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Evaluation and Forward Scoping for the Therapeutic Goods Administration's Regulatory Strengthening Program and the Australian Expert Technical Assistance Program- Regulatory Support and Safety Monitoring

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(Public Access)

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Acronyms

Term	Definition
ACTD	ASEAN Common Technical Document
APLMA	Asia Pacific Leaders Malaria Alliance
ASEAN	Association of Southeast Asian Nations
ASEAN JACG	ASEAN Pharmaceutical Products Working Group's Joint Assessment Coordination Group
ADB	Asian Development Bank
ADR	Adverse drug reactions
AEFI	Adverse events following immunisation
AETAP-RSSM	Australian Expert Technical Assistance Program for Regional COVID-19 Vaccine Access – Regulatory Support and Safety Monitoring
APEC	Asia Pacific Economic Cooperation
BMGF	Bill and Melinda Gates Foundation
CHS	Indo Pacific Centre for Health Security
CIP	WHO Coalition of Interested Parties
CMC	Chemistry Manufacturing and Control
COVID-19	Coronavirus disease 2019
DFAT	Australian Government Department of Foreign Affairs and Trade
eCTD	electronic Common Technical Document
EOPO	End of program outcome
EUA	Emergency Use Authorisation
GBT	Global Benchmarking Tool (WHO)
GEDSI	Gender Equality, Disability, and Social Inclusion
GFATM	The Global Fund to Fight AIDS, Tuberculosis and Malaria
GHD	Global Health Division (division of DFAT)
GMP	Good Manufacturing Practice
JIMT	Joint Incident Management Team
LMS	Learning Management System
MA	Market Authorization
MEL	Monitoring, evaluation and learning
MELF	Monitoring, evaluation and learning framework
MFDS	Ministry of Food and Drug Safety (South Korea)
MOU	Memorandum of Understanding
NCIRS	National Centre for Immunisation Research and Surveillance
NGO	Non-Governmental Organisation
NIID	National Institute for Infectious Diseases (USA)
NRA	National Regulatory Authority
PICs	Pacific Island Countries
PMTP	Pacific Medicines Testing Program
PMS	Post Marketing Surveillance
PNG	Papua New Guinea
PQ	Prequalification

Term	Definition
PV	Pharmacovigilance
RSP	Indo-Pacific Regulatory Strengthening Program
RVAG	Regional Vaccine Advisory Group
SEARO	WHO South East Asian Regional Office
SPC	The Pacific Community
SRA	Stringent Regulatory Authority
TGA	Therapeutic Goods Administration
UNICEF	United Nations Children's Fund
VAHSI	Regional COVID-19 Vaccine Access and Health Security Initiative
WHO	World Health Organization
WLA	WHO Listed Authority
WPRO	WHO Western Pacific Regional Office

Lexicon of Relevant Terminology

The following are definitions of key terms used in this report:

Advanced therapies or **advanced therapy medical products:** A term used to describe innovative therapies. International regulators use this term to include gene, cell and tissue therapies. See https://www.tga.gov.au/advanced-therapies.

Biological therapeutics

Also referred to as Biologicals, are those class of medicines which are grown and then purified from large-scale cell cultures of bacteria or yeast, or plant or animal cells. Biologicals are a diverse group of medicines which includes vaccines, growth factors, immune modulators, monoclonal antibodies, as well as products derived from human blood and plasma. What distinguishes biologicals from other medicines is that these are generally proteins purified from living culture systems or from blood, whereas other medicines are considered as 'small molecules' and are either made synthetically or purified from plants.

Mutual recognition: This is a process of recognition of the capabilities of the National Regulatory Authority (NRA) in a region to allow for mutual acceptance of the NRA review and authorisation of a medicinal product by engaged NRAs. (See OECD- Mutual Recognitionf (oecd.org))

Regulatory convergence or harmonisation: The process of aligning, or bringing some common ground, to the processes of regulatory affairs in partner countries, sub regions or regions. (See Regulatory reliance for convergence and harmonisation in the medical device space in Asia-Pacific | BMJ Global Health for example).

Regulatory hub: A peer group of NRAs (or single NRA) to provide a centre of regulatory best practice for a sub-regional platform. The aim is that regulatory best practice is exercised, observed and disseminated amongst the local NRAs that are engaged.

Regulatory information platform: A collective, shared database of regulatory decisions, guidance, recommendations and risk benefit management decisions. This may be a core resource for a regulatory hub.

Regulatory providers' forum: A forum/place where interested parties in the regulatory strengthening space in the region can exchange and coordinate strategies and priorities, including engagement strategies and training/information delivery.

Sub-regional platforms: Coalitions or groups of nations within a region for a common purpose (e.g. WHO Pacific Sub-Regional Platform). A sub-regional regulatory platform can assist countries to perform core regulatory functions that cannot be undertaken by countries on their own, especially in the context of constrained resources. The mechanism can be voluntary in the beginning and is not meant to replace national systems. It may in turn provide a point of focus for a regulatory hub (see above).

Executive Summary

Preamble:

This is the publicly available version of the DFAT commissioned TGA RSP and AETAP-RSSM Evaluation and Scoping Report, modified for public accessability. Public dissemination of this report is aligned to DFAT's aid transparency principles and guidelines. Personal identifiable information relating to interviewees, respondents or participants and other confidential information are not included in this report. Engaged parties have been contacted for agreement on public dissemination of this version of the report. All efforts have been made to ensure the meaning and context of this report and its recommendations are consistent with the original report.

Introduction

This report provides an independent evaluation of the work to date of the Therapeutic Goods Administration's (TGA) Regulatory Strengthening Program (RSP) and the Australian Expert Technical Assistance Program Regulatory Support and Safety Monitoring (AETAP-RSSM) as well as options for a future TGA-DFAT partnership.

The Indo-Pacific Regulatory Strengthening Program (RSP) is an AUD$11.24 million program funded through DFAT's Health Security Initiative (HSI) that was launched in October 2018. It is due for completion in June 2023, including a no cost extension from July 2022 to June 2023. The RSP's goal is to strengthen capability of national regulatory authorities (NRAs) to increase the availability of quality, safe and effective medicines and medical devices. The AETAP-RSSM is a two-year AUD$8.6 million program (April 2021 to June 2023) funded through DFAT's Regional COVID-19 Vaccine Access and Health Security Initiative (VAHSI). Its goal is to support partner countries' efforts to deliver safe, effective and accessible COVID-19 immunisation programs based on a health and regulatory systems strengthening approach. It is noted that although the two programs have different objectives, there are significant operational and functional overlaps in terms of regulatory co-operation.

The evaluation/scoping work

Design of a new phase of health security programming is being considered by DFAT. This evaluation of the DFAT-funded work of TGA (2018-present) and the scoping is designed to inform a future TGA-DFAT partnership. This report addresses 5 key questions related to achieving end of program outcomes (EOPOs) and the enablers and barriers to that, aspects of the program model to be modified, and the desired program outcome, country specific approach and regional cooperation mechanisms for a future phase of work *(see section 3.6 for the questions).*

Independent consultants Dr Barry Walker and Dr Kathryn Dinh, with backgrounds in regulatory affairs and programme evaluation respectively, conducted the review and

scoping between May and September 2022. This included a focused desktop review of documents, tailored interviews with 36 people (including some group interviews) and written comments from 8 people including Indo-Pacific representatives of national regulatory authorities (NRAs), donors, WHO, other complementary providers of regulatory strengthening activities, DFAT and TGA *(see Annex 3)*. Stakeholder mapping and a high-level needs gap analysis was undertaken from this data, and a realist evaluation approach was used to analyse the barriers and enablers of TGA's work and to contextualise the program outcomes achieved.

A Steering Committee consisting of TGA and DFAT staff with close working knowledge of the RSP and AETAP-RSSM programs provided input at key stages during the evaluation/scoping work and a sensemaking workshop involving the Steering Committee and other TGA and DFAT staff was conducted to test and qualify preliminary findings. This was a rapid exercise and thus findings and future options represent the data gathered and analysed in the time available.

Evaluation findings

The evaluation examined the context, *mechanisms* (social and psychological drivers of decision-making) and activities that if combined, provide a more holistic understanding of the process and intermediate outcomes of the RSP and AETAP-RSSM. More detail is provided in the relevant sections of the report.

- **Context:** The RSP was designed and began implementation pre-COVID-19 and the initial AETAP-RSSM design included face-to-face interaction. Due to COVID-19 travel restrictions and other impacts, both programs had to be adapted quickly. AETAP-RSSM needed to respond to needs for rapid market authorisation (MA) of COVID-19 vaccines and other products and for support in pharmacovigilance (PV) for the vaccines. This led to high public visibility of the role of national regulators but also significant pressure on the NRAs to rapidly register high quality products. In addition to the COVID-19 pandemic, civil unrest and natural disasters also restricted TGA's engagement in some countries.
- **Mechanisms:** There was universal high regard among interviewees for the quality and integrity of TGA's work. A majority of interviewees (NRAs, regulatory strengthening providers, DFAT and TGA staff) thought that TGA should play a supportive and mentoring role in regional collaboration efforts. A desire for more face-to-face time with TGA to deepen relationships as well as for technical assistance (TA) was noted. TGA has been mindful of the need for increased development experience in the team.
- **Activities:** TGA provided TA in MA, PV and good manufacturing practice (GMP). It contributed to CoRE's teaching modules, held partner forums and spent considerable time liaising with other stakeholders working in regulatory strengthening in the region.

Process outcomes and challenges: TGA has built good working relationships with numerous NRAs.

: TGA's flexible and responsive approach was highly valued by partners and made a positive contribution to Australia's strategic engagement with partner countries.

: Coordination and communication could be improved between TGA and the DFAT-funded partners (CoRE, USP) as well as with other providers of regulatory strengthening activities in the region.

Program outcomes: The RSP and AETAP-RSSM have delivered some important outcomes in strengthening national regulators and facilitating access to COVID-19 vaccines in partner countries (AETAP-RSSM) in rapidly changing and complex circumstances. Equally as important, TGA's programs have laid a significant foundation for a future TGA-DFAT partnership through building working relationships with partners regulating medicines and other products and strengthening TGA's regional reputation as one of quality and integrity. There is currently a rare alignment of Australian political will, prioritisation of health security in the region and high public visibility of the importance of regulators, and the opportunity this presents for TGA's further contribution to the Indo-Pacific region should be embraced.

Significant outcomes achieved by the RSP and AETAP-RSSM programs included:
- The successful joint assessment with the Thai FDA of the antimalarial tafenoquine – the first new treatment for the radical cure of *P.vivax* malaria in 60 years.
- The strengthening of regulatory capacity in Fiji which led to the Department of Health taking steps to formally recognise the role of the Chief Pharmacist and her team.
- Supporting the expedited approval of safe, quality and effective COVID-19 vaccines in partner countries including Indonesia, Fiji, Lao PDR, PNG, Vietnam, the Philippines and Thailand which enabled quick access to donated vaccines, including those from Australia.

Further outcomes are described in *3.5 Outcomes* on page 25. Relative to the length of time the RSP has been operating, the number of demonstrable examples of intermediate or end of program outcomes is limited. However, given the context and mechanism factors described above, there are clearly good reasons why this is the case and some important, identifiable process outcomes have also been achieved which represent significant progress in their own right. The positive engagement and adaptability of TGA's response over the period are recognised and have enabled progress to be made in the face of difficult operational and functional limitations.

Gender equality, disability and social inclusion

While scope to address gender equality in TGA's work was limited as it was not a primary focus of activities, most gains reported were likely to have occurred anyway without any active intervention by TGA. For example, there were instances where the female dominated workforce resulted in a majority of training participants being women. A recent DFAT

internal review found that RSP's progress to implement gender equality strategies was below what was expected. To address this, a GEDSI analysis of TGA's programs will soon be conducted and will provide recommendations for strengthening gender equality, disability and social inclusion.

Progress towards end of program outcomes

For the RSP, progress towards EOPOs 1-3 is as expected, and for EOPOs 4 and 5 somewhat less than expected as coordination and communication with partner organisations could be improved. The impact of COVID-19 on travel, and face-to-face and direct meetings is understood and recognised, and TGA responded to these challenges in a flexible and responsive manner. For AETAP-RSSM, progress against EOPOs 1 and 4 is as expected, and for EOPO2 somewhat less than expected as timely access to COVID-19 vaccines was not always possible, due to factors mainly beyond TGA's control. Progress against AETAP-RSSM's EOPO3 is significantly less than expected, although this outcome appears to be inappropriate as the program was designed as a rapid response program rather than one for longer-term health systems strengthening.

TGA's Future Work

Needs Gap Analysis and Stakeholder Mapping

The needs gap analysis and stakeholder mapping generated the following findings:

- Future support in a sustainable fashion for NRA/MoH regulatory strengthening is critical, with a focus on safety of medicines and biological therapeutics. This includes safety monitoring, PV systems and processes, and developing reporting systems and action plans.
- To better enable NRAs/MOHs to fulfil their regulatory functions, strengthening both the technical capability and regulatory maturity of the NRAs in the region is important through both regional activities and bilateral engagement. Support activities will depend on the maturity of the NRA and in the Pacific, on country priorities and the capacity and remit of MOH staff.
- There is a need for improved cooperation between providers of regulatory strengthening activities in the Indo-Pacific region. This could include continued and enhanced collaboration between the TGA and mSupply, USP and/or CoRE who each deliver discrete functions which can complement the TGA's capacity building work with NRAs.

There are clear gaps in capability of NRAs in the region, often due to simple, but hard to fix factors, such as staffing levels, degree of functional expertise and technical experience. This does not fall within the purview of the TGA but should be acknowledged.

There are a number of major regulatory strengthening providers in Southeast Asia and the Pacific, with overlapping, and in some instances, potentially competing interests, whereas other areas of the regulatory landscape remain relatively vacant of support. For example, the MA functions of an NRA/MoH receive significant support from a range of support providers, whereas pre-clinical and early product development activities have little support. Table 5 provides further detail. In a comparison between Southeast Asia and the Pacific combined and Southeast Asia, Africa and South America combined, the majority of NRA strengthening activity in the former regions quite rightly focus on market authorisation (MA), chemistry manufacturing and control (CMC) and PV areas. Pre-clinical and clinical areas are somewhat less well provided for, as is GMP and manufacture review (including onsite inspection). The TGA has provided support across the GMP space including GMP clearance assessments. Regional NRAs are constrained in their capacity to undertake inspections and assessments outside their own borders *(see Table 5).*

Recommendations for a future TGA-DFAT partnership

Based upon the findings in this report, the Consultants recommend that TGA and DFAT enter into a further phase of their partnership conducting regulatory strengthening activities in ODA-eligible countries in the Indo-Pacific.

The report identifies a series of options for this future work framed as high-level recommendations and starting with the development of a 5-year strategy. It recognises that TGA and DFAT will need to consider the recommendations and then decide on a way forward, including through a management response to this report. If a strategy is developed, this will need to be followed by an operational plan which will detail how the strategy will be implemented including governance, human resources, budget and risk management arrangements and year on year activities. Adoption and final prioritisation of the recommendations, as well as detailed planning for implementing the strategy is beyond the scope of this report and is the responsibility of TGA and DFAT. The main recommendations are outlined below:

- Clear commitment from DFAT to funding and providing support to a future partnership with TGA.
- Develop (with key country and regional partners) a 5-year (and 10-year stretch) strategy that outlines TGA's vision, goal, end of program outcomes, scope of work, delivery mechanisms, partnerships and ways of working. It is recommended that this strategy:
  o Includes an objective to contribute to strengthening partner country regulatory capacity and improved regional co-operation to ensure the production, distribution and timely access to quality and safe medical products in the Indo-Pacific region.
  o Continues but decreases the overall proportion of response mode programming to country requests as has occurred in the last few years under both RSP and AETAP-RSSM, while increasing planned, systematic regulatory strengthening activities identified together with country partners in country-specific work plans. This in no

way diminishes the clear and recognised benefit of response mode activity in recent years. Instead, it acknowledges a shift towards a more integrated, long-term approach to regional engagement and a decrease in demand for rapid COVID-19 vaccine support.

- o Maintains a continued, but more targeted delivery of TA in MA, PV and falsified medicines. This can include advice and guidance on management of GMP manufacturing.
- o Continues collaboration with CoRE and USP and working with mSupply and NCIRS.
- o Continues to take a tiered approach to programming, with a strategic approach for more mature NRAs and process/product-related support with less mature NRAs or where an NRA is non-existent.
- o Continues to support regional regulatory hubs – coordinating with the developing sub-regional entities being coordinated by ASEAN and WHO.
- o Initiates a Regional Providers' Forum (funders and agencies involved in provision of regulatory strengthening activities) to improve coordination and collaboration.
- o Builds on existing processes and successes in the Asia Pacific region in regulatory harmonisation and convergence. For example, support the ongoing development of the ASEAN Common Technical Document (ACTD).
- o With relevant partners, provides advice on the development of information technology applications in the region, including MA software and PV systems.
- o Considers secondments or placements between the TGA and DFAT.

In addition, the strategy could consider the following in relation to TGA's partnership with DFAT:
- o DFAT to strengthen the nature of its partnership with TGA by leveraging its resourcing and utilising posts and regional diplomacy to support regulatory strengthening activities as well as sharing of information on country and regional trends. This will require an increase in human and other resources (post and the Global Health Division - GHD).
- o TGA and DFAT to plan and identify how to strengthen TGA's work with other significant players in the region (WHO, BMGF, ASEAN, regional donors for example).
- o Consider implementing formalised and regularised annual and potentially semi annually, consultation meetings between senior-level DFAT and TGA staff.

Acknowledging the robust MEL systems that TGA has established, the recommendations in this report include the prioritisation of monitoring and reporting on programmatic outcomes in the last year of RSP and AETAP-RSSM activity. The placements and senior-level meetings could also commence prior to the development of the new strategy.

More detail on all sections of this Executive Summary is provided in the remaining sections of this report.

1. Background

This section describes the rationale for regulatory strengthening activities and the work of TGA in the Indo-Pacific region. Note: For information about the operating context for TGA's work, see *4.1 Context* below.

1.1 Background to Regulatory Strengthening

National Regulatory Authorities (NRAs) are responsible for ensuring that new medical products meet internationally agreed standards of quality, safety, and efficacy. They are also responsible for ensuring products continue to comply with these standards whilst available on the market. NRAs in low resource settings, or those tasked with regulatory responsibility in the absence of an NRA, often lack the ability or capacity to implement their core functions (e.g. MA, post market surveillance (PMS), and PV) effectively. This can result in poor regulatory practices, delays in accessing new and priority medicines and medical devices and the use of outdated treatments and substandard and/or falsified (SF) products. These issues can consequently hinder national disease control efforts and drive antimicrobial resistance (AMR), which are both health security threats to neighbouring countries and the Indo-Pacific region.

1.2 TGA's Work in Regulatory Strengthening

TGA is currently implementing three DFAT-funded programs in the region: (1) the Indo-Pacific Regulatory Strengthening Program (RSP) funded under the Health Security Initiative for the Indo-Pacific region, (2) Australian Expert Technical Assistance Program for Regional COVID-19 Vaccine Access – Regulatory Support and Safety Monitoring (AETAP-RSSM) funded through the Regional COVID-19 Vaccine Access and Health Security Initiative (VAHSI), and (3) the Pacific Medicines Testing Program (PMTP) under Australia's Pacific Step Up. Through these development programs, TGA has gained extensive experience in building regulatory capacity and supporting medicine testing for NRAs, and often MoH staff in the absence of an NRA, in the region. TGA has been working closely with almost all of the 18 partner countries under VAHSI. This report focuses on the progress of, and future scoping for RSP and AETAP-RSSM only, with PMTP being out of scope. There is a recognised overlap in operational activities between RSP and AETAP-RSSM. Although the program outcomes differ, several of the operational and functional activities of both programs are similar. For example, in targeted regulatory strengthening, both programs have conducted joint dossier reviews and shared regulatory decision processes. For this reason, the programs are discussed together in certain sections of the report.

1.3 Indo-Pacific Regulatory Strengthening Program

The RSP (including USP, CoRE and mSupply) is an AUD$11.24 million program in the Indo-Pacific being funded through DFAT's Health Security Initiative (HSI) for almost five years (October 2018 to June 2023). Its goal is to strengthen capability of NRAs to increase the availability of better quality, safer and more effective medicines and medical devices. The AETAP-RSSM is a two-year AUD$8.6 million program (April 2021 to June 2023) in the Indo-

Pacific being funded through DFAT's Regional COVID-19 Vaccine Access and Health Security Initiative (VAHSI). Its goal is to support countries to deliver safe, effective and accessible COVID-19 immunisation programs through regulatory systems support.

The expanded goals of the RSP are:
• Strengthened capability of NRAs to increase the availability of better quality, safer and more effective medicines and medical devices through improved regulatory practice and collaboration
• Improved regulatory practice through increased cross-country reliance and work sharing in the Indo Pacific
• Improved development partner coordination to support NRA maturation in all aspects of regulatory practice.

DFAT funds two partners under RSP to complement the work of TGA in regulatory strengthening. It funds course scholarships (AUD$0.65 million, February 2020 June 2022) for partner NRA staff to complete The Duke National University of Singapore's Centre for Regulatory Excellence (CoRE) Graduate Certificate in Health Products Registration. United States Pharmacopeia (USP) is funded by DFAT (AUD$1 million, September 2020 September 2022) to strengthen national drug quality control laboratories in Cambodia and Laos to international accreditation, WHO prequalification and ISO/IEC standards.

TGA has worked with NRAs, MoHs, malaria and tuberculosis disease control programs, the WHO and other key partners in building the capabilities of NRAs/MOHs to achieve its program goals. An additional partner of note is the mSupply Foundation, which is developing software for medical product registration, cold chain monitoring and for a medical stocks inventory. TGA's collaboration with this coalition of partners for both programs has resulted in some linkages and insights by TGA into the public health situation of countries and government priorities related to the COVID-19 pandemic, including understanding current and future challenges in regard to the approval and safety monitoring of COVID-19 vaccines. AETAP-RSSM, while being a separate and distinct program to the RSP, has benefitted from the relationships initially established through RSP.

RSP has been designed to deliver the following end of program outcomes (EOPOs):

EOPO 1: Improved NRA regulatory practices and systems that have addressed deficiencies identified through WHO GBT assessments, TGA in country/virtual missions and NRA priorities.
EOPO 2: Increased use of reliance and/or work sharing mechanisms by NRAs to improve regulatory efficiency and collaboration.
EOPO 3: Registration without undue delay of new and priority products by NRAs for infectious diseases.
EOPO 4: Improved coordination between NRAs, national disease programs and relevant stakeholders, to help ensure timely access to new products.

EOPO 5: Improved coordination of regulatory strengthening activities with other partners working in the region.

Under the RSP, TGA has used a tiered approach based upon the maturity of each regulator/MoH and drawing upon available Institutional Development Plans using the WHO's Global Benchmarking Tool (GBT) in order to develop country-specific plans. The GBT has provided a recognised framework to enable targeted support while also assisting in understanding the regulatory functions that are priorities for technical assistance. However, country requests for technical assistance (TA) have not always aligned with gaps identified by the GBT.

In addition to this work, there is recognition that efficiencies can be achieved through the implementation of reliance mechanisms that still allow for sovereign decision making but draw upon the work done by trusted partners. Therefore, the RSP has been working to significantly improve the ability of NRAs to utilise and participate in collaborative procedures such as the ASEAN Pharmaceutical Products Working Group's Joint Assessment Coordination Group (JACG). The RSP has also facilitated coordination with disease control programs, such as those for malaria and tuberculosis, to support efforts to access the most effective products.

1.4 Australian Expert Technical Assistance Program for Regional COVID-19 Vaccine Access – Regulatory Support and Safety Monitoring (AETAP-RSSM)

As part of VAHSI, TGA is delivering technical assistance through its Australian Expert Technical Assistance Program for Regional COVID-19 Vaccine Access – Regulatory Support and Safety Monitoring (AETAP-RSSM). AETAP-RSSM is an AUD$8.6 million program that commenced in April 2021 and is due to end in June 2023. The goal of AETAP-RSSM is to support Pacific and Southeast Asian countries' efforts to deliver safe, effective and accessible COVID-19 immunisation programs, based on a health and regulatory systems strengthening approach and in line with best practice standards. AETAP-RSSM has the following end of program outcomes (EOPOs):

EOPO 1: Greater assurance of the quality, safety and efficacy of COVID-19 vaccines that have been introduced into partner countries;
EOPO 2: Improved capacity of national immunisation programs to deploy regulated COVID-19 vaccines in partner countries in a timely manner;
EOPO 3: Improved systems and processes that are fit for purpose for the ongoing safety monitoring of COVID-19 vaccines in partner countries; and
EOPO 4: AETAP-RSSM's collaborations and support for the access and safety monitoring of COVID-19 vaccines are valued by partner countries.

TGA has provided TA to some partner countries participating in VAHSI, responding to country needs and requests. It has collaborated with the National Centre for Immunisation, Research and Surveillance (NCIRS), which is also being funded by VAHSI, to interpret reports on vaccine adverse events following immunisation and provide training in the Pacific.

2. This Report

2.1 Purpose

This report describes the results of an independent evaluation of the work of the RSP and AETAP-RSSM from 2018 to the present and provides options and recommendations to guide a future TGA-DFAT partnership to support regulatory strengthening in the Indo-Pacific. It is premised upon a commitment by DFAT to continue to fund and partner with TGA.

2.2 Scope

The scope of this work was initially set out in a terms of reference. The scope was subsequently adjusted in discussions on design and the evaluation/scoping questions below illustrate the final scope of work. Further edits and changes have been applied as required. (see preamble and statement of limitations).

This work includes an evaluation with limited scope, high-level landscape and needs analysis and recommendations for the next five years of TGA's work. There is also the consideration of a stretch view to broader outcomes desired over a 10-year period.

2.3 Evaluation/scoping Team

This work was conducted by two independent consultants: Dr Barry Walker, a regulatory advisor who has previously worked for the National Institute for Biologics Standards and Control and Dr Kathryn Dinh, an international development Monitoring, Evaluation and Learning consultant who has worked with DFAT's health security and vaccine access programs since 2019.

2.4 Steering Committee

A steering committee, consisting of TGA and DFAT staff with significant knowledge of both TGA programs, provided input at key stages during the evaluation/scoping work, including participation in a sensemaking workshop to test and qualify preliminary findings.

2.5 Methodology

The methodology for this work consisted of the following, with the retrospective evaluation results informing the future scoping options:
- Desk review of key documents (see *Annex 1* for list of documents reviewed)
- Interviews and consultations with key regional stakeholders associated with regulatory strengthening in Southeast Asia and the Pacific. See *Annex 2* for a list of interviewees and those who provided written comment.
- High-level landscape analysis of entities working in regulatory strengthening in Southeast Asia and the Pacific.
- High-level regulatory strengthening needs gap analysis for Southeast Asia and the Pacific.

- Analysis of evaluation findings using elements of a realist evaluation approach *(see below)* and identification of recommendations including options for a future TGA-DFAT partnership.
- Testing and qualifying preliminary findings with TGA and DFAT in a sense making workshop.
- Writing a report that addresses the evaluation/scoping questions and provides evidence-based recommendations for the future work of TGA.

Realist evaluation

Realist evaluation is an approach which seeks to understand "What works, for whom, in what respects, to what extent, in what contexts, and how?" (Pawson & Tilley, 1997). It is an approach for framing questioning and analysis that incorporates the context and underlying social or psychological drivers that cause the reasoning and decision making of actors '*mechanism*' in considering the outcomes of program activities. Realist evaluation was used for this evaluation to understand the reasons why there has been good engagement between TGA and some partner countries and not in other countries, as well as to understand the barriers and enablers to achieving the interim and end of program outcomes.

The initial intention for the evaluation was to use a realist evaluation approach to map out 'context + mechanism=outcome' or 'CMO' statements for select partner countries to understand engagement, barriers and enablers for each country and then to generalise findings where possible. However, the consultants were not able to gather sufficient data to be able to do this at a country level, instead opting to provide findings at an aggregate level across both TGA programs and all partner countries.

2.6 Evaluation questions, methods and data sources

The following *table 1* lists the evaluation/scoping questions and the corresponding methods and data sources used for each question. A box with a blue question number in it in the remaining sections of the report indicates where each question has been addressed.

Table 1: Evaluation/scoping questions and corresponding methods and data sources

Evaluation

Evaluation/scoping questions	Method / data source
EQ1: To what extent did RSP meet its **end of program outcomes?**	RSP and AETAP-RSSM progress reporting (document review), interviews
EQ2: What were the key **enablers** and **barriers** to achieving these outcomes and how were they managed? Which aspects of the **model could be modified** to increase its ability to achieve the intended outcomes?	Realist evaluation (modified), interview questions and document review Note: Insufficient data for country specific *context mechanism activity=outcome* findings, generalisable program-wide findings only

Scopings

Evaluation/scoping questions	Method / data source
EQ3: What could be **TGA's desired outcome** for its contribution to the regulatory environment in the Asia Pacific by the end of HSI 2.0?	Landscape analysis, needs gap analysis, interviews & document review
EQ4: Does the TGA need to develop a more **country specific approach** to engagement and capacity building, and, if so, what needs to be considered?	Document review, interviews
EQ5: What role should TGA play in facilitating **convergence** or **harmonisation** of the regulatory landscape across the Asia Pacific region?	Landscape analysis, needs gap analysis, interviews & document review

2.7 Limitations

The limited time and resources necessitated a tightly constrained scope for the evaluation and forward scoping work. This included a limited number of interviews and defined document review. Thus, the opinions of the interviewees can be said to be *indicative* but not *representative* of stakeholders working in medical product regulation and regulatory strengthening in the region. Similarly, a more extensive document review *may* have added content to the landscape and needs gap analysis or more forward-looking options.

There are recognised gaps in detail in this report, including analysis and recommendations at a country level, and these are recommended to be addressed through the development of a comprehensive 5-year strategy and implementation plan underpinning a future TGA-DFAT partnership. The development of a strategy is a critical first step, which will then need to be operationalised. While this report provides high-level recommendations to inform the strategy, detailed operationalising of the strategy is beyond the scope of this work.

2.8 Audience for the Report

This is a publicly accessible version of the DFAT commissioned, TGA RSP and AETAP-RSSM Evaluation and Scoping Report.

3. Evaluation of RSP and AETAP-RSSM EQ2

3.1 Introduction

This section describes the evaluation of the RSP and AETAP-RSSM's progress to date using a realist evaluation approach and reviewing this progress against the programs' end of program outcomes (EOPOs). Using such an approach helps to contextualise the results for both programs within the broader operating environment in which the programs function.

The following sections describe the contextual factors, mechanisms and activities that contributed towards or impeded the achievement of program outcomes. *Mechanisms* means the underlying social or psychological drivers that cause the reasoning and decision making of those who interact with the programs.

3.2 Context

This section describes some of the main contextual factors that impacted the implementation of the TGA programs as described by interviewees. Given the COVID-19 pandemic and the other factors, this was a particularly challenging, unpredictable and unprecedented time to be implementing activities. Such a context needs to be considered in assessing program outcomes.

COVID-19 pandemic

The COVID-19 pandemic caused significant disruption and re-orientation of health services starting from late 2020 and continuing until today. This created both challenges and opportunities for the work of TGA:

Challenges

- The RSP was designed pre-COVID-19, and so programming had to be adapted quickly and to a significant degree because of the pandemic.

- AETAP-RSSM was designed at a point in time where international travel and face-to-face support was envisaged by early to mid-2021. Subsequent lockdowns and travel restrictions had significant ramifications on program design (see points below) and meant that this program also had to be adapted quickly.

- A significant portion of health services in partner countries was diverted to the COVID-19 response, resulting in many activities planned by TGA and partner countries being put on hold.

- An intensification of COVID-19 vaccine donations led to unplanned demand for rapid TA by TGA for vaccine registration.

- Restricted travel instituted because of the COVID-19 pandemic meant that TGA's planned face-to-face training and mentoring activities had to be delivered remotely

for most of 2020 and 2021. This meant that some activities that could only be done in person had to be delayed and that the ability to build deep and trusting working relationships was limited. It is noted that RSP's face-to-face activities were delivered from late 2018 until the COVID-19 pandemic was declared.

- The emergence of new COVID-19 variants and vaccines as well as new age cohorts that could be vaccinated all required ongoing adaptation of TGA's activities to respond to country requests for information and advice.

- WHO, also working in regulatory strengthening in the region, had a limited capacity to respond to specific country needs in a timely manner.

Opportunities

- The global demand for rapid deployment of COVID-19 vaccines raised the profile and general understanding of the role of national regulatory authorities as well as the process of the WHO's Emergency Use Authorisation.

- As one of only two Stringent Regulatory Authorities in Southeast and East Asia and the Pacific), TGA was well positioned to provide information and technical assistance in the registration of COVID-19 vaccines.

- Other actors were also supporting the COVID-19 response in the region e.g. NZ MedSafe and the Bill and Melinda Gates Foundation (BMGF). This gave TGA opportunities to meet and collaborate with these parties.
- TGA was able to work closely and cooperatively with Fiji's NRA, the Fiji Pharmaceutical and Biomedical Services Centre (FPBS) working as an initial focus of activities in the Pacific, where successes could then be leveraged across the region to assess and generate further demand for regulatory support.

Other contextual factors

The following were other events that unfolded in the region that likely impacted TGA's ability to implement activities:

- The occurrence of internal political disruption in some parts of the region impacted enagement

- Geological and climate impacts have limited some countries capacity engage with TGA.

Organisational factors

As well as the above, there were several internal, organisational challenges and opportunities that TGA had to manage in order to deliver its work:

Opportunities

- The onboarding of new staff at TGA increased its capacity to respond.

- TGA's programs were managed to enable it to be responsive to requests from

partner countries in a timely manner. This in turn built TGA's reputation in the region as an organisation that: provides high quality technical assistance, draws upon robust technical knowledge and experience, can respond to country specific requirements in a timely way, and acts with integrity.

Challenges

- The restructure and integration of the RSP and AETAP-RSSM teams and recruiting and onboarding of new staff took considerable time and resources to manage.

- TGA has recognised a gap in development experience, which in turn has impacted the level of engagement possible with some NRA's and countries.

- The Australian Government Department of Health's (DoH) travel approval processes have been challenging for TGA staff – particularly for travel at short notice.

- TGA has been building collaborative relationships with many NRAs/MOHs in the region and this is necessarily a gradual and ongoing activity that will require investment for years to come. Strengthening regulatory systems is also a long-term process. The shorter-term nature of DFAT funding (5 years for RSP, 3 years for AETAP-RSSM) and lack of certainty of funding beyond these timeframes has limited TGA's ability to design activities that would take longer than five years to implement. However, a new partnership with DFAT will enable TGA to build upon the previous phase and plan for the next 5 years. During the development of the strategy for the next phase of regional support (*see Section 6*), clear articulation of medium to longer-term outcomes will be needed as well as delivery mechanisms supporting a sustainable improvement in NRA/MoH regulatory capacity. This could include planning for streamlining of regulatory processes including legislative change if needed. It could also include supporting sub-regional networks of NRAs to foster regulatory consistency and reliance systems for faster MA processing.

- It is noted that the TGA is currently operating under a cost recovery model, with additional funds being available from other parties for specific projects or activities. The cost recovery model required generation of operating costs through fees, charges and cost recovery of its regulatory functions. **(See Link to Parliamentary Library and Link to TGA Cost Recovery Statement 2022)**. It is recognised that a cost recovery funding model for national regulatory authorities is an outlier globally.

3.3 Mechanisms

According to a realist evaluation approach, *mechanisms* are a critical consideration in designing and appraising program outcomes. In discussing the collaborations and outcomes for RSP and AETAP-RSSM, a number of mechanisms that are likely to have influenced the outcomes have been identified.

Partner Country NRAs & MoH Staff

 All stakeholders

- Among all stakeholders external to TGA and DFAT, there was universal high regard for TGA's technical expertise. This high regard likely resulted in TGA being perceived as a trusted organisation with high integrity. There were mixed views on the role TGA should play in regional collaboration, including in harmonisation and reliance. The **majority** view was that TGA should play a support rather than a lead role. This could include contributing to existing mechanisms run by multilaterals including the ASEAN Pharmaceutical Products Working Group's Joint Assessment Coordination Group (JACG) and the Pacific Sub-Regional Platform coordinated by the WHO.

- A view expressed by a few interviewees was that on some occasions the TGA's communication could be improved and although a minority comment, it needs to be reiterated that communication with partners is a high impact activity that needs to be managed in a culturally responsive way. It is stressed that this was the experience of a minority of interactions with TGA. It highlights how critical it is to engage staff with both technical, developmental and culturally responsive skills and expertise. Cultural responsiveness means *being open to new ideas that may conflict with the ideas, beliefs and values of your own culture, and being able to see these differences as equal*[1]. **NRAs**

- During the COVID-19 pandemic, NRAs in partner countries were under intense pressure to rapidly evaluate and register COVID-19 vaccines and other products and to ensure their quality and safety. Some required assistance at short notice to be able to evaluate vaccine dossiers, particularly to facilitate access to vaccine donations. Many of the PICs which do not have dedicated regulatory capability were particularly reliant on this assistance for COVID-19 vaccine approval.

- TGA has established relationships to differing degrees with NRAs in the region, some of which involve open collaboration and sharing of information and others are more limited or purely based upon an on-call need for support.

- Some NRAs expressed the desire for increased face-to-face interaction with TGA – in-country time to both strengthen capacity as well as to deepen the relationship between the agencies. As one NRA representative put it, the point is not only about achieving the goal, but also the working relationship.

  In building working relationships, there is *procedural trust* in structures and/or processes and *interpersonal trust* based upon a judgement of honesty, values and credibility. TGA's remote work due to COVID-19 is likely to have established procedural trust, whereas increased face-to-face interactions are now needed to

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[1] Agency for Clinical Innovation 2022, *Culturally responsive practice,* available at:
https://aci.health.nsw.gov.au/projects/consumer-enablement/how-to-support-enablement/culturally-responsive-practice[2] Furlong, G 2005, *The conflict resolution toolbox*. Wiley. p.142 & Mnatsakanova, S 2020, *Why managing trust is critical in a donor-recipient partnerships,* available at: *https://partnershipbrokers.org/w/wp-content/uploads/2020/04/PBA-Paper_013_Susanna-Mnatsakanova.pdf*

build interpersonal trust. Strengthening both types of trust will likely lead to increased communication and collaboration, a deeper understanding of diverse interests, and improve problem solving and delivery of results[2].

- It was clear from the NRAs/MoH staff interviewed, that there was a keen interest in exchanging more information with TGA including for biological products, and advanced therapeutics. Information sharing, in particular the rationale and reasoning for MA and PV decisions has significant benefits to all parties and all levels of NRA/MoH staff. It can provide fresh insights into established thinking, and conversely, provide lessons learned in regulatory thinking and risk management.

- A few interviewees noted that part of TGA's value is in their perception that it is an independent (neutral) entity providing regional support. They noted that some other providers of regulatory support have potential (real or perceived) conflicts in the way they provide TA relating to commercial partnerships.

- Some of the more experienced NRAs expressed a desire to build more advanced capabilities, anticipating future demands on their services. These included regulatory capacity in advanced therapeutics and biologicals and regulatory skills to support early stage product development.

Partner governments/ministries of health

- A few interviewees identified existing and potential tensions between the provision of technical assistance and sharing of information with TGA and the importance of national sovereignty in decision making for product registration. It was recognized that these issues are closely linked to a country's national health security. This has likely influenced how, and to what extent, a partner has engaged with TGA and further underlines the importance of trust between NRAs/MoH staff in undertaking regulatory strengthening work.

- Relations between DFAT and partner governments' departments of health may have negatively influenced NRAs' engagement with TGA in some cases where DFAT has either scaled down or ceased health-related country programming. Looking forward, DFAT could exercise considerable additional influence within the higher levels of partner governments managing their country health interests. This could include raising political awareness of the importance of regulatory strengthening programs.

TGA

- TGA has displayed a willingness to respond to a surge in demand-based requests from NRAs/MoHs as a result of the COVID-19 pandemic. Most interviewees) said

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[2] Furlong, G 2005, *The conflict resolution toolbox*. Wiley. p.142 & Mnatsakanova, S 2020, *Why managing trust is critical in a donor-recipient partnerships,* available at: *https://partnershipbrokers.org/w/wp-content/uploads/2020/04/PBA-Paper_013_Susanna-Mnatsakanova.pdf*

that TGA's flexibility and responsiveness was highly appreciated, and effective.

- TGA would like to continue building strong working relationships with NRAs/MoHs in the Asia Pacific. This is a critical activity.

- TGA is aware of the need to strengthen its capability in development programming and culturally responsive practice, as well as its experience in working in low to middle income country contexts. Working more closely with DFAT including exploring the option of secondments, placements or a similar exchange, partnering and learning from relevant agencies in the region and recruiting staff with development expertise could all potentially strengthen this capability.

- TGA has identified that it is sometimes difficult meeting the expectations for TA from partner NRAs. This has occurred where the requests for TA have exceeded TGA's capacity to respond, or where the requests from the NRA to build specific capacity have been misaligned with TGA's perception of what type/ level of capacity development is appropriate and/or needed. This tension between meeting country demands but ensuring TA is appropriate needs to be carefully managed and TGA's boundaries clearly but sensitively communicated. This is addressed in the discussion on strategy later in this report.

3.4 Activities

The key activities undertaken by TGA through its RSP and AETAP-RSSM programs included the provision of information, training and advice in the following key areas (not an exhaustive list):

- Market authorisation (MA) – including conducting joint assessments [RSP & AETAP-RSSM]

- Pharmacovigilance (PV) [RSP & AETAP-RSSM]

- Good manufacturing practice (GMP) [RSP & AETAP-RSSM].

It is noted that PV activities were initially secondary priorities in the RSP design, with the view that PV would be addressed by the WHO. However, when it became apparent that WHO would be unable to provide sufficient support in PV, this was incorporated into core RSP programming.

 Other activities included:

- Teaching inputs for modules of CoRE's Graduate Certificate in Health Products Regulation [RSP]

- Feedback to mSupply during development of regulatory software (Conforma) [RSP]

- Coordination with stakeholders working in regulatory strengthening in the Asia Pacific including WHO (HQ, WPRO, SEARO), USP, CoRE, NRAs, PDPs, BMGF, APLMA and others. This involved participation in coordination mechanisms/meetings [RSP &

AETAP-RSSM]

- Holding RSP Steering Committees and Forums [RSP].

3.5 Outcomes

Context and mechanism need to be taken into account in appraising the outcomes for both RSP and AETAP-RSSM. These provide a more holistic understanding of what has been achieved and reasons for the extent of progress.

3.5.1 Process outcomes and challenges

Given the long-term nature of building relationships with NRAs and strengthening regulatory capacity, acknowledging achievements in the *process* of implementing the RSP and AETAP-RSSM programs is important as these are both key markers towards achieving the outcomes and also contribute towards Australia's political capital in the Indo-Pacific region. Some key process outcomes include:

- The provision of high quality, responsive, and country-specific training, support and information sharing with NRA/MoH partners in the region has enabled TGA to build good working relationships and what appears to be at least a degree of procedural trust. This includes the in-country and Canberra based face-to-face technical assistance and meetings which were highly valued by partners.

- TGA spends considerable time and resources in communicating and collaborating with other regulatory providers in the region and provides input into regional forums and mechanisms. For example, TGA has met regularly with WHO Headquarters and regional offices, has worked with the WHO to improve the relevancy of the GBT and has participated in GBT assessments in the region. Despite such collaborations, the interviewees identified some areas in which improvements in communication and coordination could be made. These include coordination and transparency of training activities between TGA, WHO, CoRE, USP and other providers of training; communication with WHO country offices; and longer-term strategic planning between TGA and the DFAT-funded partners USP and CoRE. This points to the need for a providers' forum to coordinate regulatory strengthening.

- TGA's work responding to on-call country requests has been highly valued by partners and has been particularly important in supporting countries' COVID-19 vaccination responses. This has contributed to Australia's strategic engagement and work in gaining political capital with Indo-Pacific partner governments, primarily through interaction between posts and ministries of health and Australia's participation in regional mechanisms. Success is evidenced by a number of accelerated EUA timelines for COVID-19 vaccine acceptance and subsequent vaccine roll-out as well as expedited approval for other therapeutics. However, it was pointed out by a few interviewees that while this on-call approach does not always lead to the systematic strengthening of regulatory systems and processes, it has

potentially opened doors for further regulatory strengthening work that should be followed up. Clearly, both types of work will need to be balanced in the next phase of programming.

- TGA has developed online training modules in order to provide on-demand training for country partners in technical issues from a regulatory perspective. In 2021, a learning management system to house the modules and track engagement was launched. The modules include case studies, real data analysis and hands on experiential learning so that they are practical and relevant to the needs of NRAs. The first module, on assessing and approving additional manufacturing sites for products, was designed more for mature regulators and was shared with 10 partner countries. However, as this was shared at a time when the LMS was not in place, the number of people who have completed it is not available.

3.5.2   Program outcomes

While relationships with NRAs/MoHs have taken considerable time to establish, and a significant amount of TGA's recent work has been reactive in supporting registration of COVID-19 vaccines, there have nonetheless been some clear intermediate outcomes achieved. TGA contributed to the following outcomes (the program linked to the activity is noted in brackets). As already noted it should be recognised that Covid 19 had significant impacts on both programmes, in particular in activities where in country interactions were key components of EPO delivery. Addition PV work with NRA's was required as a consequence of gaps in regional support activities across numerous partners through covid impacts.

- **Successful joint assessment with Thai FDA for tafenoquine [RSP].** The antimalarial tafenoquine was developed by Medicines for Malaria Venture (MMV) in partnership with GlaxoSmithKline. It was registered in Australia in 2018 by TGA, which then supported the Thai FDA to register it in 2019. This was the first new treatment for the radical cure and prevention of *P.vivax* malaria in 60 years and the first-ever single dose treatment for this indication.

- **Strengthened capacity of staff responsible for regulatory activities and MoH/legislative recognition of the regulatory function – Fiji [AETAP-RSSM].** TGA provided documentation to Fiji on the provisional approval of the AstraZeneca COVID-19 vaccine in Australia which expedited the donation of vaccines from Australia. TGA has supported the approval of other products and strengthened Fiji's capacity in PV and in using reporting software. Improving this capacity in turn, boosted the recognition and function of the Chief Pharmacist and her team within the DoH and resulted in a move to formally recognise their role:

- **Supported regulatory approval for COVID-19 vaccines in Indonesia, Fiji, Lao PDR, PNG, the Philippines and Vietnam which enabled Australian vaccine donations to proceed [AETAP-RSSM].** For example in PNG, TGA provided information on its evaluation of a

COVID-19 vaccine which enabled PNG ministerial exemption and emergency use authorisation for the vaccine. In Vietnam, TGA prepared and translated summaries of their approval of Moderna and Pfizer paediatric COVID-19 vaccines and presented this, alongside NCIRS, to Vietnam. This facilitated almost 14.5 million paediatric vaccine doses donated by Australia in May 22, which were used to bolster Vietnam's vaccination campaign for children, including those aged 5-12 years.

- **Expedited assessment and approval of the AstraZeneca VAXZEVRIA manufacturing site Siam BioSciences in Thailand [AETAP-RSSM].** TGA collaborated with the Thai FDA on the submission and assessment of this site. The approval of this site by TGA facilitated WHO's granting of Emergency Use Listing for the site, and thus the export and use of the COVID-19 vaccine from Siam BioSciences.

- **HIV product evaluations in Thailand [RSP].** TGA supported the Thai FDA's evaluation of the HIV medicines Delstrigo and Pifeltro.

- **Evaluation of chloramphenicol with PNG Pharmaceutical Services Standards Branch (PSSB) [RSP].** TGA supported the PNG PSSB to evaluate chloramphenicol, including provision of an evaluation report template and checklist.

- **Strengthened pharmacovigilance systems in the region.**

- **Gender equality, disability and social inclusion (GEDSI)**

Gender equality

While TGA reported on gender equality, and scope to address this in TGA's programs was limited as GEDSI is not a primary focus of activities, outcomes were mainly those that were likely to have occurred without any active intervention by TGA or were not clearly described. One example of this was the high female participation in events held by TGA, but this was mainly attributed to the female dominated workforce in the medical products regulatory sector. RSP and AETAP-RSSM reports describes pre-market processes for drug approval promoting the inclusion of gender diverse, older, pregnant and lactating women in clinical trials and data reporting but it is unclear how TGA has contributed to improved practice in this regard. Similarly, TGA reports supporting equal participation of women in leadership roles through mentorship and other support which is commendable but it is unclear the extent to which TGA proactively identified women for this activity. A recent internal DFAT review (June 2022) of the RSP found that progress to implement strategies to promote gender equality was below what was expected. A GEDSI analysis of TGA's programs is soon to be conducted.

USP conducted a review of the gender dimensions of human resources hiring policies and practices in national partner laboratories and this review found few women in management roles, no gender specific policies on recruitment but adherence to national legislation on gender discrimination. However, while acknowledging that TGA would not have direct influence over the leadership of partner agencies, neither TGA nor USP has yet to provide

evidence of developing activities to encourage women's leadership.

Disability and social inclusion

In order to support people with a disability to be equally engaged in programming, TGA reports making adjustments to access to webinars, such as the use of closed captioning, as well as audits of accessibility of the TGA workplace which have resulted in modifications. However, TGA hopes to further strengthen the way is addresses GEDSI following the analysis mentioned above.

3.6 Future reporting

Relative to the length of time the RSP has been operating, the number of demonstrable examples of intermediate and end of program outcomes is limited. However, given the context and mechanism factors described earlier, there are clearly good reasons why this is the case and some identifiable process outcomes have also been achieved. While TGA has established robust systems and tools for monitoring progress, its ability to monitor changes to regulatory systems and processes as a result of TGA activities has been hampered by its limited ability to travel and observe changes in the practices of partners in-country. TGA will need to focus on systematically measuring and reporting on programmatic outcomes for the remainder of this phase, and should have more opportunity to do so given the re-introduction of travel and country visits. This is important to demonstrate the value of RSP and AETAP-RSSM, the extent to which they delivered results as intended and for accountability purposes. TGA should ensure that a future phase of programming once again has a strong monitoring, evaluation and learning framework (MELF) and systems which emphasise the monitoring and reporting of outcomes. The MELF could also include an indicator to track the value of TGA's partnerships.

There is clearly more that could be done to actively address GEDSI in both the current phase of RSP/AETAP-RSSM programming as well as it being built into any future phase. Steps taken by TGA to address this include identifying a member of the TGA Team who is now supporting activities addressing gender equality and the abovementioned GEDSI analysis of TGA's work which will provide recommendations.

3.7 Progress towards end of program outcomes   **EQ1**

The following tables provide an assessment of progress of the RSP and AETAP-RSSM towards the end of program outcomes (EOPOs), based upon the evidence analysed for this evaluation. It is noted that the EOPOs were developed during the initial design of both programs. As explored in the preceding sections of this report, there are many factors that determine the achievement of outcomes for both programs, including significant factors beyond the control of TGA, and the ratings should be viewed with this context in mind.

All but one of the EOPOs (cited below) remain relevant and appropriate to the activities of TGA. Progress against the EOPOs is discussed in more detail below.

Rubric to assess progress towards end-of-program-outcomes:

Green. Progress is as expected at this stage of implementation, it is likely that the objective will be achieved. Standard program management practices are sufficient.
Amber. Progress is somewhat less than expected at this stage of implementation. Restorative action will be necessary if the objective is to be achieved.
Red. Progress is significantly less than expected at this stage of implementation. The outcome is not likely to be met given available resources and priorities.

3.7.1   RSP

The progress of EOPOs 1-3 is as expected, and for EOPOs 4-5 somewhat less than expected (*see Table 2*).

Table 2: RSP – Progress against EOPOs

EOPO	Progress
EOPO 1: Improved NRA regulatory practices and systems that have addressed deficiencies identified through WHO GBT assessments, TGA in country/virtual missions and NRA priorities.	As expected
EOPO 2: Increased use of reliance and/or work sharing mechanisms by NRAs to improve regulatory efficiency and collaboration.	As expected
EOPO 3: Registration without undue delay of new and priority products by NRAs for infectious diseases.	As expected
EOPO 4: Improved coordination between NRAs, national disease programs and relevant stakeholders, to help ensure timely access to new products.	Somewhat less than expected
EOPO 5: Improved coordination of regulatory strengthening activities with other partners working in the region.	Somewhat less than expected

The evidence for these ratings is as follows:

EOPO 1: There is evidence that TGA addressed priorities identified by country partners and in country/remote missions.

EOPO2 & EOPO3: There is evidence that reliance mechanisms were used by TGA in collaboration with some partner NRAs, such as the examples of the registration of tafenoquine and the HIV products in Thailand, chloramphenicol in PNG and the COVID-19 vaccines in multiple partner countries (AETAP-RSSM).

EOPO4: There is some evidence of coordination between TGA and NRAs, MoHs, PDPs, WHO and others in the registration of new products. However, this evaluation found that the coordination particularly between TGA, PDPs, WHO and some NRAs/MoHs could be strengthened. Coordination between national disease programs and NRAs is beyond the control of TGA – this EOPO could be reworded in the next phase of activity.

EOPO5: There is evidence that TGA has placed significant effort in communicating with its partners USP and CoRE, WHO (Headquarters, regional and country offices) and has had some meetings with BMGF, ASEAN mechanisms, PDPs and other stakeholders. While it is acknowledged that the level of engagement needs to be balanced with resources put into technical work, this evaluation found that in some instances proactive communication between TGA and other stakeholders could be improved and strategic collaboration with a longer-term vision could be strengthened, leading to a more coordinated approach to regulatory strengthening in the region.

3.7.2   AETAP-RSSM

The progress of EOPOs 1 and 4 is as expected whereas for EOPO 2 this is somewhat less than expected and EOPO 3 significantly less than expected (*see Table 3*).

Table 3: AETAP-RSSM – Progress against EOPOs

EOPO	Progress
EOPO 1: Greater assurance of the quality, safety and efficacy of COVID-19 vaccines that have been introduced into partner countries	As expected
EOPO 2: Improved capacity of national immunisation programs to deploy regulated COVID-19 vaccines in partner countries in a timely manner	Somewhat less than expected
EOPO 3: Improved systems and processes that are fit for purpose for the ongoing safety monitoring of COVID-19 vaccines in partner countries	Significantly less than expected
EOPO 4: AETAP-RSSM's collaborations and support for the access and safety monitoring of COVID-19 vaccines is valued by partner countries	As expected

The evidence for these ratings is as follows:

EOPO1 – There is clear evidence that TGA supported evaluation processes to ensure that COVID-19 vaccines were introduced into partner countries that had been assessed as products of high quality, safe and efficacious by the TGA, such as the introduction of AstraZeneca produced by CSL into Indonesia, Fiji and PNG.

EOPO2 – While there are clear examples where TGA supported a partner country's immunisation program to gain access to COVID-19 vaccines, timely access was not always possible. However, this was often not in TGA's control and was due to multiple other factors including availability of vaccines, the ability of DFAT and other donors to be responsive to the demands of partner governments and the existence and efficiency of national deployment systems and processes for vaccines once they were delivered in-country.

EOPO3   While EOPO 3 is an appropriate health systems strengthening outcome for TGA's work, VAHSI-funded programs were designed neither for health systems strengthening nor to achieve sustainable outcomes. Given the long-term nature of regulatory strengthening work, plus the short 2-year timeframe of AETAP-RSSM, EOPO 3 appears to be unrealistic and so full achievement of this EOPO would not be expected. This EOPO could be incorporated into a design of a new phase of TGA's work.

EOPO4 – There is evidence that TGA's support was valued by partner governments, particularly where TGA facilitated rapid approval of COVID-19 vaccines into countries. In addition, as noted earlier, there were significant impacts on operational delivery of key elements due to COVID 19 impacts on in country visits and training.

3.8   Future monitoring of progress against EOPOs

In order to achieve most of the EOPOs, TGA could place increased attention to coordination between themselves, NRAs/MoHs and other stakeholders working in regulatory strengthening/support in the region. They could also continue to support registration of COVID-19 vaccines as needed, although the demand for this support is likely to decrease. Given the short-term duration and responsive nature of AETAP-RSSM, it is not expected that

EOPO 3 will be achieved, and this should be accepted by DFAT, or the EOPO modified so that it better reflects the nature of support activities under AETAP-RSSM.

4. Options for forward planning

This section starts by examining the current regulatory landscape in the Indo-Pacific in order to contextualise the subsequent options that are outlined for a future five-year TGA-DFAT partnership commencing in 2023.

4.1 Regional regulatory landscape overview

USAID funded PQM+ Program led by The United States Pharmacopeia (USP) has undertaken a comprehensive review - the *Regulatory and Quality Assurance Landscape of South and Southeast Nations* (7 Feb 2022). This has been shared with the TGA and DFAT and forms the basis for this overview. In the report, the reviewer based their assessment upon analysis of responses to a range of questions based on the following selected key WHO GBT functions of an NRA:

• GBT 01: National regulatory system (RS)

• GBT 02: Registration and market authorization (MA)

• GBT 04: Market surveillance and control (MC)

• GBT 05: Licensing establishments (LI)

• GBT 06: Regulatory inspections (RI)

• GBT 07: Laboratory access and testing (LT)

The questionnaire findings were grouped into two main categories: (1) the legal and regulatory framework, which forms the basis of all national regulatory functions and (2) factors that contribute to the effectiveness of the NRA.

Developing countries' NRAs face many complex challenges reflecting a host of technical, managerial, resource, and other constraints. However, developing countries have made significant strides in strengthening both the organisational structures and functions of their NRAs. Where these NRAs fall within the current regulatory and quality assurance landscape was the object of the report.

Country engagement in TGA programs

There are only 3 ML3 NRAs recognised in the region and the option of these NRAs working alongside TGA in a next phase to strengthen regional regulatory capability has significant potential.

The PQM+ Program report notes that all countries it assessed have legal provisions, regulations, and guidelines for MA of medical products. These regulations require manufacturers to: provide relevant data related to safety, efficacy, and quality; define types and scope of variation and documentation; and authorise NRAs to withhold, suspend, withdraw, or cancel MA due to quality or safety issues. Furthermore, regulations in nearly all countries exempt certain products from routine MA procedures. These include pandemic medical products (e.g. vaccines), donated medicinal products, and products that use decisions or information from other NRAs. There are variations in the legislative details contained in these regulations and the effectiveness of implementation; however the underlying legal and executive framework is generally present.

The PQM+ program landscape analysis report of the region notes a range of agencies, NRAs and NGOs that are engaged in diverse regulatory and medicines support activities. Some of the key engagements are noted in Table 5 below.
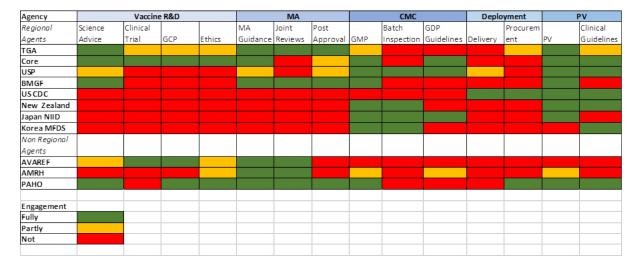
Table 4: Providers of regulatory strengthening within and outside the Indo-Pacific region and the areas of activity (extensively adapted from PQM+ Survey version)

Agency	Vaccine R&D				MA				CMC		Deployment		PV	
Regional Agents	Science Advice	Clinical Trial	GCP	Ethics	MA Guidance	Joint Reviews	Post Approval	GMP	Batch Inspection	GDP Guidelines	Delivery	Procurement	PV	Clinical Guidelines
TGA	Green	Yellow	Yellow	Yellow	Green	Red	Yellow	Yellow	Red	Red	Red	Yellow	Green	Yellow
Core	Green	Red	Red	Green	Green	Red	Green	Green	Red	Red	Red	Green	Green	Green
USP	Yellow	Red	Red	Red	Yellow	Red	Yellow	Green	Red	Red	Yellow	Red	Green	Green
BMGF	Green	Red	Red	Red	Red	Red	Red	Red	Red	Red	Red	Red	Green	Green
US CDC	Red	Red	Red	Red	Red	Red	Red	Red	Red	Red	Green	Green	Green	Green
New Zealand	Red	Red	Red	Red	Red	Red	Red	Green	Green	Green	Green	Green	Green	Red
Japan NIID	Red	Red	Red	Red	Red	Red	Red	Green	Green	Green	Green	Green	Green	Red
Korea MFDS	Red	Red	Red	Red	Red	Red	Red	Green	Green	Red	Red	Red	Red	Green
Non Regional Agents														
AVAREF	Green	Yellow	Green	Yellow	Green	Red	Red	Yellow	Red	Yellow	Red	Red	Red	Red
AMRH	Red	Green	Green	Yellow	Green	Green	Green	Yellow	Green	Yellow	Green	Yellow	Yellow	Green
PAHO	Green	Red	Red	Green	Green	Green	Green	Green	Red	Red	Green	Green	Green	Green
Engagement														
Fully	Green													
Partly	Yellow													
Not	Red													

Table 4 lists key agencies/agents PQM+ program has noted as being engaged in regulatory strengthening in the region. Some other global agencies in the Africa and South American region are included for comparison. The table shows that the majority of strengthening support activity by these agencies/providers is focused on MA, CMC and PV.

4.2 Key needs and gaps

The PQM+ program report provides their view on key needs in the region which are outlined below:

- Future support in a sustainable fashion for NRA strengthening is critical, with a focus on safety of medicines and biologics. This includes safety monitoring,

pharmacovigilance systems and processes, and developing reporting systems and action plans.

- To better enable NRAs to fulfil their functions, strengthening both the technical capability and regulatory maturity of the NRAs in the region is needed through regional activities and bilateral engagement.
- There is a need for improved cooperation between delivery partners, both at the level of operational delivery as well as cooperative engagement with country partners, at senior government as well as NRA levels.
- There are clear gaps in capability, often due to simple, but hard to fix factors, such as staffing levels, degree of functional expertise and technical experience. For example, in 11 of the regional countries assessed by PQM+ program, 3 have sufficient staff, 6 are understaffed, and 2 are needing to recruit.

4.3 Gender equality

Effectively addressing the needs of women and girls is a cross-cutting priority of Australia's development program, as indicated in DFAT's Gender Equality and Women's Empowerment Strategy. The Strategy acknowledges that health programming for women is more effective when it is led by women and that women's priorities must be taken into account in program design.

At a global level, there is a growing focus on equity within international strategies, policies and practice including those related to regulatory strengthening. Sex and gender considerations have been included in the World Health Organisation's Global Benchmarking Tool for the evaluation of national regulatory systems. Sustainable Development Goal 5b commits all UN member states to ensuring women's access to all benefits of scientific development, including development of therapeutic products and new medicines. One of the principles in the Sydney Statement on Global Health Security, recently affirmed at the Global Health Security Conference in Singapore (June-July 2022) states that interventions must be inclusive and equitable. Addressing and then monitoring and evaluating steps to address gender equality within TGA programming going forward will be important.

Based upon the evaluation findings a future TGA-DFAT partnership will need to involve the strengthening of activities to address gender equality. While gender equality will likely remain a secondary objective of TGA activities, there are ways in which TGA could strengthen how it is addressed. These could include mainstreaming gender equality in training activities, actively training in considerations of specific medical product safety issues relating to women and encouraging local research on this to inform regulatory practice. TGA could continue to encourage country partners to collect sex disaggregated data and to use this data to guide decision-making by embedding the process in standard operating procedures. It could proactively support women in regulatory leadership and decision-making roles by identifying enablers and barriers to accessing these roles and steps TGA could take to address these. It could encourage partner organisations to adopt policies,

strategies and guidelines that promote gender equality and/or are informed by gender analyses.

A consultant is about to start a GEDSI analysis of TGA's work and will provide recommendations which could inform the design of future activities. It is likely that TGA will also need to develop a gender equality strategy for a new TGA-DFAT partnership. Partner country perspectives of gender equality, gender norms and sensitivities will need to be taken into consideration and strengthening the capacity of the TGA team to systematically address gender equality in all aspects of their work will be required.

4.4 Disability and social inclusion

Adjustments have been made in the TGA workplace and to virtual webinars to enable participation of people with disabilities. However, TGA acknowledges that more could be done to address disability and social inclusion through their programs and this will be guided by the results from the upcoming GEDSI analysis. This can inform the design of future work, with specific activities to address disability and social inclusion and particularly for at-risk populations. Building the capacity of the staff at TGA to integrate disability considerations into their work will be required.

4.5 Indigenous peoples

It is likely that a future TGA-DFAT partnership will need to consider whether and how activities may impact on, or enhance the interests and health of, Indigenous people and communities, particularly work in partner countries.

5. Scoping considerations for a future TGA-DFAT partnership

Based upon the findings in this report, there would be significant value in DFAT funding a future partnership with TGA in regulatory strengthening in the Indo-Pacific.

This section outlines a series of key considerations for this new partnership over five years following the completion of the RSP and AETAP-RSSM programs. The considerations are based upon the evaluation findings, the landscape and needs gap analyses, the document review and interviews and written comments.

The existing projects will continue until mid-2023. This provides a clear window for future planning and provides an opportunity for high-level coordination discussions to be initiated between TGA and DFAT and with partners.

EQ3

5.1 Strategic planning

A significant finding is that an overall strategy for the upcoming work of TGA over the next 5 years is a critical first step. The development of a targeted strategy for a future TGA-DFAT partnership could provide a clear vision, goal and operational and priority framework for activities as well as alternative pathways of delivery in the face of further complex developments in the region. Built into this strategy will need to be activity priorities, short, medium and long-term anticipated outcomes, known operation restrictions and areas of flexibility. This strategy will need to acknowledge and set out TGA resources and strengths, as well as areas of lower priority. A strategy provides a delivery framework which facilitates prioritisation and indicates the balance of response mode and planned regulatory strengthening activities. It could also describe resource management, longer-term strategic planning, coordination and communication with other actors (through co-development of these sections) and engagement strategies.

It is recommended that such a strategy is developed in partnership with DFAT, and in collaboration with DFAT's related, existing partners (e.g. USP and CoRE), providers of regulatory strengthening activities and country partners. In particular this should include the engagement of stronger partners in the NRA and provider environments. It is recognised that a strategy will require adaptation to each partner country's capacity for medium to long strategic regulatory planning.

Key points for consideration in developing the strategy

The following could be the key components of the strategy:

- Vision, goal and end of program outcomes
- Scope of work
- Tiered programming

- Regional cooperation including regulatory convergence/harmonisation
- Information technology
- Ways of working
- Providers forum for regulatory strengthening
- Partnership between DFAT and TGA
- TGA organisational considerations
- Monitoring and evaluation.

These points are expanded upon below.

The strategy and operational plan to implement the strategy could also consider the following aspects of programming: governance, human resourcing, budget, year on year activities, risk management and program management.

5.2 Vision, goal and end of program outcomes

The vision and goal need to align with global and regional trends in health security and pandemic preparedness, the new Australian Government's regional and ODA priorities, the strategic direction of TGA and the goal of the future phase of DFAT programming.

They could consider TGA's contribution to strengthening partner country regulatory capacity and improved regional co-operation to ensure the production, distribution and timely access to quality and safe medical products in the Indo-Pacific region.

Anticipated end of program outcomes should be part of the strategy.

5.3 Scope of work   EQ4

The scope of the training and engagement activities of TGA's programs to date has been extensive. However, there has been a clear focus on targeted regulatory strengthening, both with response mode engagement on specific country requirements as well as wider response activities involving the COVID-19 vaccine rollout. This has involved more complex interactions including joint product reviews for Emergency Use Applications as well as deeper information sharing agreements including dossier review considerations and scientific advice as needed. This country-specific approach is highly valued and should continue, as there are other actors such as the WHO and CoRE that are providing more general regulatory strengthening in the region.

The proportion of on-call regulatory strengthening and support through training, advice and targeted product reviews (so called response mode engagement) as against a more regional and longer-term delivery plan with a view to strategic regional outcomes should be agreed and clearly outlined in the strategy. This should sit alongside alternatives and responses learnt from COVID-19, in the event of further disruption.

A recommended balance could be 70% strategic and planned activities and 30% responsive, on-call programming.

The work TGA has already completed in conducting both targeted regulatory strengthening in response to need, as well as building an understanding of thematic gaps in capacity that could be addressed strategically and systematically in the future is acknowledged. Both response mode as well as more strategic regulatory strengthening activities such as embedding regulatory culture, PV and AEFI reporting models etc. will be required and can continue to build upon the foundations TGA has already established.

In terms of technical areas, TGA should continue to provide country-level technical assistance in the core areas of MA, GMP and PV, as required by countries (*see 5.4 programming considerations below*).

Depending on the resources available and prioritisation in the strategy, TGA could consider limited TA in advanced therapeutics, biologics, substandard and falsified medicines and continuing its regional leadership role that currently involves a TGA staff member as Chair of the WHO Member State Mechanism Steering Committee on Substandard and Falsified Medicines), and scientific advice for early new product development in response to planned increases in manufacturing capability in the region.

5.4 Programming considerations

Targeting country specific needs in regulatory strengthening will require a balance between the day-to-day operational needs of the NRA/MoHs and the larger strategic view in supporting an increase in the overall maturity level of the NRA or relevant government department. This complex balancing act will benefit from the continuation of a tiered, country-specific technical assistance framework taking into account the existing maturity level of the NRA or regulatory capacity of the MoH, along with due regard to regional public health priorities, receptiveness to TGA's support and capability gaps. These plans are critical to ensuring NRA/MoH and partner government engagement and relevant TA delivery. It is acknowledged that TGA has already been operating using a tiered approach model. The approach recommended here could consider the following:

- **ML3 NRAs:** Where many of the key operational functions are established, technical support, while still needed, becomes less of a priority. In such instances overall strategic regulatory thinking around MA priorities and the risk management arguments to be considered for MA are likely to be of a higher priority in terms of overall benefit to the NRA going forward.

In additionTGA could be actively partnering with identified NRA's in the provision of regulatory strengthening to other NRAs in the region. Using this approach, these NRAs could be both providers and recipients of TA with the TGA both building the capacity of these regulators in the provision of TA to others, while continuing to provide support in areas which lack capacity. This represents a sustainable approach supporting South-South collaboration in the region.

- **NRAs at ML 1 or 2**: Where some or many functional areas are weak or where there is no functional NRA, then targeted process and product specific training in technical aspects and co-development of processes and procedures for specific regulatory functions is more likely to be appropriate. Where a more comprehensive strengthening program is planned, inputs by multiple providers of regulatory strengthening may be more appropriate, bringing together strengthening of a number of aspects of related regulatory function to provide a pathway towards a coherent, strengthened national service.

- **Stand-alone activities:** The NRA functional areas in the WHO GBT listed in section 4.9 above cover the key operational areas of an NRA. They are distinct functions but when combined and integrated can result in a mature, high functioning NRA. However, key elements (such as MA in particular) can almost stand alone and provide limited, but vital functions for access to key medicinal products of high priority, particularly where resources and capability are constrained or NRA maturity/MoH capacity level is low.

- **Regulation of manufacturing:** Establishing autonomous manufacturing capability is becoming a priority for many countries in the Indo-Pacific region, as issues with cost and supply chain concerns become more pressing. Where there are sub-regional platforms, or coalitions of countries of interest, then the possibility of regional manufacturing capability becomes a real possibility. This raises the future requirement for operational regulatory oversight of manufacturing capability and ongoing assessment of compliance. Although not a critical gap or need at this point, this area will grow in importance in the near future and interviewees (NRAs including mature NRAs) cited a need to build onsite and desk-based compliance assessment capability now, in order to be ready for when manufacturing capability increases.

- **Geopolitical:** Like all development assistance and interaction between countries, Australia's support for regulatory strengthening in the region takes place in a geopolitical context. Geopolitics has had a more pronounced impact on global health in recent years, particularly during the COVID-19 pandemic (for example – see link here Geopolitics and Global Health). DFAT and TGA should continue to monitor the geopolitical context and its impact on the region's regulatory environment and the program.

EQ5

5.5 Regulatory cooperation

There was a perceived need among interviewees for closer sub-regional engagement which could facilitate both accelerated MA for high need public health products as well as improved product safety and characterisation (detecting falsified medicines for example). This is a complex area and there is clear recognition by the partners of the complexity of this vision and need for long-term planning and development. However, a number of significant steps have already been made with the development of regional reliance and common recognition processes. These can have regional impacts on speed of access to new drugs for local high priority health needs. For example, the ACTD (ASEAN Common Technical Document) and other initiatives have been in play for some time. Although traction is variable, there is support in the region and guidance, support and advice from the TGA and DFAT as to the regional public health benefits of the ACTD could help to further embed this process in a sustainable fashion. The Providers' Forum *(see 5.8 below)*, if established, could further engage with this process.

The benefits on facilitating approval of a wide range of country and region-specific high priority medical products is understood and has gained significant traction through the COVID-19 experience. During the COVID-19 pandemic, significant barriers to co-operation were reduced or eliminated as countries and others recognised the risk to public health through failure to accelerate access to critical vaccines. Joint reviews of MA dossiers, awareness of the power of common recognition processes, increased in-depth information sharing along with formal structures through MoU's to facilitate such sharing, became a reality.

It is recognised that the capability for engagement in this longer-term strategy of regulatory cooperation will vary according to NRA/regulatory maturity. This will likely operate much like the tiered approach noted in 5.4 above. It is important to note that the proposed Regional Providers' Forum *(see 5.8 below)* may be a core facilitator of regional regulatory cooperation. How the TGA and DFAT partner to manage these complex issues is expected to be detailed in the strategy.

There is potential for greater involvement of ML3 NRAs in this process, both in terms of partnering with TGA to provide TA to other NRAs in the region *(see 5.4 above)* and also to continue to take a leading role in regional mechanisms such as the ASEAN JACG.

There is support across the region for engagement in processes, agreements or partnerships that could facilitate regulatory load sharing among NRAs, supporting weaker NRAs and MOHs without a regulator in gaining safe access to public health priority products, and filling gaps in NRA resources/capabilities.

Risk management in the MA process is a complex process which, for weaker NRAs, benefits from input from stronger NRAs where these processes have been worked through for high-risk complex therapeutics. Importantly the process of risk management is context specific,

balancing the specific national public health issue, aspects of relationships between individual countries prescribing practices, dispensing intersections, infrastructure along with the medical product being considered and both regional and local pressures. Engagement by the TGA in this space, initially with strong NRAs in the region, could embed the rationale and underlying risk calculus processes into regulatory thinking. This is an important capability which will become more so as potentially disease specific drugs/antivirals or similar products come onto the horizon for region specific diseases. Small molecules and pharmaceuticals pose a less complex regulatory assessment pathway than biologics, advanced therapeutics or personalised medicine, however issues around falsified medicines and substandard products remain areas of significant national and regional concern. Moreover, NRAs in the region may soon be required to assess advanced therapeutics which require complex risk benefit analyses. Consideration should be given within the strategy to the possibility of TGA engaging in this space, helping to establish the most effective balance between direct capability and reliance relationships in the region.

5.6 Information technology

Information technology (IT) is critical infrastructure needed to support development and policy frameworks, enabling the potential of regional regulatory data hubs so that decisions, processes and outcomes of MA reviews as well as clinical study enquiries etc. can be shared safely.

High-level political and regulatory NRA-level engagement could provide pathways to political recognition of the functional importance of compatible IT systems, both internally across all functions of an NRA, as well as regionally between NRAs. Maintaining a common benchmarked IT capability allows for increased integration of regulatory data management both nationally and in the region. The impact of limitations of information technology cannot be overstated and the need to move away from paper-based systems to eCTD (Electronic Common Technical Document) type approaches will have significant benefit to regional convergence of systems and regulatory processes. In conversation with TGA it has been noted that a number of NRAs still predominantly use paper-based systems and the feedback indicates that key information can be difficult to ascertain e.g. current status in process, key data areas in dossiers, even point of contact channels with sponsor and manufacturer etc. Moreover, where IT systems and regulatory software are compatible or conform to recognised standards, information sharing and a common understanding of decisions between NRAs becomes more straightforward.

DFAT and TGA are currently engaged in this space in targeted ways. However, there is opportunity to assess where working with other provider partners may bring a more

coordinated regional software acceptance plan into place. While it is recognised that the TGA is not in a position to support any specific IT package, its expertise in advising on the risks and benefits of a particular approach, and facilitating a compatible IT environment in the region is valued and needed.

Integrated regulatory software could result in the following benefits:
- Reduced authorisation timelines through start to end documented and live tracking of MA applications, reducing loss of reporting and response requirements, and indeed in some instances loss of the application entirely.
- Live traceability of applications, notification and flagging of approval and authorisations, live data updates to dossiers and post marketing data and managing ongoing CMC or Quality Control (QC) issues.
- Robust systems for PV and AEFI reporting, response warnings and follow up. This enhances the safety of medicines.
- Reporting and response systems for ensuring data flagging of poor quality drug identification, falsified medicines, falsified approval history, dossier falsification, and providing track and trace response capability.

5.7 Ways of working

The need for improved communication and coordination has been a repeated theme raised during this evaluation/scoping work, and it is recommended this is explicitly addressed as part of the new strategy.

It is important to recognise that face-to-face visits and extended visits, both in-country and Canberra were seen as vital, acknowledging the disruption of COVID-19 to this type of activity. These face-to-face activities need to be continued in a strategic manner, taking into account response mode activities.

Information sharing and extending the scope of MoUs or agreements between NRAs/MoHs and other government departments to facilitate different types of information exchange were also seen as a gap. Actions taken during COVID-19 to reduce these barriers were acknowledged. Further action in this area is needed.

5.8 Regulatory providers' forum

A regulatory providers' forum would be a mechanism to extend partnerships and regional thinking between agencies involved in the provision of regulatory strengthening activities. While there are existing communication channels between many of these actors, greater communication and strategic coordination between a wider group of agencies would be beneficial to all parties.

A forum process, or cooperative collaboration approach, could help to coordinate activities in regional regulatory strengthening, medicines safety, supportive funding, direct engagement, training provision and other areas. It could identify overlaps or duplications and coordinate targeted support in countries. This concept could also enhance and support the development of regional hubs, through bodies such as ASEAN, WPRO or SEARO. Providers that could be involved include: TGA, USP, CoRE, WHO, USAID, BMGF, the Asian Development Bank (ADB), PMDA (Japan) MFDS (South Korea), NZ Medsafe. Others may wish to be engaged in the future.

There was strong support among interviewees (donors, DFAT, BMGF, WHO) for the development of this concept of a regulatory providers' forum.

The need for strategic and cooperative engagement between relevant funding and direct support agencies to fill priority regional needs is clear. The potential benefit of peer-to-peer engagement with ML3/4 NRAs to develop regional hubs of best practice that will result in a cascade of best practice processes "down" and across the region is widely acknowledged.

While they are not providers or funders of regulatory strengthening activities, other organisations that TGA could continue to collaborate and communicate with include Medicines for Malaria Venture (MMV), the Asia Pacific Leaders Malaria Alliance (APLMA), Path, TB Alliance and the Foundation for Innovative New Diagnostics (FIND).

5.9 Partnership between TGA and DFAT

Health security, including continued infectious disease control as well as pandemic preparedness, has become a priority discussion in the region, including an increase in urgency for regional regulatory strengthening. These are politically relevant discussion points and useful "hooks" for engaging at the political level on regional regulatory strengthening.

There is potential for an enhanced peer to peer partnership between DFAT and TGA in the next phase of DFAT health security-related funding to support a range of activities that the TGA would find more difficult to implement if acting alone. This partnership would require an increase in DFAT's support for the work of TGA above what has been the case under RSP and AETAP-RSSM, primarily through enhanced political engagement and human resources (time required by Global Health Division (GHD) staff and posts). DFAT's enhanced support could include:

- Engaging with PICs for ongoing TGA TA and liaison with the DFAT sections responsible for the Pacific Medicines Testing Program (PMTP). The sharing of cross program learning, synergies and relationships could be strengthened between DFAT and TGA staff working on PMTP and TGA's new activities.

- Conducting high level diplomatic meetings with the relevant ministries of Japan, Korea, US, NZ, and with organisations such as BMGF, ADB and WHO to facilitate a coordinated and optimised range of regulatory inputs into the region, targeting gaps and needs.
- Meeting with ministries of health and/or relevant departments in partner countries, particularly where TGA has had limited engagement and would like this to increase or where there is existing bilateral health programming. This could include TGA-DFAT joint travel and engaging and equipping DFAT posts with the information needed for active involvement. This engagement with DFAT posts could include:
    - involving them in country-level planning under a new TGA-DFAT partnership, particularly in countries where there is bilateral health programming
    - providing background information on the new TGA-DFAT partnership
    - providing a briefing note on how post could support the specific work planned by TGA in a country which could include discussion points for posts in their meetings with the MoH/NRA and the required outcomes of the engagement and/or brokering meetings for TGA with government and other DFAT in-country partners
    - seeking input from posts as to how to best engage with regulators/MoHs where there are challenges, and
    - developing country case studies describing the practical ways in which posts have supported the work of TGA in other countries and the outcomes achieved to build posts' understanding of the ways they could support TGA.

    This work with posts could be effective when combined with TGA engaging simultaneously (where feasible) with national regulators - helping to increase engagement and achieve regulatory 'quick wins' in order to increase political support for such regulatory collaboration.
- Contributing to coordination between PDPs and TGA (through a DFAT program which funds PDPs). This would be particularly useful for coordinating plans for the PDPs to lodge product applications in partner countries and TGA's support for product registration processes.
- Contributing to coordination between mSupply and TGA, with a view to encouraging convergence of Regulatory IT systems.
- Sharing of information and expertise on country and regional trends.

This enhanced support by DFAT needs to align with the approach, resourcing and staffing in the design of a future phase of the Health Security Initiative. It will also need to be coordinated and align with DFAT's wider engagement with partner governments in the Indo Pacific.

5.10   TGA organisational considerations

There is potential for cross engagement between DFAT and TGA, with a structured plan for placements TGA to DFAT and/or DFAT to TGA to better inform both agencies as to the culture, language and priorities in each other's operating environment. For example,

secondments/placements could be for a set period of time or a member of staff could spend one day a week in the other agency and vice versa. This has time and resource implications; however, the benefits have been strongly supported by a number of the interviewees in DFAT and TGA and are recommended in this report. This recommendation is subject to the practical and functional issues these placements may raise.

A further option would be to hold regular TGA-DFAT senior management meetings to discuss progress, regional trends and opportunities and program risks. These meetings could include geographic and other DFAT leads where relevant.

6. Risk management (SWOT)

This matrix provides a high-level view of key strengths, weaknesses, opportunities and threats (a so-called 'SWOT assessment') for a future TGA-DFAT partnership. It provides a high-level quick overview of the projected landscape and areas of benefit and concern, with pointers to possible mitigation areas. This SWOT analysis informed the ratings given to the recommendations below and could inform the development of the strategy for a future TGA-DFAT partnership.

Strengths

- Improved safety of medicines in region
- Faster approvals, stronger evidence-based approvals based around TGA strengths
- Regional harmonisation and potential recognition processes (feeds into above)
- Resource management and skills sharing
- Trust building – TGA as a trusted resource.

Weaknesses

- Country-specific engagement variable between govt and NRA MoH
- Funding timeline limited
- TGA capacity to deliver in some areas
- Appropriate skillsets for political/regional engagement
- Country sensitivities

Opportunities

- Faster approvals of priority medicines
- Improved safety of medicines in region
- Enhanced regional convergence and improved recognition processes
- Change in political landscape around Australia's engagement in Asia Pacific
- High public awareness of the role of regulators due to COVID-19 vaccines
- Resource management and skills sharing

Threats

- Australian interaction in the region can be positive and negative
- Regional issues that affect engagement
- Change in political landscape around Australia's engagement in Asia Pacific
- Sustainability of TGA's funding and engagement as well as of its regulatory strengthening activities

7. Key recommendations

Strengthening the regulatory capacity of partner countries in the Indo Pacific is a long-term exercise. Due to the sensitive nature of collaboration in the regulatory context, particularly where it involves the sharing of information, strong working relationships based upon trust need to be established before detailed technical assistance and support can be provided. This has taken time for the TGA and is still a work in progress. As a result, outcomes for RSP/AETAP-RSSM have been limited. Despite this, and given the long-term nature of regulatory strengthening, this evaluation has found that there is significant technical and strategic value as well as potential for impact in continuing the work of TGA in the Indo Pacific.

Based upon the findings in this report, it is recommended that DFAT funds a future TGA-DFAT partnership for regulatory strengthening activity in the Indo-Pacific. The following recommendations are mainly focused on this new partnership following the conclusion of RSP and AETAP-RSSM. Each recommendation is given a series of ratings based upon need, feasibility, potential for impact and timeframe *(see explanatory table below)*. More than one rating is given for some recommendations. The **priority** rating in the last column is based upon a combined assessment of the ratings in the preceding four columns.

Explanation of Ratings

Rating	Explanation
Need	This is the need of countries within the Indo-Pacific region. Ratings are high, medium and low.
Feasibility	This is the feasibility of TGA conducting, addressing or being involved in an activity. Ratings are high, medium or low.
Potential for Impact	This is the potential level of impact that the activity could have on a country, the Indo-Pacific region or TGA itself (for recommendations 6 & 7). Ratings are high, medium and low.
Timeframe	This is the timeframe for achieving change in the recommended activity. Ratings are long (5-10 years), medium (2-5 years), and short (1-2 years).
Priority	This column considers the ratings in the preceding four columns, and then rates the priority for TGA's programming as either high, medium or low.

#	Recommendation	Need	Feasibility	Potential for Impact	Timeframe	Priority
1	Strategy: TGA and DFAT to develop a five-year strategy for a new TGA-DFAT partnership funded by DFAT, incorporating elements that will continue from both RSP and AETAP-RSSM. The strategy could include: • Clear vision, goal and anticipated end of program outcomes in regulatory strengthening that align with the goal and objectives of DFAT's next phase of health security programming and takes into account pandemic preparedness • 10-year stretch objectives • Sections for strategic planning with CoRE, USP, mSupply and NCIRS The strategy could also incorporate recommendations 2a to 5 below.	HIGH	HIGH	HIGH	MEDIUM	HIGH
2a	Scope of work Technical areas: TGA to continue to provide country-level technical assistance in the core areas of MA, GMP and PV. : Merge activities provided under RSP and AETAP-RSSM. : Consider limited TA in advanced therapeutics, substandard and falsified medicines : Include a long-term planned approach to GEDSI.	HIGH	HIGH	HIGH	SHORT TO MEDIUM	HIGH
2b	Types of programming: TGA to maintain a tiered, country-specific technical assistance framework taking into account the existing maturity level of the NRA or regulatory capacity of the MoH, along with due regard to regional public health priorities. : Establishing autonomous manufacturing capability is becoming a priority for many countries in the region.	HIGH	HIGH	HIGH	SHORT TO MEDIUM	HIGH
2c	Regulatory cooperation (convergence, reliance, harmonisation etc): TGA to support existing processes for regional regulatory cooperation, including the ASEAN JACG and the WHO Pacific Sub-Regional Platform. : TGA, with DFAT's support, to work towards supporting other NRAs in the region as a more sustainable model of regulatory strengthening. : TGA to work with DFAT in providing input on any proposed regulatory legislative changes in partner countries that support convergence.	MEDIUM	MEDIUM	HIGH	MEDIUM TO LONG	MEDIUM

#	Recommendation	Need	Feasibility	Potential for Impact	Timeframe	Priority
	: DFAT to collaborate with other donors to strengthen regulatory cooperation through the regulatory providers' forum (see below). : TGA to assess how to support the ASEAN Common Technical Document process. : TGA to support building of common capacity and understanding on risk management and assessments for MA of new products and PV planning.					
2d	Information technology: TGA to support and advise on the implementation of IT systems used to facilitate compatible regulatory processes where possible. This could include continued work with mSupply and contributing to early steps for a joined-up data base on regulatory decision making. Early steps could include TGA agreements for sharing documents bilaterally or between sub-regional groups of countries.	MEDIUM	LOW TO MEDIUM	MEDIUM TO HIGH	MEDIUM TO LONG	LOW TO MEDIUM MEDIUM
3	Ways of working: TGA to continue to build working relationships and trust and increase face-to-face engagement with country partners through in-country visits and capacity strengthening and forums in Australia. : TGA and DFAT to clearly define the proportion of time and resources spent on planned activities (systematically building regulatory capacity which could increase in a future partnership with DFAT) and responsive requests. A 70% planned (building upon previous responsive support), 30% on-call split might be appropriate. : TGA to strengthen regular communication and coordination with DFAT partners USP and CoRE, including through joint design of relevant elements of the strategy. : TGA and DFAT to capitalise on the current high profile and awareness of the role of regulators and advantages of NRA collaboration generated by the COVID-19 response, and the new government's high interest in the Indo-Pacific region to foster high-level Australian government support for TGA's work, increased engagement with some partner countries and NRA/partner government buy-in to NRA collaborative processes.	HIGH	HIGH	HIGH	SHORT TO MEDIUM	HIGH

#	Recommendation	Need	Feasibility	Potential for Impact	Timeframe	Priority
4	Regulatory providers' forum: TGA and DFAT to initiate a regulatory providers' forum, together with other actors such as WHO, BMGF and USP. This forum will coordinate regulatory strengthening activities, including training and support and cooperative regulatory processes such as reliance, in the Indo Pacific. Such a forum would include MFDS (South Korea), NIID (Japan), NZ MedSafe and others funding and conducting activities in the region.	HIGH	HIGH	HIGH	SHORT	HIGH
5	Partnership between TGA and DFAT: Strengthen the partnership approach between DFAT and TGA, including the allocation of greater resourcing from DFAT (GHD program management and time spent by posts) by: - GHD engaging posts in country-level planning of a new TGA-DFAT partnership and brokering meetings with MoHs/partners; and GHD providing background information to posts on how to support the work of TGA. - DFAT specifically engaging with PICs for ongoing TGA TA and facilitating cross program learning with PMTP. - DFAT facilitating TGA support for ASEAN JACG and the WHO-coordinated Pacific Sub-Regional Platform. - DFAT conducting diplomatic meetings (Japan, Korea, NZ, US etc.) to optimise regulatory inputs and coordination in the region. DFAT to enhance coordination (where appropriate) with other relevant DFAT-funded programs – e.g. PDP Fund, mSupply, NCIRS so that there is increased visibility of planned activities and where each partner can add value to the other.	HIGH	MEDIUM TO HIGH	HIGH	SHORT TO MEDIUM	HIGH
6	TGA organisational management: Increase the knowledge and experience of development and culturally responsive practice within the TGA team in order to strengthen work with country partners. : Explore organising the secondment or placement of a TGA member of staff into DFAT's Global Health Division or having a DFAT member of staff seconded/placed in TGA for a limited period/regularly to improve mutual	MEDIUM	MEDIUM	MEDIUM TO HIGH	SHORT TO MEDIUM	MEDIUM TO HIGH

#	Recommendation	Need	Feasibility	Potential for Impact	Timeframe	Priority
	understanding of activities and ways of working, as well as in development practice through closer work with DFAT.					
7	Measuring outcomes: Use the robust monitoring systems established by TGA to increase focus on measuring and reporting on interim and end of program outcomes for the remainder of this phase of activity and ensure that MEL systems for a future TGA-DFAT partnership continue to emphasise the monitoring of outcomes. : In the MELF for a future partnership with DFAT, include an indicator to measure the value of TGA's partnerships with regional stakeholders.	HIGH	MEDIUM	HIGH	SHORT TO MEDIUM	HIGH

7. Annex : Sample Interview Guide

The following is a sample interview guide for TGA's country partners that was used for this evaluation/scoping work.

COUNTRY PARTNERS
Evaluation
1. From 2019 until now, what support or technical assistance has TGA provided to your agency/department?

2. Did this assistance contribute to improvements in the regulatory practices and systems of your agency/department? If so, how?

3. Did other organisations also provide technical assistance in these areas? How did their support contribute to improvements to your regulatory practices and systems?

4. What sorts of challenges did the operating context from 2019 to now pose in achieving these improvements in regulatory practice?
E.g. pressures for rapid product approvals to support the COVID-19 response, limited human resource capacity etc.

5. Could you please give some suggestions as to what would have helped to strengthen the working relationship between TGA and your agency/department?

Future Scoping
1. In the next five years, in what ways could TGA best support your agency/department?

2. Does the TGA need to develop a more tailored approach to its engagement with your country and agency/department? If so, what needs to be considered?

3. In the next five years, and mindful of emerging priorities in the region, in what ways do you think TGA could best contribute to strengthening the regulatory environment in the Asia Pacific?

4. What role could TGA play in facilitating convergence or harmonisation of the regulatory landscape across the Asia Pacific region?

5. Do you have any other feedback or suggestions for TGA's work to date or potential future work in regulatory strengthening with your agency/department or more broadly in the Asia Pacific?

Statement of limitations

The authors have made every effort to ensure the accuracy of the information used; information detailed in this public report is based upon the information available at the time the authors conducted the work and has been edited for public access - at the request of DFAT. Over 30 Internal and External document sources were drawn upon for this report, in addition to the face to face or online interviews – including written submissions. This revised report has been prepared for the Client (DFAT) for publication in the public domain. All intellectual property rights in documents created by the authors remain the property of the authors. The authors do not accept any responsibility for the use of, or reliance on, the contents of this report by the Client or any third party.