Australian Government
Department of Foreign Affairs and Trade

Australian Aid

PRODUCT DEVELOPMENT PARTNERSHIPS FUND MID-TERM REVIEW: ANNEXES

FINAL: 8 October 2020

CONTENTS

ANNEXES

ANNEXES

1. DOCUMENT REVIEW LIST

The following is the list of documents reviewed for the PDP Fund Mid-Term Review.

- G20 Extraordinary Leader's Summit Statement (CEPI)
- G7 Statement (CEPI)
- CEPI Business Plan 2019-22
- CEPI Investor Council minutes 27 Nov 2019
- CEPI Investor Council minutes 13 Mar 20
- CEPI Covid19 Update Public 2 April 20
- CEPI Annual Progress Report 2019
- CEPI Partnership with UQ 17 Jan 19
- CEPI Programme Document Updated April 19
- CEPI Progress Report 2018
- CEPI Funding Agreement 2019
- CEPI Board and investors COVID-19 update 31 Mar
- CEPI Investment Design FINAL
- CEPI – CEPI extends funding call to accelerate development and global manufacture of COVID-19 vaccines 21 Jul 20 https://cepi.net/news_cepi/cepi-extends-funding-call-to-accelerate-development-and-global-manufacture-of-covid-19-vaccines/
- CEPI website https://cepi.net/
- CEPI DFAT Standing Brief April 20
- CEPI summaries from Investors Council meetings
- FIND PDP Annual Funder Report 2018 (May 19 version)
- FIND DFAT Grant Agreement 2018
- FIND Work Plan and Budget 2018
- FIND Work Plan and Budget 2019
- FIND Milestone 2019 DFAT Report 20 May 20
- FIND DFAT 2020 Work plan 1 Apr 20
- FIND GDA C19 Dx Investment Case
- FIND Global Diagnostics Alliance Ppt
- FIND Access Strategy 2018
- FIND Covid19 Additional Information for Australia
- FIND website https://www.finddx.org/
- IVCC PDP Funders Report 2017-18
- IVCC PDP Annual Funder Report 2019 FINAL
- IVCC 2019 Activity Report
- IVCC PDP Reporting Template 2019
- IVCC DFAT Annual Funder Report 2019 FINAL

- IVCC 2019 Activity Report
- IVCC DFAT Project Budget: Actuals and Forecast 2018-23
- IVCC DFAT Grant Agreement 2018
- IVCC DFAT Work plan 2018-19
- IVCC DFAT Budget 18-19
- Original IVCC DFAT Budget Revised 2
- IVCC DFAT Work Plan 2019-20
- IVCC DFAT IPI Work Plan & Budget 2020
- IVCC Gates Open papers related to gender
- IVCC Technical Regulatory and Market Access in the Indo-Pacific Reports 2019
- IVCC IPI Plan Overview
- IVCC website https://www.ivcc.com/
- COVID-19, Malaria and IVCC - IVCC website 6 Apr 20
- MMV DFAT Grant Agreement 2018
- MMV DFAT Work Plan & Budget 2018
- MMV DFAT Work Plan & Budget 2019
- MMV DFAT Work Plan and Budget 2020
- MMV 2018 PDP Annual Funder Report
- MMV 2018 General Progress Summary for DFAT
- MMV 2019 PDP Annual Funder Report
- MMV 2019 Report for DFAT
- MMV 2019 Work Plan and Budget
- MMV PDP Funders Group PowerPoint Feb 20
- MMV Supported Projects PowerPoint Dec 19
- MMV studies related to gender - various
- MMV website https://www.mmv.org/
- TB Alliance PDP Annual Report & Appendices 2018 DFAT
- TB Alliance DFAT Grant Agreement 2018
- TB Alliance Annual Plan 2019
- TB Alliance Annual Plan 2018
- TB Alliance DFAT Annual Activity Plan 2020 FINAL
- TB Alliance PDP Annual Report 2019_DFAT FINAL
- TB Alliance Audited Financials 2019
- TB Alliance 2019 Annual Report
- TB Alliance website https://www.tballiance.org/
- PDPs Joint Submission to DFAT's International Development Policy Review: Product Development Partnerships and Health Security in the Indo-Pacific February 20
- DFAT PDP Evaluation and Options 2013-2018
- DFAT PDP Evaluation 2013-2018 Management Responses
- DFAT PDP Aid Quality Check 2019
- DFAT Trends in vaccines 1 May 20
- DFAT PDPs Investment Design Document
- DFAT Final Aid Quality Check PDPs 2013-18
- DFAT Aid Quality Check PDP Fund 2019
- DFAT Aid Quality Check PDP Fund 2020
- DFAT Correspondence with PDPs and other actors 2019-2020
- DFAT Internal briefs 2019-2020
- DFAT CHS briefing paper on Global Health R&D Dec 19

- DFAT Australia's $352m pledge to international vaccine Press Release 5 May 20
- DoH (Australia)- $66million for coronavirus-related research 2 Jun 20 https://www.health.gov.au/ministers/the-hon-greg-hunt-mp/media/66-million-for-coronavirus-related-research
- DFID R&D Results Framework 2019
- PDP 2.0 DFID/PDP Funder Group Study Preliminary Report July 20
- DFID/ PDP Funder Group Study PowerPoint and handout for PDP Funders Group
- PDP Funders Group newsletters and correspondence
- Gavi press release - Gavi launches innovative financing mechanism for access to COVID-19 vaccines 23 Jun 20
- GHIT - Uniting Efforts for Health Challenges and opportunities for innovation, access and delivery of health technologies: Why a global dialogue? Feb 19 report
- GHIT website https://www.ghitfund.org/
- RIGHT Fund website http://www.rightfund.org/
- Korea Biomedical Review More public-private partnership needed to spur research of less-profitable areas 15 Jun 20 http://www.koreabiomed.com/news/articleView.html?idxno=7902
- APLMA Thailand approves new radical cure for vivax malaria: Press Release Apr 20
- APLMA The APLMA Leaders' Malaria Elimination Roadmap: A 5-year Review of Progress (2015-2019)
- APLMA Virtual Roundtable on Innovations for Malaria: Asia Pacific Concept Note 2020
- Wellcome Trust, Achieving Equitable Access to Healthcare Interventions Feb 2020
- The Global Fund, WHO: Tackling Bottlenecks that Impede Access to Health Innovation 12 Jul 19
- McNeil M (2018). No success without access: Perspectives from funders, PDPs and international agencies on challenges and opportunities around access to new products developed by PDPs (Draft).
- Agency for Science, Technology and Research ASEAN DXD Initiative & 1st Call for Proposal https://www.a-star.edu.sg/Research/funding-opportunities/asean-dxd-initiative
- Bill and Melinda Gates Medical Research Institute website https://www.gatesmri.org/
- Ivivo Gates Foundation Plots a Fresh Metric for Market Access: Lives Saved Nov 2019
- Unitaid statement: Unitaid responds to global call to action partnerships for COVID-19 24 Apr 20
- Unitaid FIND - FIND and Unitaid Launch Call for Expression of Interest to Accelerate Availability and Manufacturing Scale-Up of Rapid Diagnostic Tests for COVID-19 9 Jul 20
- US DHHS FDA Tropical Disease Priority Review Vouchers: Guidance for Industry Oct 16
- WHO A Global Framework to Ensure Equitable and Fair Allocation of COVID-19 Products: WHO Member States Briefing 2 July 20
- WHO ACT-Accelerator update 7 July 20
- WHO PDP Funder's Group slides 17 Feb 20
- WHO TPP harmonized methodology Dec 19
- UNDP GHIT Government of Japan Access & Delivery Partnership 30 Jan 19
- BMGF, Terry, Yamey Portfolio to Impact Model 2019.
- BMGF Young 2019 Pipeline Portfolio review and cost model
- Various press releases on COVID-19

2. INTERVIEW PARTICIPANT LIST

Name	Organisation
Mel Spigelman	TB Alliance
Willo Brock	TB Alliance
Anu Mahalingashetty	TB Alliance
David Reddy	MMV
Charlie Masding	MMV
Andrea Lucard	MMV
George Jagoe	MMV
Nick Hamon	IVCC
Fred Yeomans	IVCC
Jason Richardson	IVCC
Sharon Saacks	FIND
Ayushi Agnihotri	FIND
Jo Mulligan	DFID
Kei Katsuno	GHIT
Bahati Ngongo	BMGF
Jeff Chertack	BMGF
William Hall	Wellcome Trust
Alexandra Cameron	UNITAID
Kellen Thomas	Mylan
Anil Soni	Mylan
Kristy Tomas	Therapeutic Goods Administration (TGA)
Michael Wiseman	TGA
Marie Lamy	APLMA
Leanne Robinson*	Burnet Institute
Suman Majumdar*	Burnet Institute
Jody McVernon*	Peter Doherty Institute for Infection and Immunity
Robin Davies	CHS
Bridie Rushton	CHS
Stephanie Williams	CHS
Nic Notarpietro	CHS
Camilla Burkot	CHS
Alex Stephenson	CHS

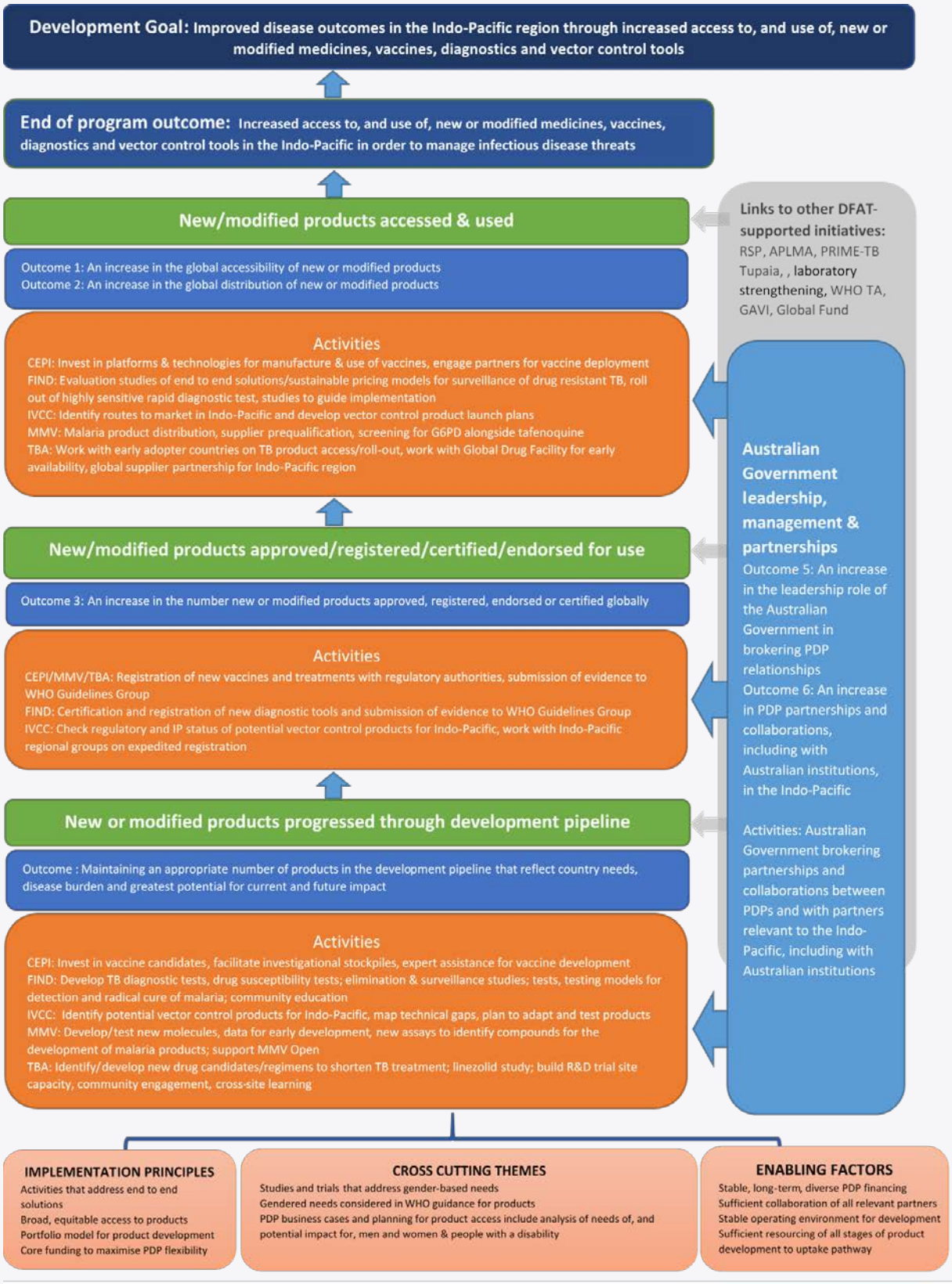
* Questions on the PDPs included in interviews conducted as part of a separate process on the progress of the Health Security Initiative.

3. SAMPLE INTERVIEW GUIDE

The following is a sample interview guide used in this review for PDPs. It is noted that as each guide was tailored, no two guides were the same.

1. Could I have a brief update on [XX] activities being funded by DFAT?
2. Could you provide 1-2 examples of how [X PDP] has provided technical assistance in the Asia Pacific to support countries' adoption of new products?
3. In terms of [X PDP]'s advocacy work, are there examples you could provide of tangible *outcomes* of your advocacy work in the Asia Pacific e.g. changes to national or regional policies, plans, strategies, or initiatives?
4. Could you provide 1-2 examples of how DFAT has supported [X PDP]'s work in the region by brokering linkages with other organisations, governments, other DFAT-funded programs or through other support? Can you give me an example of where these linkages have not been working so well?
5. Was there any value in [X PDP] attending the RSP Forum in 2019? If so, what were the key outcomes for [X PDP] of the meeting?
6. Could you give me an example of a partnership with an Australian institution that [X PDP] has developed within the contractual period. How it has contributed to [X PDP]'s work and describe the mutual benefits.
7. Do you have issues or concerns with how you are tracking or will track against the activities outlined in the contractual agreement with DFAT, particularly considering COVID-19?
8. What do you think about the level of engagement of DFAT in the work of your organisation? In what ways could DFAT better support or facilitate the implementation of activities in the remaining funding period?
9. Which strategies are [X PDP] putting in place in the next 2-3 years to help ensure the sustainability of its funding?
10. What are the key strategies [X PDP] will use to ensure increased access to its products in the next 5 years? Where does [X PDP] see the line of involvement of MMV should end and where other partners should continue the process?
11. What are examples of the key ways in which [X PDP] plans to interact with the following bodies to facilitate access to new products and address bottlenecks in the Asia Pacific in the next 2-3 years? Where relevant, please discuss: WHO, Global Fund, APLMA/APMEN, ASEAN.
12. Where do you think DFAT would strategically be best placed to work to address some of these access bottlenecks?
13. Going forward, what are your key strategies to ensure product development becomes more demand driven, appropriate and relevant to country needs?
14. Are there any other points you would like noted for this review?

4. PDP FUND PROGRAM LOGIC



Note: Product development is a continuous process, thus the terms outcomes (rather than intermediate outcomes) and activities (rather than outputs) are used as the timeframes and nature of these vary by product and PDP.

5. PDP FUND INDICATORS FROM THE MONITORING EVALUATION AND LEARNING FRAMEWORK

Outcome/impact description*	Indicator #	Indicator
Impact (5-10 years)		
Impact: Improved disease outcomes in the Indo-Pacific region through increased access to, and use of, new or modified medicines, vaccines, diagnostics and vector control tools		Estimated people cured per annum, based on introduction of novel medicines (and bioequivalent generics)
		Estimated people correctly diagnosed and put on treatment, based on introduction of novel diagnostics (cumulative)
		Disease -specific incidence for disease(s) targeted by new vaccines/vector control tools
End of program outcome		
EOPO: Increased access to, and use of, new or modified medicines, vaccines, diagnostics and vector control tools in the Indo-Pacific in order to manage infectious disease threats		Targets reached for indicators 1,7,8,9
		Evidence demonstrating significant progress against indicators 3, 4
Accessibility - Uptake (Post approval implementation, new products distributed)		
Outcome 2: An increase in the global distribution of new or modified products	1	Total number of products procured or distributed globally
Outcome 1: An increase in the global accessibility of new or modified products	2	Evidence of PDPs engaging Indo-Pacific countries through advocacy or providing technical assistance related to adoption of new products
	3	Evidence demonstrating impact of research on gender, equity and the most vulnerable
	4	Evidence of PDP implementation of a fair allocation system for COVID-19 vaccines or diagnostics
Accessibility - Development (New products approved, registered, certified, endorsed for use)		
Outcome 3: An increase in the number new or modified products approved, registered, endorsed or certified globally	5	Examples of key product development milestones/breakthroughs
	6	Evidence of national policies, plans, strategies, treatment guidelines, roadmaps and leadership initiatives which are influenced by donor-funded research/programmes
	7	Total number of products that have been included in WHO guidance per year for treatment, diagnosis or prevention of diseases
	8	Total number of products registered per year in one or more countries (cumulative)
Research & translation (new/modified products developed/trialled)		
Outcome 4: Maintaining an appropriate number of products in the development pipeline that reflect country needs, disease burden and greatest potential for current and future impact	9	Total number and spread of projects in the development pipeline.

Partnerships, leadership and management		
Outcome 6: An increase in PDP partnerships and collaborations, including with Australian institutions, in the Indo-Pacific	10	Total number of PDP partnerships in Australia and the Indo-Pacific region
Outcome 5: An increase in the leadership role played by the Australian Government in brokering collaborations between PDPs and with partners relevant to the Indo-Pacific	11	Evidence that the Australian Government played a role in brokering collaborations between PDPs and with other partners relevant for the Indo-Pacific that improved and streamlined research activities
PDP project management		
Outcome 8: PDPs are managed efficiently, represent good value for money and a sustainable model for product development	12	Total annual budget, expenditure and variance
	13	Evidence demonstrating value for money
HSI Program Linkages		
Outcome 7: There are clear links and complementary activities between the PDP work and other DFAT-supported initiatives	14	Evidence of linkages made, or complementary activities established with other relevant DFAT investments on the product development to uptake pathway
* The outcomes and most of the corresponding indicators are not classified as, or under, *intermediate outcomes* as is the case in other HSI investments. This is because product development is an ongoing process, so that depending on the PDP and the product, some outcomes will be achieved during the funding period and some will be achieved at the end of the funding period.		

6. PIPELINE STAGES IN THE PDP FUNDER TEMPLATE MAPPED AGAINST PDP PIPELINES

The following table maps the names given to the product development pipeline stages in the PDP Funder Template against the activities carried out at each stage of the PDPs' pipelines. This rubric is used for Table 2 on page 14 of the main report.

Pre-clinical/feasibility (from early product conception/ identification to initial safety studies/proof of principle)	MMV: Research and early translational CEPI: Pre-clinical IVCC: Proof of concept, lead optimisation, early stage TBA: Lead identification, lead optimization, preclinical development, FIND: Concept and feasibility
Clinical/pre-development - IVCC (phase 1, phase 2, phase 3; IVCC-advanced safety and efficacy testing)	MMV: Late translational (from entry into human) and product development CEPI: Clinical phase 1,2,3 IVCC: Pre development (Phase 1 and 2) TBA: Phase 1, Phase 2A/2B, Phase 3 FIND: Development (includes verification and lab validation studies)
Trialling (non-clinical evaluation of product effectiveness)	MMV: N/A CEPI: N/A IVCC: Development/Field Evaluation TBA: N/A FIND: Evaluation (validation in settings of use) and evaluation demonstration (ease of use, cost effectiveness analysis etc)
Complete (trials complete, on market, addressing access issues such as regulatory approval, PV, post market surveillance)	MMV: Regulatory review, complete CEPI: Registration/introduction IVCC: Products launched TBA: Marketing products FIND: Registration (SRA) and product on market

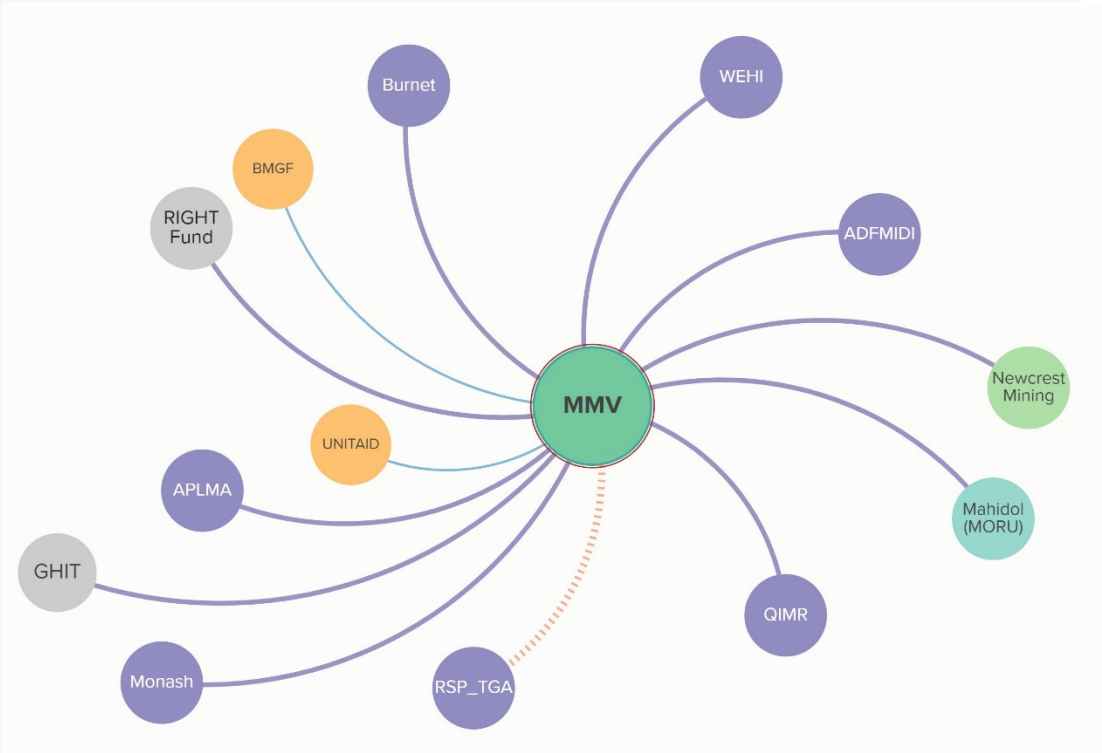
7. COLLABORATIONS BETWEEN PDPS AND HSI-FUNDED PROGRAMS

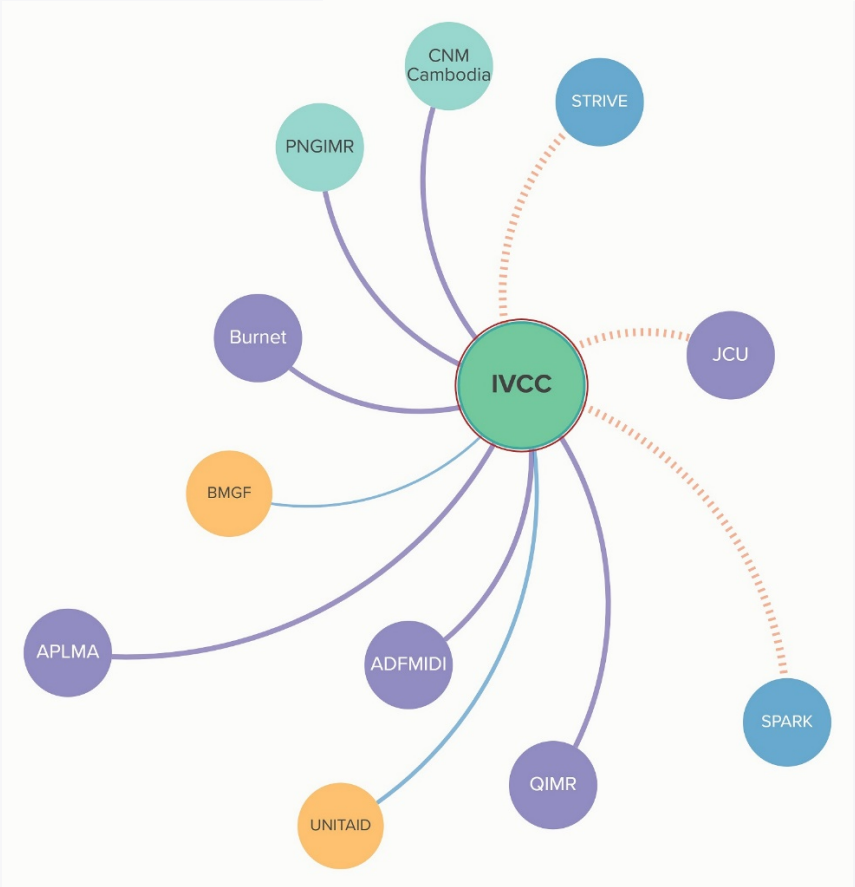
The table below lists the types of collaborative relationships between the PDPs and other HSI-funded programs and examples of the outcomes and benefits of such collaborations.

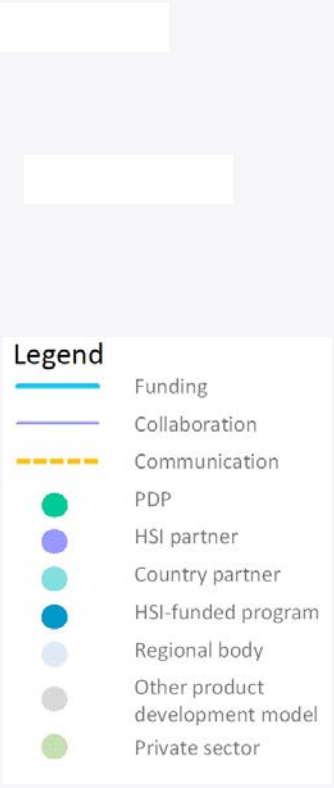
HSI-funded program	PDPs collaborators	Points of collaboration	Examples of collaborative benefits
Regulatory Strengthening Program (RSP)	MMV/GSK	• Product registration in Australia • Product registration in the region • Regular communication	• TGA guidance for MMV on the registration process in Australia • MMV updates on submission of tafenoquine dossier in RSP partner countries • RSP provides information to MMV on regulatory environment in RSP partner countries • Newly established reliance pathway between Thai FDA and TGA enabled TGA assessment reports for Tafenoquine to be shared with Thai FDA (with GSK approval) and product approval in 109 working days instead of the average 220 working days (Apr 20)
	TB Alliance/ Mylan	• Product registration in Australia • Product registration in the region • Ad hoc communication	• TGA guidance for TB Alliance on the registration process in Australia • TB Alliance/Mylan presented their roll-out plans for BPaL at the RSP Forum (Sept 19)
	FIND	• Ad hoc communication	• FIND interested in collaborating more closely with the RSP on regulatory pathways in the region
APLMA/ APMEN	MMV	• MoU (2019)– regulatory harmonisation support work & advocacy for improved case management	• APLMA provides high-level advocacy to regional partners re benefits of new products and pending filing of dossiers • APMEN Vivax Working Group collaborates with national disease programs on technical level advocacy and communication with NRAs • APLMA organises malaria week, giving PDPs the opportunity to talk about their pipelines and product roll out plans to senior officials • APLMA has developed Policy Road Maps for high level advocacy for getting products to market. E.g. a roadmap for accelerating market access to radical cure for vivax malaria for Thailand was developed with the Thai Division of Vector Borne Diseases, Thai FDA, MMV and TGA.
	IVCC	• IVCC member of Vector Control	• APLMA and UNITAID launched VCAP, promoting innovation and access to vector control tools in Asia Pacific, including engaging with regulators

		for the Asia Pacific (VCAP) Steering Group • MoU with APLMA/APMEN in development	• APLMA supported IVCC in identifying respondents for the landscaping reports • IVCC landscaping reports funded by HSI launched at VCAP regulatory meeting (2019) • APLMA developing policy road map for introduction of vector control tools in Cambodia
HSI operational research partners	FIND	• Collaboration on building operational research capacity	• FIND: exploring regional research platform with Burnet/discussion on PRIME TB/joint grant applications • Burnet provides technical expertise, networks; FIND provides a global view which is impact-orientated
	IVCC	• IVCC – Burnet Institute contract lead for NATNAT	• Burnet Institute is the lead contractor for IVCC's project NATNAT (PNG) • Collaboration between IVCC's Project NATNAT in PNG, and STRIVE-PNG (Burnet, JCU, PNGIMR and other partners) and SPARK (PDI, JCU, WEHI and other partners) including sharing data and information, ensuring respective work well integrated.
	TB Alliance	• TB Alliance – collaboration on PRIME TB	• Collaboration between Burnet (PRIME TB) and TB Alliance for PRIME-TB.

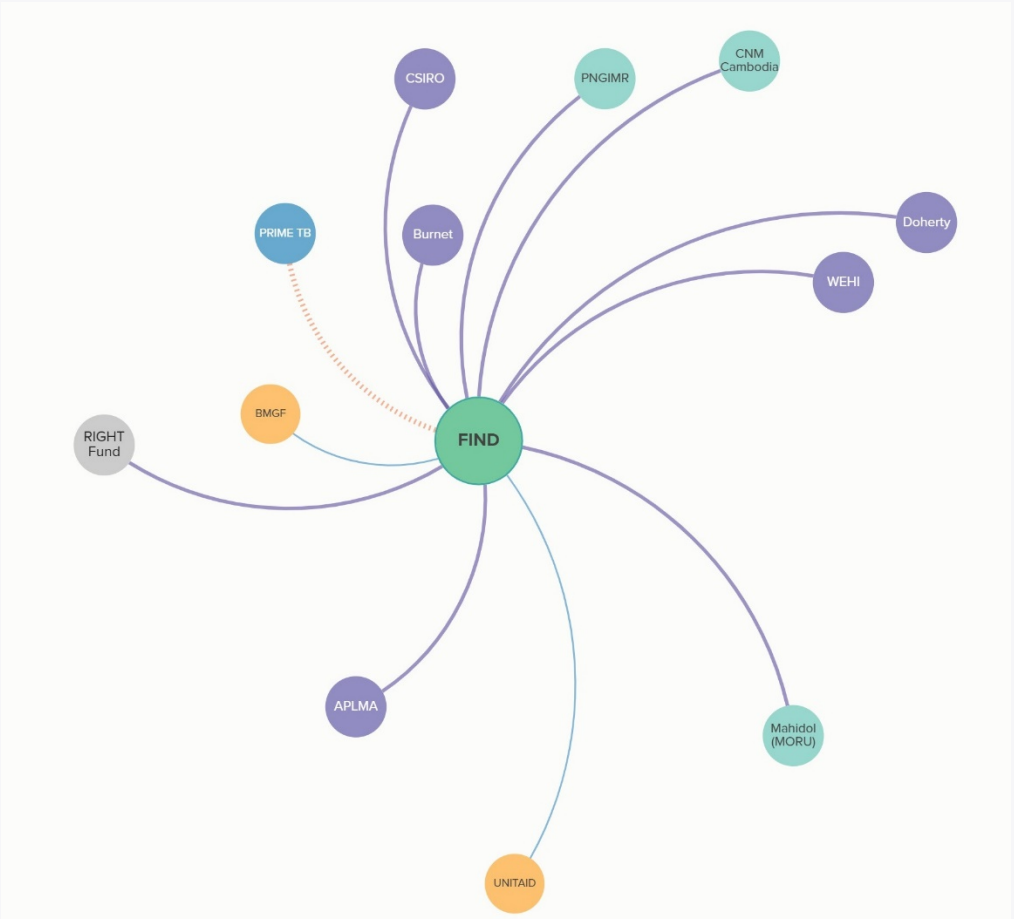
8. ECOSYSTEMS IN THE INDO-PACIFIC BY PDP

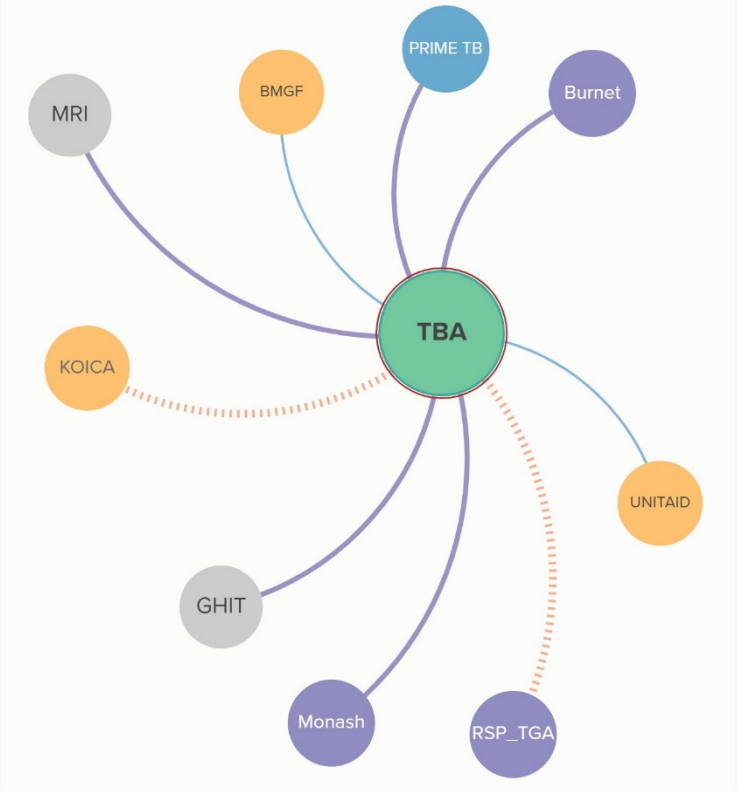






ECOSYSTEMS IN THE INDO-PACIFIC BY PDP CONT.





9. FUTURE DIRECTIONS IN PRODUCT DEVELOPMENT AND ACCESS [EQ8]

The following section describes key trends and future challenges in product development and access. There are many existing discussion papers that capture some of the global trends and challenges in these areas. Some of these papers are referenced in Annex 1 and are widely available. This section draws upon these papers but does not seek to replicate them. Instead it focuses on developments identified through the document review and the interviews that are most relevant to the work of DFAT as well as those that are focused on the Indo-Pacific region.

9.1 TRENDS AND CHANGES IN THE PDP LANDSCAPE AND HOW PDPS OPERATE

GLOBAL

Covid19 Response

- The **longer-term impacts of COVID-19 on the progress against the diseases** addressed by the PDPs will be significant. For example, the Stop TB Partnership has estimated that under a three-month lockdown, at least five years of progress on the TB response will be lost. Further it estimated that under a protracted 10-month restoration of services, the world could see an additional 6.3 million cases of TB between 2020 and 2025 and an additional 1.4 million TB deaths during that same period. If such projections are realised, this will place significant demands on product development and access.
- The **ACT-Accelerator** may generate **valuable lessons** to inform how product development and access partners coordinate, communicate and collaborate in the future.
  See Section 8 on the COVID-19 for further discussion.

Pipeline

- Between 1995 and 2005 only 13 new drugs were developed to respond to neglected tropical diseases. In 2017 there were **109 active R&D projects** for neglected tropical diseases with late stage testing underway for treatments and vaccines for seven compounds. In a recent 2019 presentation, a DNDi representative pointed to a **'watershed period'** in PDP development in the next five years, with the anticipated completion of many new products. They gave the example that five PDPs anticipate that they will have over 50 products completing development over the next five years.
- MMV are exploring product development with **monoclonal antibodies** as the costs of production are decreasing and the potential public health benefits are high.
- Given the double burden of communicable and non-communicable diseases for a growing number of LMICs, and based upon a WHO recommendation, FIND is starting to explore the inclusion of **non-communicable diseases** within its portfolio.
- Drug resistant TB, malaria and HIV are all increasing and there is a need for product pipelines to continue to **innovate because of drug resistance** in current regimens.

Innovation

- **Multiplexed point-of-care testing** – the use of one specimen for simultaneous on-site detection of different chemical substances that are indications for different diseases. Such testing could significantly increase timely access to multiple diagnostic tests in resource-poor settings.
- PDPs e.g. MMV are looking to develop new products with **monoclonal antibodies**. These are laboratory-produced proteins that act like human antibodies in the immune system and can target specific antigens. Monoclonal antibodies are given intravenously. This will require completely new processes for access.
- The DFID/PDPFG Preliminary report identified that **AI screening and development of compounds at early discovery phase** of R&D can significantly accelerate identification of promising candidates. One interviewee gave the example of how AI was used to identify 69 different potential hit leads for COVID in two weeks.

Funding for PDPs

- In 2017, there were 538 product candidates for neglected diseases with an estimated USD16.3 billion (range US$13.4-19.8 billion) needed to move these candidates through the pipeline. The 2018 G-Finder survey found that in 2017, **70% of total funding** for neglected disease product development was for products directed at **TB, malaria and HIV/AIDS**. However, rheumatic fever, leptospirosis, Buruli ulcer and trachoma all received less than 0.1% of global funding respectively. As a result, a Duke study concluded that the proportion of funding for neglected diseases was often poorly correlated with the overall disease burden.
- The estimated **funding gap** between current investment and what is needed to launch one of each of 18 key missing neglected disease essential medicine products in the next five years is at least $1.5 to $2.8 billion annually (Young et al., 2020).
- PDPs have noted a shift in donor funding from portfolio funding to individual project funding, which reduces their ability to be agile and responsive and, in some cases, increases inefficiencies.
- **BMGF** is either the highest or second-highest funder of all four PDPs: MMV, TB Alliance, FIND and IVCC. It has indicated that it will **continue funding all the PDPs at a similar level** (grants renewed for MMV and IVCC in 2020, with a new grant to commence for IVCC in 2022) with the exception of a small decrease in funding for TB Alliance as the MRI has commenced work in development of TB products in collaboration with TB Alliance.

New funding mechanisms

- Some PDPs are exploring new funding mechanisms for their work. For example, FIND is looking at **loan structures** (e.g. malaria work funded through loans with the European Investment Bank); direct country procurement from essential diagnostics lists; and preferential funding of developers willing to hand over their know how to local manufacturers. MMV established the **Foundation Fund** in 2019 to invest extraordinary revenue (such as from the GSK Krintafel partnership) to improve business sustainability.

R&D Capacity Building

- The DFID/PDP FG Preliminary Report noted that while PDPs have contributed to R&D **capacity building** in LMICS, there needs to be better **coordination and collaboration** among PDPs and other partners and a more horizontal rather than siloed (i.e. for specific diseases or products) approach taken.

SOUTHEAST ASIA & THE PACIFIC

- Demand stimulation for vector control technologies among **private sector** organisations that are **large employers** in the region is one strategy being explored by IVCC. It is a consideration for the NATNAT program with companies such as Newcrest Mining, Ramu Sugar and Exon in PNG. MMV is also working with Newcrest Mining.
- FIND is exploring expanding its work with the **Burnet Institute** by establishing a **research platform** in the region.
- MMV and FIND have one **regional advisor** each in Southeast Asia. This has increased their ability to engage with regional and Australian actors such as APLMA and TGA.
- The DFID/PDP FG Preliminary Report highlighted the opportunity for increased funding and engagement in product development by **MICs**. This could include countries in the region such as Thailand and Malaysia.

9.2 NEW MODELS FOR PRODUCT DEVELOPMENT

New product development models for diseases affecting LMICs are enhancing the product development ecosystem, and not necessarily detracting from PDP activity and funding as some had earlier feared. PDPs are often working in collaboration with the new models. In some cases, e.g. MRI, this will result in a small reduction in funding for the TB Alliance as the MRI takes on some of the portfolio of work. Some of the new models are described briefly here. For more detail, see Annex 10.

- **The Bill and Melinda Gates Medical Research Institute (MRI)** was launched in 2018. It had a start-up budget of US$270M and has an annual operating budget of US$100M. Its mandate includes developing products as well as improving the clinical development process. The MRI employs a 'full-service enterprise model' meaning it operates along the full product development to uptake continuum in collaboration with partners. The MRI sees itself as an addition to the PDP ecosystem rather than replacing it.

  The MRI is working with four companies and BMGF under the TB Drug Accelerator on investigational TB drug regimens. The MRI TB pipeline consists of TBA-7371, Sutezolid and SPR720, with the first two being conducted in collaboration with the TB Alliance. BMGF established the PAN-TB collaboration with members including Otsuka, Johnson and Johnson, Evotec, GSK, MRI and soon to include the TB Alliance. This collaboration will focus on Phase 2 regimen evaluation studies which will likely utilise sites in the Asia Pacific in 2021.

- **GHIT** was established 2013 and is designed to advance innovations from Japan as well as work with global entities. Half of its funding comes from the Japanese Government and the remaining funding comes from sources such as pharmaceutical companies and initially from BMGF. It is working with MMV, the TB Alliance and Australian institutions.

  According to GHIT, a key lesson learnt to date has been the importance of a governance structure with clear separation between the funders and the decision-making process for which products to develop. Another lesson learnt has been the importance of the right leadership to be able to bring together the public and private sectors and to ensure strong collaboration.

- **Korean RIGHT Fund** was established in mid-2018 and is funded by the Government of Korea, Korean pharmaceutical companies and international funders. Their current pipeline consists of vaccines (cholera and DTwP-BepB-IPV-Hib), low-cost manufacturing for a malaria drug (with MMV) and diagnostics (2nd generation G6PD test and POC test for MDR TB (with FIND).

- **ASEAN Diagnostic Initiative** was co-launched in 2018 by the Diagnostic Development Hub in Singapore (DxD Hub) and the Philippines' ASEAN Network for Drugs, Diagnostics, Vaccines and Traditional Medicines Innovation (ASEAN-NDI), in collaboration with FIND. The Initiative will collect diagnostic needs from countries within ASEAN and develop products to meet those needs. Under the model, countries will commit to purchasing certain volumes of the new products.

- **Global Research Collaboration for Infectious Disease Preparedness (GloPID-R)** network was established in 2013 to ensure rapid initiation of research in outbreaks.

- **CARB-X (Combating Antibiotic Resistance Bacteria Biopharmaceutical Accelerator):** - this is a US$500million non-profit partnership focused on early-development pipeline of new antibiotics, vaccines and rapid diagnostics. Wellcome Trust is a major funder.

- **Global Diagnostics Alliance** (GDA) is in development. It will be led by FIND working with WHO, UNITAID, World Bank, UNICEF, Global Fund, Clinton Foundation, and other public and private donors. It will work on aggregating country demand, modelling to help country decision-making, centralizing pre-orders, co-funding, technical assistance for LMICs, developing TPPs, and evaluations to inform country decision-making.

9.3 OPPORTUNITIES AND CHALLENGES FOR PRODUCT ACCESS

The following outlines some of the opportunities and challenges for product access that have been identified primarily through the interviews for this review. There are several papers on access published by global initiatives or as a result of international meetings, and as such, this section does not seek to replicate the content of these papers which are widely available. This section also includes access opportunities and challenges that may be specific or relevant to actors in Southeast Asia and the Pacific.

GLOBAL

Opportunities

- Among the interviewees for this review, there was a level of impatience with the number of global discussions or papers on access issues with little practical action resulting. However there was significant appetite among several interviewees (APLMA, BMGF, Unitaid) for a '**critical path**' or equivalent approach to map the steps needed to ensure product uptake of specific products and to identify the relevant actors best placed to be involved at each step. A sticking point of such an approach has been in identifying mechanisms for the governance, leadership and coordination of such access work, to bring together all relevant actors.
- Part of Wellcome Trust's Access Strategy will be to support the online **Master Alliance Provisions Guide** (MAP Guide), developed by the Global Health Innovator Alliance Accelerator. This will provide a list of different approaches that have been taken by public, corporate, philanthropic and multilateral

institutions to address key access issues in global health agreements. This could inform the critical path' approach described above.

- Another part of Wellcome Trust's Access Strategy will be to support development of an **Annual Global Forum** (AGF) to accelerate the late-stage pipeline of critical medical and health products. It will involve funders, regulators, financing institutions and the global community. At the time of this report, Wellcome had commissioned consultations with key stakeholders on the scope of the Annual Global Forum. Some interviewees pointed to the need for a mechanism that had a mandate to make decisions rather than only share information. A first meeting of the AGF is planned for 2021.
- In January 2020, the **WHO** launched the **Emergency Use List procedure** for assessing and listing unlicensed products to expedite their use during **public health emergencies.**

Challenges

- The **boundaries** between the PDPs traditionally involved in **product development** and the product sponsors traditionally involved in **access** are shifting. PDPs are finding that they are increasingly involved in access activities and note that pharmaceutical companies are simultaneously decreasing their role. For the pharmaceutical sector, one consideration is the significant short-term costs involved in post market research and registration and the diminished return on investment as a result. For the PDPs, this means the need for additional capabilities, capacity and funding of access activities, as well as new partnerships, so that they can adopt an 'end to end' approach.
- Some PDP and private sector interviewees noted a need for **earlier, proactive and consistent elaboration of TPPs and the clinical data needed by the WHO** so that PDPs could incorporate this information into planning the types of studies required for the product to be added to WHO policy and guidance. This, they said, would result in less work needed post registration and expedited drug access.
- There are **complex** and **fragmented international funding** sources for access.
- The **rate that new products come on to the market** makes it challenging for countries with limited capacity to assess the products, update national guidelines and instigate the processes for introduction of new products.
- Country approaches to **regulating non-pharmaceuticals** (e.g. diagnostics, insecticides or bed nets) vary widely, with some countries having no clear regulatory process in place to assess such products.
- **Responsibility and capacity for post-marketing pharmacovigilance** (such as tracking adverse events) is sometimes poorly defined or inadequate, particularly where a PDP has licensed the production and supply of a product to several generic firms. There have been initiatives supporting national pharmacovigilance systems, such as ADP's support of the development of a surveillance system in Indonesia to monitor and enable the introduction of bedaquiline for MDR-TB treatment.
- FIND noted a need to find a balance between innovation and practical solutions. For example, while there is strong potential in the use of electronic decision tools – dedicated algorithms i.e. **AI and machine learning** to help guide care and surveillance, some governments are less likely to have the appetite to implement such tools outside of research, and there are barriers such as local capacity, guidance and regulation of such tools to consider.
- **Accessible pricing of vector control products** is an issue as there are a decreasing number of companies able to produce the required chemicals. In addition, development of the next generation of bed nets requires the manufacture of new chemical compounds which is costly and time consuming.
- There is **under-utilisation of regimens to treat drug resistant strains**, so that such regimens are falling short of having population-level impact.

SOUTHEAST ASIA & THE PACIFIC

Opportunities

- IVCC notes that there is a significant consumer market for VCTs in the region and so consideration is being given to product development through this delivery channel, rather than only donor funded.
- The **Access and Delivery Partnership (ADP)** was launched in 2013 and supports countries to strengthen the policies, human capacities, systems and regulations needed to ensure access to products. The core partners of the ADP are UNDP, WHO, TDR and PATH.
- **Uniting Efforts for Innovation, Access and Delivery** was launched in 2019 by the Government of Japan, ADP and GHIT. Uniting Efforts states that it is a platform to improve innovation, access and delivery of products for unmet health needs in LMICs, It held its first meeting in early 2019.
- Several interviewees noted the importance of **regulatory strengthening activities** in improving access in Southeast Asia and the Pacific and their interest in further collaboration in this space. Interviewees indicated the potential for: stronger linkages with the RSP and some PDPs, closer integration of RSP with work of APLMA; better communication of TGA activities and what it plans do in the region with other stakeholders; ongoing work with ASEAN processes; and coordination with similar work being carried out with KOICA and others. BMGF are interested in further collaboration with DFAT in regulatory strengthening and communicating with regional governments.
- APLMA is developing **policy road maps** for several different products categories in countries in the region – mapping the processes needed for the introduction of a new product. These will need to be operationalised.

Challenges

- According to some of the PDP interviewees, **NRA registration processes** in Southeast Asia and the Pacific are complex, diverse and take considerable time to complete (up to 18-24 months in some markets). An established and well utilised process for **regional registration**, such as exists in the EU or Africa (the African Medicines Registration Harmonization Initiative), does not exist in Southeast Asia and the Pacific.
- The waiver process for importing products prior to regulatory approval in countries in Southeast Asia is historically complicated.
- **ASEAN** has been working on **harmonisation** schemes for the region through its Pharmaceutical Product Working Group (PPWG), its development of ASEAN Common Technical Document (ATCD)and an ASEAN Common Technical Requirements (ATCRs) and use of the Joint Assessment Procedure for Pharmaceutical Products (JAPPP) through the Joint Assessment Coordination Group). However, to date only one product has passed through the assessment process. TGA noted that some countries need improved technical capacity to be able to participate in such a joint process and to build greater experience working with other NRAs.

10. CASE STUDY: SUPPORTING THE PRODUCT DEVELOPMENT TO UPTAKE PATHWAY

AN END-TO-END APPROACH TO ENSURE NEW PRODUCTS GET TO THOSE WHO NEED THEM

HSI is supporting development of new drugs, diagnostic tests, vaccines & vector control tools

HSI investments are addressing barriers to access to new products at key points along the product development to uptake pathway

Between 1995 and 2005 only 13 new drugs were developed to respond to neglected tropical diseases (NTDs), communicable diseases disproportionately affecting populations living in poverty. [1] By 2017, there were 109 active research and development (R&D) projects for NTDs.[2] Product development partnerships (PDPs) are responsible for almost a fifth of the total funded R&D for these diseases.[3] PDPs are non-profit entities that bring together the public and private sectors to research, develop and support access to new products that target diseases disproportionately affecting those in resource-poor settings. While PDPs have increased development of new drugs, diagnostic tests, vector control tools and vaccines, there are a number of steps needed to get these products to those who need them and barriers that need to be overcome. This is called this the 'product development to uptake pathway' (Figure 1).

Recognising that new products were faltering along this pathway and not reaching the market, the Health Security Initiative (HSI) has funded a series of initiatives from product develop right through to product access that are addressing these barriers. At the **product development** stage, the HSI's **PDP Fund** is supporting the following four PDPs over five years: Medicines for Malaria Venture (MMV), TB Alliance, Foundation for Innovative New Diagnostics (FIND) and the Innovative Vector Control Consortium (IVCC). It is also funding the Coalition for Epidemic Preparedness Innovations (CEPI) to support its core work in vaccine development for emerging infectious diseases for three years to December 2022.

In order to ensure the safety, quality and efficacy of new products before they are sold, HSI established the **Regulatory Strengthening Program (RSP)** in partnership with the Therapeutic Goods Administration (TGA). The RSP works with national regulatory authorities to strengthen the **regulatory processes** for medicines and medical devices in Laos, Cambodia, Indonesia, Myanmar, PNG and Vietnam, including improving capacity to monitor products once they are in the market (**post-market surveillance**). At the same time, the HSI funds the **Asia Pacific Leaders Malaria Alliance** (APLMA) which is working with partner governments at a **policy level for country-level roll-out** of new products and facilitates connections between PDPs, regulatory agencies and national malaria control programs.

As part of gaining **WHO approvals** for products to be included in their guidance and recommended product lists, products are tested in different contexts. The HSI funds **operational research projects** in countries across the Indo-Pacific which are improving country research capacity, and in some cases informing product testing. For example, IVCC's NATNAT project will test vector control tools in PNG.

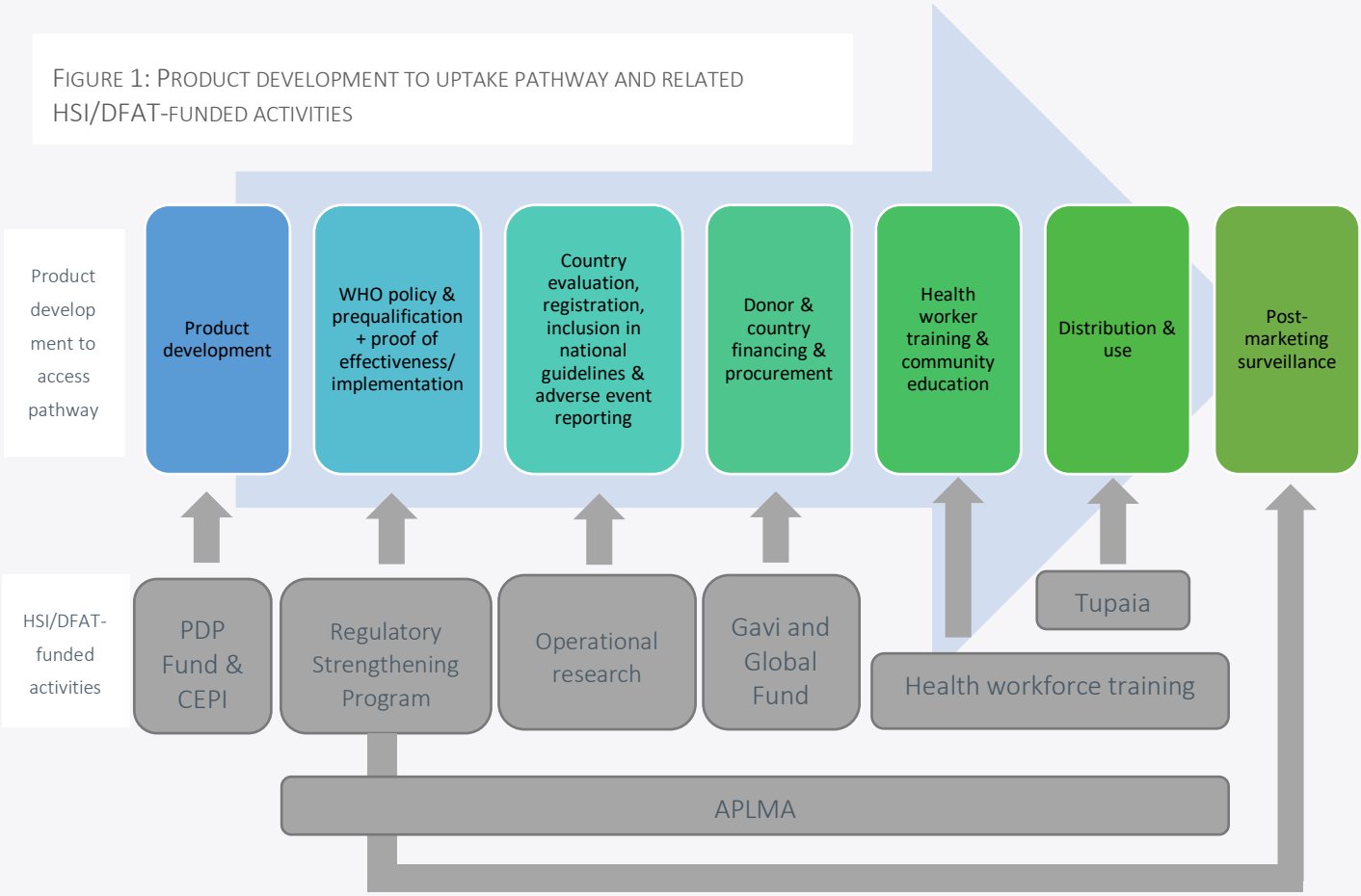
[1] Moran, M 2005, A Breakthrough in R&D for Neglected Diseases: New Ways to Get the Drugs We Need, PLOS Medicine 2 (9): e302, p. 828

2 International Federation of Pharmaceutical Manufacturers & Associations 2017, Doing our part: Innovating to Fight Neglected Tropical Diseases, <https://www.ifpma.org/wp-content/uploads/2017/04/IFPMA_Innovating_to_Fight_NTDs_April2017_FINAL.pdf> [accessed on 25 July 2019]

3 G-FINDER & Policy Cures Research 2019, G-FINDER: Global Funding of Innovation for Neglected Diseases, < https://s3-ap-southeast-2.amazonaws.com/policy-cures-website-assets/app/uploads/2020/02/07161934/GF-6pSummary2019.pdf> [accessed 14 September 2020]

The wider DFAT Health Portfolio is funding both **Gavi, the Vaccine Alliance**, and the **Global Fund**. Both are mechanisms that pool donor funding to combat diseases, including global procurement of products for use by country disease control and prevention programs.

FIGURE 1: PRODUCT DEVELOPMENT TO UPTAKE PATHWAY AND RELATED HSI/DFAT-FUNDED ACTIVITIES



Before products are sold in the market, **health workers** need to be **trained** in how to use them and **communities** need to be aware of and understand the products in order to create demand. While the HSI is not directly supporting these activities for new products, it is equipping health workers with knowledge and skills in areas such as surveillance and infection prevention control and communities in detecting and responding to emerging infectious disease outbreaks – capacities which could also support the roll-out of new products.

The HSI support the **Tupaia** program which has established a system – mSupply - to manage stocks and monitor use of medical products. mSupply is being rolled out in several countries in the Pacific and will help improve efficient **product distribution and availability**.

There is active collaboration and communication between these HSI-funded initiatives which has resulted in demonstrable added value. For example, the MMV-developed antimalarial tafenoquine was approved by the Thai Food and Drug Administration in 50 per cent of the average time due to the RSP (TGA) setting up a system to share its drug assessment reports with the Thai FDA. APLMA helped to facilitate the process.

While the HSI is working across the product development to uptake pathway, there are many remaining barriers to access that require global and regional cooperation. Efforts to overcome these barriers have largely been fragmented. The HSI is engaging in global, regional and bilateral mechanisms to help to address these barriers.