the focus of previous National Capability Audits undertaken in 2012 and 2017.

MEDICAL COUNTERMEASURES
Highlights

Scale-up of vital manufacturing processes for in-demand therapeutics

DMTC is collaborating with academic and industrial partners across Australia to develop novel manufacturing processes which can be scaled to produce in-demand therapeutics, a key contributor to supply chain resilience.

The COVID-19 pandemic has brought to light several critical areas that Australia needs to focus on to achieve sovereign sustainability. One of these is establishing scalable manufacturing processes that can be used to rapidly produce a range of therapeutics, which may have been in higher than expected demand or at risk of interrupted supply. Diverse supply chains are important in ensuring supply chain resilience in times of crisis.

Two projects in the MCM portfolio focus on delivering novel and scalable manufacturing processes for in-demand therapeutics.

One of these projects is a collaboration between 60 Degrees Pharmaceuticals Australia (60P), the University of Melbourne (UoM), Australian strategic biopharmaceutical consulting company Biointelect and CSIRO. This project is accelerating the development of a unique flow chemistry manufacturing process, designed by experts at the UoM, for a therapeutic asset that has recently been approved for the prevention of malaria.

While malaria is not endemic to Australia, it remains both a public health threat, as well as a threat to Australian defence force personnel. Australians are susceptible to the disease when travelling in tropical regions, such as in our neighbouring South East Asian nations, and there are several hundred imported cases annually. However, there is concern that malaria could become endemic to Australia, as mosquito vectors begin to travel to far North Queensland, and local transmission could become a future issue.

This project is also important from a supply chain perspective, as the intellectual property and manufacturing will be retained in-country. If successful, this project could secure the Australian supply chain for this antimalarial drug. Furthermore, the manufacturing process could be applied to other key pharmaceuticals that are in global demand.

The second manufacturing project in the MCM portfolio is a collaboration between Australian chemical manufacturing company, Boron Molecular and CSIRO. The objective of this project is to pilot a scaled manufacturing plant using flow chemistry for an in-demand therapeutic asset. A synthetic route to produce the therapeutic asset will be established, and a scaled flow reactor will be designed to test production.

Both projects utilise flow chemistry. This process enables a chemical reaction to be run continuously and allows for a higher surface area to volume ratio, improving heat removal efficiency. It is often safer, more precise, and less expensive than traditional batch manufacturing.

Both projects aim to develop Australian capability in therapeutic manufacturing and are important in mitigating the risks associated with global supply shortages of key pharmaceuticals required in Australia. Ensuring a secure and stable local supply chain builds our in-country capacity, and enhances the skills of our workforce, contributing to sovereign resilience, which is critical in the face of current global therapeutic shortages.

MEDICAL COUNTERMEASURES
Highlights

Development of a universal malaria vaccine

DMTC is collaborating with James Cook University's Australian Institute of Tropical Health Medicine (AITHM), Townsville Hospital, Glycosyn and Pfizer Hospira to develop a universal malaria vaccine candidate that can protect against all strains, species, and life-cycle stages of malaria.

The universal vaccine candidate for malaria being developed at AITHM is the only candidate to meet the globally endorsed Target Product Profile. Led by renowned malaria expert, Professor Louis Schofield, the team is working on GPIVax, a first-in-class carbohydrate-based malaria vaccine candidate that has the ability to prevent both malaria infection and disease transmission.

Malaria remains one of the world's deadliest diseases, responsible for over 400,000 deaths a year and is a threat to Australian Defence personnel deployed in tropical regions worldwide. It is also a complex disease to vaccinate against as there is a diversity of both species and strain. There is growing resistance to certain anti-malarials, which has made treatment more difficult in some endemic areas, and made the need for an effective vaccine more critical.

GPIVax has shown strong preclinical efficacy against all species and strains of the malaria parasite, and each of these life-cycle stages, blocking sequential development of the parasite. This DMTC project is stage-gated and firstly will focus on pre-clinical vaccine toxicology work. Once pre-clinical toxicology studies are successfully completed, a Phase 1 clinical study will be conducted in Australia. In addition, this project will establish a manufacturing process for the vaccine that can be scaled, and compliant with Good Manufacturing Practice (GMP) standards, to ensure a high standard of safety in production.

If successful, this DMTC project could become the first universal malaria vaccine, produced in Australia, that could be used to vaccinate and protect both locally and globally against the malaria parasite. This project also contributes to extending Australia's vaccine development capability, and is crucial for developing self-reliance and creating new market and export opportunities for Australian industry.

LOOKING AHEAD

DMTC will continue to coordinate technology solutions as part of our national COVID-19 response. Building supply chain resilience and pursuing rapid and innovative responses to the local and global challenges posed by COVID-19 will assist in the short-term response as well as contributing to longer-term economic recovery.

In view of the pandemic, Government stakeholders requested that DMTC bring forward the next audit of MCM development to 2020-2021. Renamed the **National Health Security Resilience Assessment** (NHSRA), this assessment will guide the development of future technologies that contribute to Australia's sovereign preparedness (more information can be found on the DMTC website www.dmtc.com.au).

MEDICAL COUNTERMEASURES
Highlights

Platform diagnostic for rapid point of care detection

This DMTC collaboration between industrial partner BioCifer, the USC, the UQ and CSIRO, aims to deliver a rapid point of care platform diagnostic based on molecular genetics technology that has high sensitivity and enables the detection of multiple diseases within a single test kit.

This rapid diagnostic platform operates using a three-step “test-kit” procedure, whereby an extraction protocol is used on raw samples for 5-10 minutes (including blood, tissue and swabs), without requiring centrifuge. Following the extraction, an isothermal amplification procedure is used to rapidly amplify the nucleic acids for between 5-30 minutes, and detection occurs via lateral flow strips within five minutes.

This project focuses on Nipah virus, Dengue virus and Antimicrobial Resistance (AMR) bacteria detection. A Hendra virus test is also being developed for use in this platform diagnostic.

Carbapenemases are Beta-lactamase enzymes and work as a mechanism for resistance against many types of antibiotics. Detecting carbapenemases allows screening for multi-drug resistant bacteria, which is particularly relevant in light of growing global antimicrobial resistance AMR.

Both Nipah virus and Dengue virus are not endemic to Australia, however, both are viral infections that pose significant risks to Australians travelling overseas, particularly in South-East Asia. Nipah virus has a particularly high mortality rate, and the Dengue virus has four serotypes and can cause a particularly deadly disease called Dengue haemorrhagic fever. A rapid diagnostic will assist in obtaining a more rapid diagnosis and isolation of these viral infections.

The project team are currently conducting preclinical validation for target pathogens. They have completed the primer and probe design for their rapid Nipah test and for their various resistance enzyme tests for AMR detection.

As this project is a platform technology, the primers and probes within the amplification tube can be swapped for different genetic markers, allowing for the detection of multiple diseases. It is also low-resource and cost, as no centrifuge or equipment is required for sample processing. In addition, it can deliver a similar sensitivity to laboratory-based molecular genetic tests. Such platforms are particularly important in field deployable settings, where the ADF can be exposed to multiple pathogens at one time, especially when deployed in the Asia-Pacific region.

Success of preclinical studies will allow BioCifer to scale-up production of the rapid diagnostic platform, compliant with clinical manufacturing standards, and commercialise the outputs from this DMTC project.

Pictured opposite: Mr Joshua Boyle, a Senior Scientist with Melbourne-based industry partner Boron Molecular, adjusts the continuous flow reactor used as part of the DMTC project piloting a scaled flow chemistry manufacturing plant. This project will advance in-country pharmaceutical manufacturing and enhance supply chain capacity.